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Epidemiology of injuries, treatment (costs), and outcome in burn patients admitted to a hospital with or without dedicated Burn Center (Burn-Pro); Protocol for a multicenter prospective observational study

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Abstract

Introduction

Admission to a Burn Center is indicated for patients with severe burns or with specific characteristics like older age or comorbidities. The Emergency Management of Severe Burns (EMSB) referral criteria have been implemented for optimal triaging of burn patients. Extensive injury and outcome registration exists for patients admitted to a dedicated Burn Center, but limited information is available about the organization of care and referral of burn patients presented to a hospital elsewhere. The aims of this study are to compare the burn injury characteristics, treatment (costs), Quality of Life, and scar quality of burn patients admitted to a hospital without dedicated Burn Center versus burn patients with <10% Total Body Surface Area (TBSA) burned who are admitted (or secondarily referred) to a Burn Center. If these admissions were in agreement with the EMSB referral criteria will also be determined.

Methods and analysis

In this multicenter, prospective, observational study (cohort study), the following two groups of patients will be followed; 1) All patients (no age limit) admitted with burn-related injuries to a hospital without a dedicated Burn Center in the Southwest Netherlands or Brabant Trauma Region ; and 2) All patients (no age limit) with <10% Total Body Surface Area (TBSA) burned who are primarily admitted (or secondarily referred) to the Burn Center of Maasstad Hospital. Data on the burn injury characteristics (primary outcome), EMSB compliance, treatment, treatment costs, and outcome will be collected from the patients' medical files. At three weeks and at three, six, and 12 months after trauma, patients will be asked to complete the Quality of Life (EuroQoL-5D; EQ-5D), and the patient-reported part of the Patient and Observer Scar Assessment Scale (POSAS). At those time visits, the

coordinating investigator or research assistant will complete the observer-reported part of the POSAS.

Ethics and dissemination

This study has been exempted by the medical research ethics committee (MREC) Erasmus MC (Rotterdam, The Netherlands). Each participant will provide written consent to participate and remain encoded during the study. The results of the study are planned to be published in an international, peer-reviewed journal.

Registration details

The study is registered at the Netherlands Trial Register (NTR6565; date 12-jul-2017).

Keywords

Burn; Costs; Epidemiology; Etiology; Outcome; Quality of Life; Referral; Scar; Treatment.

Article Summary

Strengths and limitations of this study:

- This study will provide insight into care of burn patients both in hospitals with and without a dedicated Burn Center
- It is a prospective, multicenter, observational study with a strong methodological design.
- Participation of over 20 participating hospitals will increase the reliability and generalizability of the data
- Although the study will be mostly relevant for the Netherlands, it is also informative for other regions.

Introduction

Burns cause significant morbidity and mortality worldwide. Globally, some studies are available on the epidemiology of Emergency Department (ED) treatments of burn injuries[1-6]. These studies focus on epidemiology, including incidence rates and trends of burn-related ED visits[3, 4, 6]. Two international publications have been written, including presentation of data on ED treatment for burns in the Netherlands[7, 8]. These data were limited to home and leisure accidents; work-related burn injuries were not included.

Depending on the severity, burn injuries may require specialized burn care. Three Dutch Burn Centers have been established in order to provide specialized burn care to specific patients. In order to enable proper triaging and referral, the Emergency Management of Severe Burns (EMSB) referral criteria have been implemented (Table 1)[9]. This should result in optimal treatment for burn patients.

In 2014, 322 patients with burns or inhalation injury were admitted to a hospital in the trauma region South-West Netherlands. Of these patients, 213 (66%) were admitted to Burn Center of Maasstad Hospital (Rotterdam), the other 109 (34%) were admitted to hospitals without specialized Burn Center. Whether or not these 109 admissions were in compliance with the EMSB referral criteria is unknown. Equally important, there is a lack of insight into the epidemiology, treatment (including treatment costs), and outcome (both clinical results and Quality and Life) of the patients treated in hospitals without Burn Center. One study is currently being conducted, in which treatment, Quality of Life, and medical costs of patients reporting with burn injuries to the Emergency Department is studied[10]. The study population (N=87) mainly consists of non-admitted patients.

In order to get insight into the epidemiology of burn patients, detailed data collection on patient characteristics, etiology, burn injury characteristics, treatment, and outcome is critical. For that reason, the Dutch Burn Repository (DBR) R3 has been established in 2009[11]. From that date onwards, all patients admitted to a Burn Center in The Netherlands are registered in this Repository. Burn patients admitted elsewhere are not included in the R3 Repository.

Three other national registries also do not provide insight into epidemiology, treatment (costs) and outcome including quality of life of all admitted burn patients. The National Injury Surveillance System (in Dutch: Letsel Informatie Systeem, LIS; www.veiligheid.nl)[12] and the National Medical Registration (in Dutch: Landelijke Medische Registratie, LMR; www.dutchhospitaldata.nl)[13] register non-admitted and admitted patients, respectively. Both are insufficient, as they register patients based on the main diagnosis, which may not always be the burn injury. The Dutch National Trauma Registry (in Dutch: Landelijke Trauma Registratie, LTR; www.lnaz.nl) registers all admitted trauma patients. It encodes burn wounds, but with limited detail, and does not contain relevant treatment and outcome data.

Based on the above, there are currently no data available that provide sufficient details about patients admitted to a hospital without Burn Center. The main aim of this study is to compare the burn injury characteristics of burn patients admitted to a hospital without dedicated Burn Center versus burn patients with <10% Total Body Surface Area (TBSA) burned who are admitted (or secondarily referred) to a Burn Center. Secondary aims are 1) to determine if these admissions were in agreement with the EMSB referral criteria; and 2) to compare the treatment and direct medical costs between these patient groups, and to compare the Quality of Life (EuroQoL-5D; EQ-5D), and scar quality (Patient and Observer Scar Assessment Scale; POSAS) between these patient groups until 12 months follow-up.

Methods and analyses

Study design

This study will follow a multicenter, prospective, observational study design (*i.e.*, cohort study). Patients will be recruited from every hospital in two large trauma regions in The Netherlands, the South-West Netherlands trauma region and Network Emergency Care Brabant. The Burn Center of Maasstad Hospital is included in the South-West Netherlands trauma area. The following 18 hospitals in The Netherlands will participate: Admiraal De Ruyter Ziekenhuis (Goes), Albert Schweitzer Ziekenhuis (Dordrecht), Amphia Ziekenhuis (Breda), Beatrix Ziekenhuis (Gorinchem), Bravis Ziekenhuis (Roosendaal), Catharina Ziekenhuis (Eindhoven), Elisabeth-TweeSteden Ziekenhuis (Tilburg), Elkerliek Ziekenhuis (Helmond), Erasmus MC, University Medical Center (Rotterdam), Franciscus Gasthuis & Vlietland (Rotterdam), IJsselland Ziekenhuis (Capelle aan de IJssel), Ikazia Ziekenhuis (Rotterdam), Jeroen Bosch Ziekenhuis (‘s-Hertogenbosch), Burn Center Maasstad Hospital (Rotterdam), Máxima Medisch Centrum (Veldhoven), Van Weel-Bethesda Ziekenhuis (Dirksland), and ZorgSaam Zeeuws-Vlaanderen (Terneuzen).

The study is registered at the Netherlands Trial Register (NTR6565; date 12-jul-2017).

Recruitment and informed consent

Eligible persons admitted with burn-related injuries (or the parents of pediatric patients) will be informed about the study as soon as possible after hospital presentation. They may receive the information at the ED or while admitted at the surgical ward. The local staff will ask permission to send contact details to the research team. Upon receipt of that permission, a local contact person in the participating hospital will provide details of the patient to the research team. The coordinating investigator or research assistant will contact the patient (or parents) to explain the study, and will send the information brochure and informed consent

form. The coordinating investigator or a research assistant will attend the patient's outpatient visit in the hospital (at approximately three weeks after admission) in order to further explain the study, answer any question the patient (or parents) may have, and for signing informed consent. This gives patients on average two to three weeks to consider their participation. As data collection also includes investigation of the TBSA and extent of burn wounds, it is not possible to give patients more time to consider their participation.

In order to reduce bias as much as possible, the follow-up measurements by the clinical investigator or research assistant will be performed using a standardized protocol.

Study population

The study population will consist of a group of patients admitted to a hospital without dedicated burn center or who are admitted to a dedicated burn center. In order to be eligible to participate in this study, a subject must meet all of the following criteria:

1) Patients with burn-related injuries (no age limit), admitted to a hospital without dedicated Burn Center in the trauma regions South-West Netherlands or Brabant; or patients with <10% TBSA burned, who are primarily admitted or secondarily referred to the Burn Center of Maasstad Hospital*
2) Provision of informed consent

* 10% has been chosen as we expect that patients admitted outside the Burn Centers will have no more that 10% TBSA burned.

A potential subject who meets any of the following criteria will be excluded from participation in this study:

1) Patients who died <24 hours due to severity of non-burn injuries
2) Patients with incomplete or unknown contact information

3) Insufficient comprehension of the Dutch or English language to understand the questionnaires

Outcome measures

The burn-related injury pattern will serve as primary outcome measure. Information on the following items will be collected from the patients' medical files:

- Burn etiology (scald, flame, contact, chemical, or other)
- Inhalation injury (yes or no)
- Setting (home, work, or other)
- Body regions burned, severity (% TBSA burned)
- Extent of burns (superficial dermal, deep dermal, or subdermal)

The secondary outcome measures are:

1) Compliance with EMSB referral criteria (yes or no)
2) Treatment
3) Health care use in hospital with associated treatment costs
4) Health-Related Quality of life (EuroQol-5D-3L (EQ-5D-3L))
5) Patient and Observer Scar Assessment Scale (POSAS)

The following treatment characteristics will be collected:

- Prehospital transport (ambulance, helicopter emergency medical services, or other
- Level of trauma care (level 1, 2, or 3)
- Required care (ward or Intensive Care Unit)
- Resuscitation (amount of fluid <24h after admission)
- Intubation (yes or no)

- Bronchoscopy (yes or no)
- Wound treatment (wound dressing, topical therapy, or other)
- Date of the first operation
- Escharotomy (yes or no)
- Type of operation (split skin grafting, full thickness skin grafting, or excision and primary closure)
- % TBSA that needed skin grafting
- Expansion of split skin graft (1:1, 1:1.5, 1:3, or 1:6)
- Total number of operations
- Indication for second, third, and any subsequent operation
- Number of outpatient department visits
- Date of discharge from hospital
- Reconstructive surgery (release/excision with split skin grafting, full thickness grafting, or laps)

In order to determine the treatment costs, the use of hospital resources will be collected from medical files directly. All direct medical costs due to treatment, complications, and events during follow-up (*e.g.*, ED visit, diagnostic work-up, therapy, events, surgery, admissions, follow-up visits) will be collected. The economic evaluation will be in accordance with the Dutch guideline and will use cost prices were possible[14]. Medical costs will be calculated by multiplying the volumes of health care use with the corresponding unit prices.

The EQ-5D is a validated questionnaire for measuring health-related quality of life[15, 16]. Its use is recommended for the assessment of quality of life in trauma patients, especially for economic assessments[17, 18]. The EQ-5D-3L descriptive system consists of five dimensions

of health (mobility, self-care, usual activities, pain/discomfort anxiety/depression), each with three possible answers. Scores are converted to a utility score ranging from zero to one, with lower scores indicating poorer quality of life. The EQ Visual Analog Score (VAS) records the respondents self-rated health status on a vertical (0-100) visual analog scale. Patients aged 16 years or older will be asked to complete the EQ-5D themselves. Pediatric patients (<16 years) will be asked to compete the youth version of the EQ-5D, or their parent(s) will be asked to complete a proxy version of the EQ-5D youth version.

The POSAS v2.0 (www.posas.org)[19] consists of two parts: a Patient Scale and an Observer Scale, which aim to provide a rating of several measured of scar quality (vascularity, pigmentation, relief/texture, thickness, pliability, surface area, pain, and itching/pruritus). Patients aged 16 years or older and parents of younger pediatric patients will complete the patient-reported part, a trained observer will complete the observer-reported part.

Other data collected

The following, additional, data will be collected in order to describe the study population, patient characteristics, additional injury characteristics, and burn-related (adverse) events:

- Patient characteristics: age, gender, American Society of Anesthesiologists (ASA) classification, comorbidities (diabetes or other)
- Additional injury characteristics: Injury Severity Score (ISS), Abbreviated Injury Score (AIS), for all nine anatomical regions as registered in the trauma registry)
- Burn-related (adverse) events: hematoma (yes or no), excessive blood loss (requiring blood transfusion), wound infection (requiring antibiotic and/or surgical treatment) (yes or no), pneumonia (yes or no), graft loss requiring surgical intervention (or vac therapy; yes or no), or other.

- Outcome related variables: duration of hospital admission, time to wound closure (calculated from date of admission and date of last wound dressing), percentage graft take 5-7 days post burn, discharge destination (home, other hospital, Burn Center, rehabilitation facility, or other), and mortality (possibly burn-related yes or no)

Study procedures

Patients will be followed for one year, with visits planned at three weeks (window 2-4 weeks), three months (window 11-15 weeks), six months (window 5-7 months), and 12 months (window 12-14 months) after admission (Table 2). One additional, optional visit is planned at six weeks (window 5-7 weeks) in case the burn wound has not closed at three weeks. The coordinating investigator or research assistant will be present at each outpatient department visit of the enrolled patients for direct collection of data. The study will not interfere with treatment or follow-up.

Patient characteristics, injury characteristics, and any other relevant data will be collected from the patient's medical files as soon as possible after signing informed consent. Treatment and other clinical data such as adverse events will be collected (partly from the patient files) at each follow-up visit. During these regular clinical visits, any radiographs or digital photos that are routinely obtained will be collected. For the purpose of the study, additional details concerning treatment and outcome that are not mentioned in the patient's hospital files, may be registered on the case report forms directly. At the one-year follow-up visit, the coordinating investigator or research assistant will document any secondary intervention that may be planned for the patient.

As soon as possible after inclusion, patients will be asked to complete the EQ-5D-3L reflecting their pre-injury quality of life. At three months, six months, and at 12 months after the primary hospital admission, patients (or the parents of pediatric patients) will be asked to

complete the EQ-5D-3L and the patient-reported part of the POSAS. The coordinating investigator or research assistant will complete the physician-reported part of the POSAS.

Sample size calculation

A formal sample size calculation for this observational study is not constructive. By including all patients treated in the trauma regions South-West Netherlands and Brabant during 18 months, as well as all patients with >10% TBSA burned who are primarily admitted or secondarily referred to a Burn Center, the maximum number of inclusions will be achieved. The larger the number of patients, the more reliable the analysis will be. Enrolling all patients possible will result in the highest reliability of data (*i.e.*, accurate point estimate with lowest possible variance). Based on the data in the annual report of Trauma Center South-West Netherland (*i.e.*, 109 patients admitted outside the Burn Center in the year 2014), we expect to include approximately 300 patients in 18 months in the two trauma regions combined.

Statistical analysis

Data will be analyzed using the Statistical Package for the Social Sciences (SPSS) version 21.0 or higher (SPSS, Chicago, Ill., USA) and will be reported following the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines. Missing values will not be replaced by imputation. Normality of continuous data will be tested with the Shapiro-Wilk test, and homogeneity of variances will be tested using the Levene's test. A p-value <0.05 will be taken as threshold of statistical significance in all statistical tests, and all tests will be two-sided. No interim analysis is planned.

First, descriptive analysis will be performed in order to report the outcome measures and other collected data. For continuous data (*e.g.,* EQ-5 and POSAS, the mean and SD (parametric data) or the median and quartiles (non-parametric data) will be reported. The only exception are cost data, these will be reported as mean with 95% confidence interval (95%

CI). The 95% CI around the mean costs will be approximated by nonparametric bootstrapping. For categorical data (*e.g.*, EMSB compliance), the number and frequencies will be reported. Data will be reported for the entire population as well as separately for the group of patients admitted to a hospital without versus with a Burn Center.

Next univariate analysis will be done. Statistical significance of difference between the two groups will be tested using a Student's T-test (parametric, continuous data; with or without equal variance assumed as applicable), Mann-Whitney U-test (non-parametric, continuous data), or Chi-squared or Fisher's Exact test (categorical data, as applicable).

Subgroups will be determined based on the patients included. Relevant subgroups can be children versus adults versus elderly, subgroups with different percentages TBSA burned, or patients admitted in compliance versus disagreement with the EMSB referral criteria. Should formal testing between the latter two subgroups be feasible, this will be done as described above.

The economic evaluation will include costs for health care. Direct and indirect, medical and non-medical cost will be measured as indicated in the Dutch guidelines for economic evaluations, using standard, published cost prices where possible[14].

Ethics and dissemination

This study will be conducted according to the principles of the Declaration of Helsinki (64th World Medical Association General Assembly, Fortaleza, Brazil, October 2013). Data will encoded and stored in a pass-word protected OpenClinica database with restricted access to the researchers only. Data will be entered ones. Quality of the entered data will be monitored by checking entry for a random sample of patients prior to database locking.

This study has been exempted by the medical research ethics committee (MREC) Erasmus MC (Rotterdam, The Netherlands). This MREC acts as central ethics committee for this trial (reference number MEC-2017-356). Approval has been obtained from the local hospital boards in all participating centers. Following review of the protocol (version 1.0 date 22-may-2017, the MREC concluded that this study is not subject to the Medical Research Involving Human Subjects Act (WMO). They concluded that the study is a medical/scientific research, but no patients are subjected to procedures or are required to follow rules of behavior. Consequently, the statutory obligation to provide insurance for subjects participating in medical research (article 7 of the WMO) does not apply. Any important changes in the protocol will be submitted to the accredited MREC. The results of the study are planned to be published in an international, peer reviewed journal and presented at national and international trauma and burn care meetings. Each participating center will provide a group author to every publication. No personal data of study participants will be presented.

Discussion

Burns cause significant morbidity and mortality worldwide, and depending on the severity, burn injuries may require specialized burn care in a dedicated Burn Centers. In order to enable optimal triaging and referral to a Burn Center, the EMSB referral criteria have been implemented[9]. Whereas extensive injury and outcome registration exists for patients admitted to a dedicated Burn Center, there are currently no data available that provide sufficient details about patients admitted to a hospital without Burn Center. Successful completion of this study will provide more insight into the percentage of patients admitted to a hospital without dedicated Burn Center. It will also provide us detailed data on patient and injury characteristics, EMSB compliance, treatment, treatment costs, relevant outcome data, and quality of life of burn patients with primary admission at a hospital without Burn Center as well as patients with <10% TBSA burned who are secondarily referred to a Burn Center. Twenty-one hospitals will participate. Inclusion has started September 18, 2017, and a total of 39 patients have been included so far. Eighteen months are planned for inclusion. With a follow-up of one year the presentation of data will be expected by the end of 2020.

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List of abbreviations used

AIS, Abbreviated Injury Scale; ASA classification, American Society of Anesthesiologists classification; 95%CI, 95% Confidence Interval; DBR R3, Dutch Burn Repository R3; ED, Emergency Department; EMSB, The Emergency Management of Severe Burns; EQ-5D, EuroQoL-5D; ISS, Injury Severity Score; LIS, Letsel Informatie Systeem (in English: National Injury Surveillance System); LMR, Landelijke Medische Registratie (in English: National Medical Registration); LNAZ, Landelijke Netwerk Acute Zorg (in English: National Network Acute Care); LTR, Landelijke Trauma Registratie (in English: National Trauma Registry); MEC, Medisch Ethische Commissie (in English: Medical Research Ethics Committee (MREC); NTR, Nederlands Trial Register (in English; Netherlands National Trial Register); POSAS, Patient and Observer Scar Assessment Scale; QoL, Quality of Life; SD, Standard Deviation; SPSS, Statistical Package for the Social Sciences; STROBE, STrengthening the Reporting of OBservational studies in Epidemiology; TBSA, Total Body Surface Area; VAS, Visual Analog Scale; WMO, Medical Research Involving Human Subjects Act (in Dutch: Wet Medisch-wetenschappelijk Onderzoek met Mensen).

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

CHVDV, DTVY, MVB, SP, EMMV and MJHV developed the study. DTVY and EMMVL drafted the manuscript. MHJV will act as trial principal investigator. DTVY, DB, AYMVPC, PARDR, MG, TMALK, KWWL, ANR, MS, LVDS, AHVDV, FCVE, PVVE, PAV, DIV, MW, CHVD and MHJV will participate in patient inclusion and outcome assessment. DTVY

and EMMVL will perform statistical analysis of the study data. All authors have read and approved the final manuscript.

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Competing interests statement

The authors declare that they have no competing interests.

Tables

Table 1: EMSB referral criteria[9]

1)	The percentage Total Body Surface Area burned (TBSA burned; >10% TBSA in adults or >5% in children)
2)	Burns of special areas (face, hands, feet, perineum, genitalia, and major joints)
3)	Full thickness burns >5% TBSA burned
4)	Electrical burns
5)	Chemical burns
6)	Burns with associated inhalation injury
7)	Circumferential burns of limbs or chest
8)	Extremes of age (children and elderly)
9)	Pre-existing medical disorders which could complicate management and prolong recovery or effect mortality
10)	Associated trauma

Table 2: Schedule of events

Event forms	**Screening**	**3 we** (2-4 we)	**6 we*** (5-7 we)	**3 mo** (11-15 we)	**6 mo** (6-7 mo)	**12 mo** (12-14 mo)
Screening	X					
Informed Consent		X				
Patient characteristics		X				
Injury characteristics		X				
Radiology		X[1]	X[1]	X[1]	X[1]	X[1]
Digital photo		X[1]	X[1]	X[1]	X[1]	X[1]
Treatment characteristics		X	X	X	X	X
Outcome details		X	X	X	X	X
Adverse Events		X	X	X	X	X
Clinical FU		X	X	X	X	X
Health Care Consumption		X	X	X	X	X
EQ-5D		X[2]		X	X	X
POSAS				X	X	X
Early withdrawal		**	**	**	**	**

*Optional visit; will only take place if wounds are not closed at three weeks.

[1]Only if treating surgeon requests these images.

[2]Asking for EQ-5D pre-burn.

** Only at time of withdrawal.

SPIRIT 2013 Checklist: Recommended items to address in a clinical trial protocol and related documents*

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	5, 9
	2b	All items from the World Health Organization Trial Registration Data Set	
Protocol version	3	Date and version identifier	17
Funding	4	Sources and types of financial, material, and other support	22
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1, 2, 3
	5b	Name and contact information for the trial sponsor	1
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	21, 22
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	21, 22

Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	4, 7, 8
	6b	Explanation for choice of comparators	N.A.
Objectives	7	Specific objectives or hypotheses	4, 8
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	9
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	10
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	10, 11
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	11-15
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	N.A.
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	N.A.
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	N.A.
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	11-14
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	14, 15, Table 2

Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	15
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	N.A.
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	N.A.
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	N.A.
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	N.A.
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	N.A.
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	11-15
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	

Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	17
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	15-16
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	16
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	15
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	N.A.; instead, quality checks of entered data are planned (page 17)
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	15
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	N.A. is not an intervention study
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	17
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	5, 17
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	17

Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	9-10
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	N.A.
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	17
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	22
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	17
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	N.A.
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	17
	31b	Authorship eligibility guidelines and any intended use of professional writers	17
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	N.A.
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	Attached
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	N.A. _____

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated.

BMJ Open

Epidemiology of injuries, treatment (costs), and outcome in burn patients admitted to a hospital with or without dedicated Burn Center (Burn-Pro); Protocol for a multicenter prospective observational study

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	SURGERY, SURGERY

Epidemiology of injuries, treatment (costs), and outcome in burn patients admitted to a hospital with or without dedicated Burn Center (Burn-Pro); Protocol for a multicenter prospective observational study

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Abstract

Introduction

The Emergency Management of Severe Burns (EMSB) referral criteria have been implemented for optimal triaging of burn patients. Admission to a Burn Center is indicated for patients with severe burns or with specific characteristics like older age or comorbidities. Patients not meeting these criteria can also be treated in a hospital without Burn Center. Limited information is available about the organization of care and referral of these patients. The aims of this study are to determine the burn injury characteristics, treatment (costs), Quality of Life, and scar quality of burn patients admitted to a hospital without dedicated Burn Center. These data will subsequently be compared with data from patients with <10% Total Body Surface Area (TBSA) burned who are admitted (or secondarily referred) to a Burn Center. If admissions were in agreement with the EMSB referral criteria will also be determined.

Methods and analysis

In this multicenter, prospective, observational study (cohort study), the following two groups of patients will be followed; 1) All patients (no age limit) admitted with burn-related injuries to a hospital without a dedicated Burn Center in the Southwest Netherlands or Brabant Trauma Region ; and 2) All patients (no age limit) with <10% Total Body Surface Area (TBSA) burned who are primarily admitted (or secondarily referred) to the Burn Center of Maasstad Hospital. Data on the burn injury characteristics (primary outcome), EMSB compliance, treatment, treatment costs, and outcome will be collected from the patients' medical files. At three weeks and at three, six, and 12 months after trauma, patients will be asked to complete the Quality of Life (EuroQoL-5D; EQ-5D), and the patient-reported part of the Patient and Observer Scar Assessment Scale (POSAS). At those time visits, the

coordinating investigator or research assistant will complete the observer-reported part of the POSAS.

Ethics and dissemination

This study has been exempted by the medical research ethics committee (MREC) Erasmus MC (Rotterdam, The Netherlands). Each participant will provide written consent to participate and remain encoded during the study. The results of the study are planned to be published in an international, peer-reviewed journal.

Registration details

The study is registered at the Netherlands Trial Register (NTR6565; date 12-jul-2017).

Keywords

Burn; Costs; Epidemiology; Etiology; Outcome; Quality of Life; Referral; Scar; Treatment.

Article Summary

Strengths and limitations of this study:

- This study will provide insight into care of burn patients both in hospitals with and without a dedicated Burn Center
- It is a prospective, multicenter, observational study with a best possible methodological design.
- Participation of over 20 participating hospitals will increase the reliability and generalizability of the data
- Although the study will be mostly relevant for the Netherlands, it is also informative for other regions.

Introduction

Burns cause significant morbidity and mortality worldwide. Globally, some studies are available on the epidemiology of Emergency Department (ED) treatments of burn injuries[1-8], including three from the Netherlands[7-9]. These data were limited to home and leisure accidents; work-related burn injuries were not included.

Depending on the severity, burn injuries may require specialized burn care. In order to enable proper triaging and referral, the Emergency Management of Severe Burns (EMSB) referral criteria have been implemented (Table 1)[10].

In 2014, 322 patients with burns or inhalation injury were admitted to a hospital in the trauma region South-West Netherlands. Of these patients, 109 (34%) were admitted to hospitals without specialized Burn Center. There is a lack of insight into the epidemiology, treatment (including treatment costs), and outcome (both clinical results and Quality and Life) of the patients treated in hospitals without Burn Center.

In order to get insight into the epidemiology of burn patients, detailed data collection on patient characteristics, etiology, burn injury characteristics, treatment, and outcome is critical. Such data are currently not available from current registries. The Dutch Burn Repository (DBR) R3 only registers data for patients admitted to a Burn Center[11]. The National Injury Surveillance System (in Dutch: Letsel Informatie Systeem, LIS; www.veiligheid.nl)[12] and the National Medical Registration (in Dutch: Landelijke Medische Registratie, LMR; www.dutchhospitaldata.nl)[13] register non-admitted and admitted patients, respectively. Both are insufficient, as they register patients based on the main diagnosis, which may not always be the burn injury. The Dutch National Trauma Registry (in Dutch: Landelijke

Trauma Registratie, LTR; www.lnaz.nl) registers all admitted trauma patients. It encodes burn wounds, but with limited detail, and does not contain relevant treatment and outcome data.

Based on the above, there are currently no data available that provide sufficient details about patients admitted to a hospital without Burn Center. It is also not clear if these are different for patients with similar burn injury severity admitted to a Burn Center. The main aim of this study is to determine the burn injury characteristics of burn patients admitted to a hospital without dedicated Burn Center. Secondary aims are 1) to determine if these admissions were in agreement with the EMSB referral criteria; 2) to determine the treatment and direct medical costs, the Quality of Life (EuroQoL-5D; EQ-5D), and scar quality (Patient and Observer Scar Assessment Scale; POSAS) for these patients until 12 months follow-up; and 3) to compare the injury pattern and outcome of these patients with burn patients with <10% Total Body Surface Area (TBSA) burned who are admitted (or secondarily referred) to a Burn Center. We expect that burn patient admission outside the Burn Center is restricted to a maximum of 10% TBSA, and that outcome is similar to that achieved for a subgroup with similar burn injury severity admitted to a Burn Center.

Methods and analyses

Study design and setting

This study will follow a multicenter, prospective, observational study design (cohort study). Patients will be recruited from every hospital in two large trauma regions in The Netherlands, the South-West Netherlands trauma region and Network Emergency Care Brabant. The Burn Center of Maasstad Hospital is included in the South-West Netherlands trauma area. The following 18 hospitals in The Netherlands will participate: Admiraal De Ruyter Ziekenhuis (Goes), Albert Schweitzer Ziekenhuis (Dordrecht), Amphia Ziekenhuis (Breda), Beatrix Ziekenhuis (Gorinchem), Bravis Ziekenhuis (Roosendaal), Catharina Ziekenhuis (Eindhoven), Elisabeth-TweeSteden Ziekenhuis (Tilburg), Elkerliek Ziekenhuis (Helmond), Erasmus MC, University Medical Center (Rotterdam), Franciscus Gasthuis & Vlietland (Rotterdam), IJsselland Ziekenhuis (Capelle aan de IJssel), Ikazia Ziekenhuis (Rotterdam), Jeroen Bosch Ziekenhuis ('s-Hertogenbosch), Burn Center Maasstad Hospital (Rotterdam), Máxima Medisch Centrum (Veldhoven), Van Weel-Bethesda Ziekenhuis (Dirksland), and ZorgSaam Zeeuws-Vlaanderen (Terneuzen). The study started in September, 2017 and the recruiting periods will be 18 months. With a follow-up of one year the presentation of data will be expected by the end of 2020.

Study registration

The study is registered at the Netherlands Trial Register (NTR6565; date 12-jul-2017).

Recruitment and informed consent

Eligible persons admitted with burn-related injuries (or the parents of pediatric patients) will be informed about the study as soon as possible after hospital presentation. They may receive the information at the ED or while admitted at the surgical ward. The local staff will ask

permission to send contact details to the research team. Upon receipt of that permission, a local contact person in the participating hospital will provide details of the patient to the research team. The coordinating investigator or research assistant will contact the patient (or parents) to explain the study, and will send the information brochure and informed consent form. The coordinating investigator or a research assistant will attend the patient's outpatient visit in the hospital (at approximately three weeks after admission) in order to further explain the study, answer any question the patient (or parents) may have, and for signing informed consent. This gives patients on average two to three weeks to consider their participation. As data collection also includes investigation of the TBSA and extent of burn wounds, it is not possible to give patients more time to consider their participation.

In order to reduce bias as much as possible, the follow-up measurements by the clinical investigator or research assistant will be performed using a standardized protocol.

Study population and eligibility criteria

The study population will consist of a group of patients admitted to a hospital without dedicated burn center or who are admitted to a dedicated burn center. In order to be eligible to participate in this study, a subject must meet all of the following criteria:

1) Patients with burn-related injuries (no age limit), admitted to a hospital without dedicated Burn Center in the trauma regions South-West Netherlands or Brabant; or patients with <10% TBSA burned, who are primarily admitted or secondarily referred to the Burn Center of Maasstad Hospital*
2) Provision of informed consent

* 10% has been chosen as we expect that patients admitted outside the Burn Centers will have no more that 10% TBSA burned. This is also in line with the EMSB referral criteria[10]. The

% TBSA will be assessed during physical examination by a research physician who has had elaborate training for this at the participating dedicated Burn Center.

A potential subject who meets any of the following criteria will be excluded from participation in this study:

1) Patients who died <24 hours due to severity of non-burn injuries (*e.g.*, severe head injury)
2) Patients with incomplete or unknown contact information
3) Insufficient comprehension of the Dutch or English language to understand the questionnaires

Outcome measures

The burn-related injury pattern will serve as primary outcome measure. Information on the following items, representing injuries and mechanism, will be collected from the patients' medical files:

- Inhalation injury (yes or no)
- Body regions burned, severity (% TBSA burned as assessed by a trained research physician)
- Extent of burns (superficial dermal, deep dermal, or subdermal)
- Setting (home, work, or other)
- Burn etiology (scald, flame, contact, chemical, or other)

The secondary outcome measures are:

1) Compliance with EMSB referral criteria (yes or no)
2) Treatment
3) Health care use in hospital with associated treatment costs

4) Health-Related Quality of life (EuroQol-5D-3L (EQ-5D-3L))

5) Patient and Observer Scar Assessment Scale (POSAS)

The following treatment characteristics will be collected:

- Prehospital transport (ambulance, helicopter emergency medical services, or other
- Level of trauma care (level 1, 2, or 3)
- Required care (ward or Intensive Care Unit)
- Resuscitation (amount of fluid <24h after admission)
- Intubation (yes or no)
- Bronchoscopy (yes or no)
- Wound treatment (wound dressing, topical therapy, or other)
- Date of the first operation
- Escharotomy (yes or no)
- Type of operation (split skin grafting, full thickness skin grafting, or excision and primary closure)
- % TBSA that needed skin grafting
- Expansion of split skin graft (1:1, 1:1.5, 1:3, or 1:6)
- Total number of operations
- Indication for second, third, and any subsequent operation
- Number of outpatient department visits
- Date of discharge from hospital
- Reconstructive surgery (release/excision with split skin grafting, full thickness grafting, or laps)

In order to determine the treatment costs, the use of hospital resources will be collected from medical files directly. All direct medical costs due to treatment, complications, and events during follow-up (*e.g.*, ED visit, diagnostic work-up, therapy, events, surgery, admissions, follow-up visits) will be collected. The economic evaluation will be in accordance with the Dutch guideline and will use cost prices were possible[14]. Medical costs will be calculated by multiplying the volumes of health care use with the corresponding unit prices.

The EQ-5D is a validated questionnaire for measuring health-related quality of life[15, 16]. Its use is recommended for the assessment of quality of life in trauma patients, especially for economic assessments[17, 18]. The EQ-5D-3L descriptive system consists of five dimensions of health (mobility, self-care, usual activities, pain/discomfort anxiety/depression), each with three possible answers. Scores are converted to a utility score ranging from zero to one, with lower scores indicating poorer quality of life. The EQ Visual Analog Score (VAS) records the respondents self-rated health status on a vertical (0-100) visual analog scale. Patients aged 16 years or older will be asked to complete the EQ-5D themselves. Pediatric patients (<16 years) will be asked to compete the youth version of the EQ-5D, or their parent(s) will be asked to complete a proxy version of the EQ-5D youth version.

The POSAS v2.0 (www.posas.org)[19] consists of two parts: a Patient Scale and an Observer Scale, which aim to provide a rating of several measured of scar quality (vascularity, pigmentation, relief/texture, thickness, pliability, surface area, pain, and itching/pruritus). Patients aged 16 years or older and parents of younger pediatric patients will complete the patient-reported part, a trained observer will complete the observer-reported part.

Other data collected

The following, additional, data will be collected in order to describe the study population, patient characteristics, additional injury characteristics, and burn-related (adverse) events:

- Patient characteristics: age, gender, American Society of Anesthesiologists (ASA) classification, comorbidities (diabetes or other)
- Additional injury characteristics: Injury Severity Score (ISS), Abbreviated Injury Score (AIS), for all nine anatomical regions as registered in the trauma registry)
- Burn-related (adverse) events: hematoma (yes or no), excessive blood loss (requiring blood transfusion), wound infection (requiring antibiotic and/or surgical treatment) (yes or no), pneumonia (yes or no), graft loss requiring surgical intervention (or vac therapy; yes or no), or other.
- Outcome related variables: duration of hospital admission, time to wound closure (calculated from date of admission and date of last wound dressing), percentage graft take 5-7 days post burn, discharge destination (home, other hospital, Burn Center, rehabilitation facility, or other), and mortality (possibly burn-related yes or no)

Study procedures, data collection methods and participant timelines

Patients will be followed for one year, with visits planned at three weeks (window 2-4 weeks), three months (window 11-15 weeks), six months (window 5-7 months), and 12 months (window 12-14 months) after admission (Table 2). One additional, optional visit is planned at six weeks (window 5-7 weeks) in case the burn wound has not closed at three weeks. Wound closure is defined as 95% closure, as judged upon wound inspection by the research physician and the local treating physician or specialized wound care nurse. In case of disagreement, consensus will be reached by discussion. The coordinating investigator or research assistant will be present at each outpatient department visit of the enrolled patients for direct collection of data. The study will not interfere with treatment or follow-up.

Patient characteristics, injury characteristics, and any other relevant data will be collected from the patient's medical files as soon as possible after signing informed consent. Treatment and other clinical data such as adverse events will be collected (partly from the patient files) at each follow-up visit. During these regular clinical visits, any radiographs or digital photos that are routinely obtained will be collected. For the purpose of the study, additional details concerning treatment and outcome that are not mentioned in the patient's hospital files, may be registered on the case report forms directly. At the one-year follow-up visit, the coordinating investigator or research assistant will document any secondary intervention that may be planned for the patient.

As soon as possible after inclusion, patients will be asked to complete the EQ-5D-3L reflecting their pre-injury quality of life. At three months, six months, and at 12 months after the primary hospital admission, patients (or the parents of pediatric patients) will be asked to complete the EQ-5D-3L and the patient-reported part of the POSAS. The coordinating investigator or research assistant will complete the physician-reported part of the POSAS.

Blinding

Patients, the research physician who determines % TBSA, wound closure, and scar quality, and the statistician will not be blinded.

Sample size

Given the epidemiologic nature of the primary aim and the lack of information of the population admitted to a hospital without Burn Center, a formal sample size calculation was not made. By including all patients treated in the trauma regions South-West Netherlands and Brabant during 18 months, as well as all patients with >10% TBSA burned who are primarily admitted or secondarily referred to a Burn Center, the maximum number of inclusions will be achieved in both cohorts. The larger the number of patients, the more reliable the analysis will

be. Enrolling all patients possible will result in the highest reliability of data (*i.e.*, accurate point estimate with lowest possible variance). Based on the data in the annual report of Trauma Center South-West Netherland (*i.e.*, 109 patients admitted outside the Burn Center in the year 2014), we expect to include approximately 300 patients in 18 months in the two trauma regions combined.

Statistical analysis

Data will be analyzed using the Statistical Package for the Social Sciences (SPSS) version 21.0 or higher (SPSS, Chicago, Ill., USA) and will be reported following the Strengthening the Reporting of Observational studies in Epidemiology (STROBE) guidelines. Missing values will not be replaced by imputation. Normality of continuous data will be tested with the Shapiro-Wilk test, and homogeneity of variances will be tested using the Levene's test. A p-value <0.05 will be taken as threshold of statistical significance in all statistical tests, and all tests will be two-sided. No interim analysis is planned.

First, descriptive analysis will be performed in order to report the outcome measures and other collected data. Data will be reported for the entire population as well as separately for the group of patients admitted to a hospital without versus with a Burn Center. For continuous data (*e.g.,* EQ-5 and POSAS, the mean and SD (parametric data) or the median and quartiles (non-parametric data) will be reported. The only exception are cost data, these will be reported as mean with 95% confidence interval (95% CI). The 95% CI around the mean costs will be approximated by nonparametric bootstrapping. For categorical data (*e.g.*, EMSB compliance), the number and frequencies will be reported.

Next univariate analysis will be done in order to compare the two cohorts. Statistical significance of difference between the two groups will be tested using a Student's T-test (parametric, continuous data; with or without equal variance assumed as applicable), Mann-

Whitney U-test (non-parametric, continuous data), or Chi-squared or Fisher's Exact test (categorical data, as applicable).

Subgroups will be determined based on the patients included. Relevant subgroups can be children versus adults versus elderly, subgroups with different percentages TBSA burned, or patients admitted in compliance versus disagreement with the EMSB referral criteria. Should formal testing between the latter two subgroups be feasible, this will be done as described above.

The economic evaluation will include costs for health care. Direct and indirect, medical and non-medical cost will be measured as indicated in the Dutch guidelines for economic evaluations, using standard, published cost prices where possible[14].

Data management and monitoring

Data will be encoded and stored in a pass-word protected OpenClinica database with restricted access to the researchers only. Data will be entered once. Quality of the entered data will be monitored by checking entry for a random sample of patients prior to database locking.

Patient and public involvement

The need for this study emerged from meetings of the Association of Dutch Burn Centers as well as the Dutch Burns Foundation, representing both health care professionals and patients. Input into the design, comparison, and outcome measures was given during presentation for the Scientific Board of the Dutch Burns Foundation. Patients were not directly involved in the subsequent writing of the protocol, nor were they directly involved in the recruitment to and conduct of the study. A summary of the main results will be made available to study participants on request.

Ethics and dissemination

This study will be conducted according to the principles of the Declaration of Helsinki (64th World Medical Association General Assembly, Fortaleza, Brazil, October 2013).

This study has been exempted by the medical research ethics committee (MREC) Erasmus MC (Rotterdam, The Netherlands). This MREC acts as central ethics committee for this trial (reference number MEC-2017-356). Approval has been obtained from the local hospital boards in all participating centers. Following review of the protocol (version 1.0 date 22-may-2017, the MREC concluded that this study is not subject to the Medical Research Involving Human Subjects Act (WMO). They concluded that the study is a medical/scientific research, but no patients are subjected to procedures or are required to follow rules of behavior. Consequently, the statutory obligation to provide insurance for subjects participating in medical research (article 7 of the WMO) does not apply. Any important changes in the protocol will be submitted to the accredited MREC. The results of the study are planned to be published in an international, peer reviewed journal and presented at national and international trauma and burn care meetings. Each participating center will provide a group author to every publication. No personal data of study participants will be presented.

Discussion

Burns cause significant morbidity and mortality worldwide, and depending on the severity, burn injuries may require specialized burn care in a dedicated Burn Centers. In order to enable optimal triaging and referral to a Burn Center, the EMSB referral criteria have been implemented[10]. Whereas extensive injury and outcome registration exists for patients admitted to a dedicated Burn Center, there are currently no data available that provide sufficient details about patients admitted to a hospital without Burn Center. Successful completion of this study will provide more insight into the percentage of patients admitted to a hospital without dedicated Burn Center. It will also provide us detailed data on patient and injury characteristics, EMSB compliance, treatment, treatment costs, relevant outcome data, and quality of life of burn patients with primary admission at a hospital without Burn Center as well as patients with <10% TBSA burned who are secondarily referred to a Burn Center. Twenty-one hospitals will participate. Although the participation of multiple hospitals may introduce treatment bias, it also makes the results more generalizable.

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List of abbreviations used

AIS, Abbreviated Injury Scale; ASA classification, American Society of Anesthesiologists classification; 95%CI, 95% Confidence Interval; DBR R3, Dutch Burn Repository R3; ED, Emergency Department; EMSB, The Emergency Management of Severe Burns; EQ-5D, EuroQoL-5D; ISS, Injury Severity Score; LIS, Letsel Informatie Systeem (in English: National Injury Surveillance System); LMR, Landelijke Medische Registratie (in English: National Medical Registration); LNAZ, Landelijke Netwerk Acute Zorg (in English: National Network Acute Care); LTR, Landelijke Trauma Registratie (in English: National Trauma Registry); MEC, Medisch Ethische Commissie (in English: Medical Research Ethics Committee (MREC); NTR, Nederlands Trial Register (in English; Netherlands National Trial Register); POSAS, Patient and Observer Scar Assessment Scale; QoL, Quality of Life; SD, Standard Deviation; SPSS, Statistical Package for the Social Sciences; STROBE, STrengthening the Reporting of OBservational studies in Epidemiology; TBSA, Total Body Surface Area; VAS, Visual Analog Scale; WMO, Medical Research Involving Human Subjects Act (in Dutch: Wet Medisch-wetenschappelijk Onderzoek met Mensen).

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

EMMVL, DTVY, MEVB, SP, MHJV, and CHVDV developed the study. MHJV will act as trial principal investigator. DTVY, DB, AYMVPC, PARDR, MG, TMALK, KWWL, ANR, MS, LVDS, AHVDV, FCVE, PVVE, PAV, DIV, MW, MHJV, and CHVDV will participate in patient inclusion and outcome assessment. DTVY, SP, and EMMVL will perform

statistical analysis of the study data. DTVY and EMMVL drafted the current manuscript. All other authors have read and approved this final manuscript. At the end of the study, DTVY and EMMVL will draft the manuscript. All other authors will interpret the data, critically revise the manuscript, and approve the final version to be submitted.

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Competing interests statement

The authors declare that they have no competing interests.

Tables

Table 1: EMSB referral criteria[10]

1)	The percentage Total Body Surface Area burned (TBSA burned; >10% TBSA in adults or >5% in children)
2)	Burns of special areas (face, hands, feet, perineum, genitalia, and major joints)
3)	Full thickness burns >5% TBSA burned
4)	Electrical burns
5)	Chemical burns
6)	Burns with associated inhalation injury
7)	Circumferential burns of limbs or chest
8)	Extremes of age (children and elderly)
9)	Pre-existing medical disorders which could complicate management and prolong recovery or effect mortality
10)	Associated trauma

Table 2: Schedule of events

Event forms	**Screening**	**3 we** (2-4 we)	**6 we*** (5-7 we)	**3 mo** (11-15 we)	**6 mo** (6-7 mo)	**12 mo** (12-14 mo)
Screening	X					
Informed Consent		X				
Patient characteristics		X				
Injury characteristics		X				
Radiology		X[1]	X[1]	X[1]	X[1]	X[1]
Digital photo		X[1]	X[1]	X[1]	X[1]	X[1]
Treatment characteristics		X	X	X	X	X
Outcome details		X	X	X	X	X
Adverse Events		X	X	X	X	X
Clinical FU		X	X	X	X	X
Health Care Consumption		X	X	X	X	X
EQ-5D		X[2]		X	X	X
POSAS				X	X	X
Early withdrawal		**	**	**	**	**

*Optional visit; will only take place if wounds are not closed at three weeks.

[1]Only if treating surgeon requests these images.

[2]Asking for EQ-5D pre-burn.

** Only at time of withdrawal.

STROBE Statement—Checklist of items that should be included in reports of ***cohort studies***

	Item No	Recommendation	Page
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	4-5
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	7-9
Objectives	3	State specific objectives, including any prespecified hypotheses	8
Methods			
Study design	4	Present key elements of study design early in the paper	9
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	9, 14-15
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	10-11, 14
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	N.A.
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	11-14
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	11-14
Bias	9	Describe any efforts to address potential sources of bias	10
Study size	10	Explain how the study size was arrived at	15-16
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	16
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	16-17
		(*b*) Describe any methods used to examine subgroups and interactions	17
		(*c*) Explain how missing data were addressed	16
		(*d*) If applicable, explain how loss to follow-up was addressed	16
		(*e*) Describe any sensitivity analyses	N.A.
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	N.A.
		(b) Give reasons for non-participation at each stage	N.A.
		(c) Consider use of a flow diagram	N.A.
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	N.A.
		(b) Indicate number of participants with missing data for each variable of interest	N.A.
		(c) Summarise follow-up time (eg, average and total amount)	N.A.
Outcome data	15*	Report numbers of outcome events or summary measures over time	N.A.
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	N.A.

		(*b*) Report category boundaries when continuous variables were categorized	N.A.
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N.A.
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N.A.
Discussion			
Key results	18	Summarise key results with reference to study objectives	N.A.
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	N.A.
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	19
Generalisability	21	Discuss the generalisability (external validity) of the study results	19
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	23

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.