OUTCOME ASSESSMENT OF THE SEVERELY INJURED

The value of a network and registry

Jan van Ditshuizen

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J.C. van Ditshuizen

Colofon

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The value of a network and registry

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PART I

INTRODUCTION AND OUTLINE

1

CHAPTER 1

General introduction and outline of this thesis

A brief history

Linguistically the word 'trauma' originates from the ancient Greek word for "a wound, a hurt, a defeat". Besides forming ideas of what trauma is, at that time, Hippocrates of Kos deviated from magicians and religion, and materialised medicine. Ways of dealing with trauma has a long history in all sort of forms, mostly described in the aftermath of bloodshed: collective attention by ancient dramatic plays as a form of catharsis, purifying rituals, or repentant actions in an attempt to absolve moral injuries to name but a few. More recently, industrialisation and technological abundances gave an impulse to more catastrophic accidents on civilian sides.

Modern society faces an ongoing challenge with five millions of trauma-related deaths annually, and approximately 10 percent loss of disability adjusted life years due to injuries worldwide. Both severe and minor trauma can have profound impact on a personal level as well. Impaired quality of life, difficulties with return to work, health care consumption, post-traumatic stress, long-term social limitations, and impact on social environment can be considerable.[1-6] In the Netherlands, the prevalence of medical treatment after unintentional trauma is around 1.5 million per year, which is approximately 900 per 10,000 inhabitants. Around five percent involves clinical admission to a hospital which is somewhat more than 40 per 10,000 inhabitants.[7]

Organisation of trauma care

Impulses for more systematically organised trauma care originates mainly from wars or high impact disasters. Such incidents ask for medical staff to be extremely organised in working processes, in high demanding situations the time element is crucial. 'The golden hour' has been a leading concept since World War I. Although time as an acute health care principle is under debate, current medical system efficacy heavily relies on organised swiftness of processes.[8-10]

In 1987 scientific research concluded that trauma care in the Netherlands was not organised enough, advising that organisation and integration of acute trauma care similar to the United States would be efficient and beneficial for Dutch acute trauma patients. Persons in need of acute health care were mostly brought to the nearest hospital, *'the right patient at the right place at the right time'* was not a theme. The catastrophic *'Bijlmerramp',* being the most deadly aviation disaster in the Netherlands, harshly pointed out lacunae in the organisation of Dutch trauma care. Eventually, this led to the implementation of inclusive trauma networks in 1999, with one of the top priorities at this point, a focus on the most severely injured patients. The ministry of health officially assigned regions with a designated level I trauma centre regionalising trauma care, several helicopter emergency medical services, regional disaster preparedness management, a bureau for organising and coordinating acute trauma care at the same time functioning as a centre of knowledge, and a trauma registry for evaluation of major trauma care.

Trauma registry

The Dutch Nationwide Trauma Registry (DNTR) was implemented in 2007 with a dataset mainly oriented on the severely injured. The DNTR is considered to be a prospective cohort, for which data is collected throughout the acute trauma health care chain. DNTR inclusion criteria are trauma < 48 hours when admitted to the emergency department, following either hospitalisation, transfer to a different hospital with the intention to be admitted, or death (excluding death on arrival), for all type of trauma. The DNTR has a 100% participation rate of all Dutch hospitals since 2019, and is legally obliged since 2021. Inclusion criteria are somewhat different from other (European) registries, whose inclusion criteria are mainly aimed at severely injured patients, leaving out patients with minor injuries, and many children or elderly, resulting in an restricted view on the total magnitude of clinically admitted trauma.[11]

The DNTR contains information on demographics, trauma setting, prehospital and emergency department vital parameters, clinical emergency interventions (e.g. embolization and craniotomy), and clinical outcome measures, such as, hospital length of stay, intensive care admission and admission duration, and in-hospital mortality. Much effort is put in coordinating and standardising the DNTR per trauma region, as well as on a national level with boards for coordinators and coders and one for medical heads of designated level I trauma centres. Inclusion criteria, data validation, injury coding, and data governance are constantly monitored and discussed.

Quality indicator major trauma

Each trauma region in the Netherlands, includes a designated level I trauma centre, surrounded with multiple non-level I trauma centres. Hospitals are designated a specific level of trauma care based on criteria established by the Dutch Trauma Association. Level I trauma centres provide most extensive care with immediate availability of trained medical specialists and supporting staff around the clock and are required to treat a minimum of 240 major trauma patients annually. Specific resources like an infusion warmer, thoracotomy set, extracorporeal membrane oxygenation, intensive care bed, operation theatre, an intervention radiologist, a neurosurgeon, and massive transfusion protocol are also non-stop available in level I trauma centres. Level II trauma centres are able to stabilise major trauma patients, but do not have all neurosurgical facilities, extracorporeal membrane oxygenation, or organ preserving facilities immediately available around the clock. Patients with minor or isolated injuries can be also admitted to a level III trauma centre.[12]

With the combination of level status and a major trauma definition, a quality indicator was established in 2014, as part of a set acute health care indicators; 90 percent of all major trauma patients should be primarily admitted to a level I trauma centre. This indicator was introduced by the National Health Care Institute (In Dutch: Zorginstituut Nederland), and once more based on a report originating from the United States published by the American College of Surgeons.[13] This report advises on volume norms, level criteria for trauma centres, and a prehospital undertriage of five percent.[14] Undertriage is defined as the proportion of major trauma patients primarily admitted to a non-level I trauma centre. Currently, in the Netherlands, some level I trauma centres do not meet 240 admitted major trauma patients,

nor does a single level I trauma centre have 90 percent of the major trauma patients primarily admitted in their respective designated trauma region.[7, 15] Injury coding with the AIS is part of the DNTR. Since the Injury Severity Score (ISS), thus major trauma (ISS > 15) classification is part of the DNTR, the aforementioned quality indicators on volume and percentage of primarily admitted major trauma patient to a level I trauma centre are extracted from the DNTR.[7, 11, 16]

Objectives and questions this thesis

In order to evaluate major trauma care from a regional perspective, the current formation of trauma networks and major trauma quality indicators raises some questions about the Dutch trauma system, based on data from the DNTR, whether or not enriched with a questionnaire

- *Are all major trauma patients identified, registered and classified as such in a regional trauma registry?*
- *What does the literature tell us on the performance of different levels of trauma care in terms of mortality and non-fatal clinical outcome measures of major trauma patients, and can these results be found in a regional trauma registry?*
- *Do major trauma patients in a network report their health status and return to work different compared with a reference population?*
- *Do major trauma patients report a different health-related quality of life and psychological health status across levels of care in a network?*

Benchmarking is based on databases of registries, therefore the quality of each separate registration is important. Trauma registrations need to be as complete and reliable as possible. However, administrative hospital data can have a large amount of omissions or might not be specific enough for trauma care evaluation.[17] Missing registrations and missing values are common, reliability of data validation and injury coding can be questionable, and are a potential source of information bias.[18-26] Epidemiological studies can also suffer from an ecological fallacy when looking at the total burden of acute trauma care, if certain subgroups are excluded.[11, 27] An inclusive population based trauma registry in a network, including all types of injuries in all hospitals, creates an ideal situation for data analysis. However, missing registrations do occur, and could introduce a selection or exclusion bias.[28, 29]

Injury coding

Injuries in trauma registries are coded with the AIS. Injury coding is dependent on medical information reported in electronic health records and the experience of coders. Radiologic reports are an important source for injury coding. Such information sources are not always explicit, uniform, and straightforward, whereas the AIS injury codes are highly detailed. The AIS not only contains injury codes on anatomical damage, but also clinical elements like coma, blood loss, and the degree of tissue damage are elements determining the severity of injuries. Some of these items are multi interpretable, or not documented well. Whenever there is doubt on scoring the injury severity of a specific anatomical part, the AIS advises to code conservatively. That could mean either a 'not further specified' AIS code, or the lowest of two

severity codes between the two most likely to be chosen codes. As we can imagine, it can be difficult to code completely reliably based on retrospective data. The educational background of coders is diverse, ranging from administrative medical personnel to experienced physicians. Interpretation of extensive medical information is mostly reserved for clinicians with medical experience.[18-20, 30] However, when medical reports are straightforward, medical coders perform similar as physicians. Various studies have shown variability between injury coders and between centres in injury coding with the AIS from its developing years on.[19, 31-33] Especially injury coding of TBI has shown significant variability.[19, 34] This raises questions on correctness of quality indicators and (sub)population analyses that are based on certain injuries or a specific ISS threshold, such as a threshold of 16 for major trauma classification. In addition, such classification is also subject to time. AIS code sets are periodically revised to better reflect contemporary performance of trauma systems. Not all trauma registries use the same AIS revision at any given time; worldwide, registries implement newer AIS revisions whenever considered necessary at a local level. differences in the classification of injury severity between AIS revisions can affect assessments of injury severity, both in individual patients and across populations.[35-43] In turn, this can compromise assessments of quality of care, or of the level of performance of trauma systems.

Classifying major trauma

A long glossary exists for the most severely injured patients, of which polytraumatised, multitrauma, severely injured, and major trauma are most commonly used. Major trauma will be used throughout this thesis, and is classified by the ISS, with a threshold of 16. The ISS is derived from AIS codes, which is an anatomically-based, mortality-weighted code set used to classify injury severity.[44-49] AIS coding, and AIS-derived scores such as the ISS, are used to identify and classify injured patients within trauma systems, and can also be used as a component of risk adjustment and benchmarking using mortality prediction models. [31, 50-53] Although based on expert opinion, the ISS has persevered for over 40 years as the 'gold standard' of injury scoring.[51, 54] The most used threshold for major trauma was adopted following evaluation of mortality rates in the North American Major Trauma Outcome Study in the 1980s.[55, 56] The ISS, however, also has substantial limitations.[34, 51-53, 57-59]

In the light of the quality indicator, the difficulty lies in recognising an individual major trauma patient at the location of the accident by (helicopter) emergency medical services, whereas the indicator itself relates to injury coding based on information of extensive assessment with all diagnostic tools available in hospitals and retrospectively registered in medical records.[60-63]

Evaluation of clinical outcome measures

Another way to assess performance of trauma care, is to look at clinical outcome measures, such as throughput times, damage control interventions, complications, length of stay, and in-hospital mortality. A prediction model on mortality (probability of survival) is available in the DNTR, and can be compared with actual survival. How hospitals perform, in terms of in-hospital mortality, is evaluated with funnel plots. These plots display the difference between actual survival and the probability of survival, of the hospitals own population. These plots are an addition on the previous mentioned quality indicators major trauma, when it comes on

evaluation of trauma care. Trauma networks are originally designed and implemented around the severely injured patients. From a concentration and spread principle, these patients potentially have a survival benefit when being admitted to a level I trauma centre. An association of level of trauma care and clinical outcome measures for major trauma patients is not part of a structured evaluation from a network perspective.

Survival rates of major trauma patients are 82-84% in the Netherlands.[64] Enormous pre-hospital and clinical effort has been put into trauma patients since Dutch trauma regions have been designated; concentration of major trauma care in designated level I trauma centres, non-stop availability of resources, specific expertise of staff, more swiftly diagnosis, and more aggressive treatment throughout the trauma chain of care, all of which resulting in saving patients with a low probability of survival.[65-67] A further reduction of mortality in the future will probably follow the law of diminishing returns, with exsanguination, post-traumatic organ failure, and secondary damage after traumatic brain injuries being the most important life-saving elements.[68, 69] Therefore, a shift has been made in evaluation of trauma care from fatal outcome measures to patient-reported outcome measures.

Patient-reported outcome measures (PROMs)

Most trauma patients survive their injuries, therefore mortality is not the main concern for medical professionals and not the main determinant of care. Life after trauma can highly impact social structures, physical activities, and psychological well-being. Most likely, many of these elements interact with each other. Non-fatal clinical outcome measures like complications, the mobility of a joint, or hospital length of stay do not adequately represent the needs and quality of life persons experience after trauma. Monitoring physical, mental, and social outcome measures can be of importance for health care workers and patients during recovery trajectories, providing discernment in expectation- and self-management.

Literature shows that up to five years after trauma, 50% of major trauma patients report signs of depression, 30% did not return to work after two years, 20% reports a likely post-traumatic stress disorder after two years, major trauma patients scored lower than populations norms for physical and psychological health two years after major trauma, and around 45% of major trauma patients reported some form of social dysfunctioning.[3, 5, 70-72]

Previous mentioned studies on PROMs are based on large cohorts of a single or multiple level I trauma centres. Hospitals have different levels of care, thus different trauma functions in a region. Therefore, case mix of trauma populations of hospitals with different levels of trauma care also differ. Many initiatives are already taken to evaluate PROMs, some of which did look at PROMs on a large scale, but trauma network analysis on PROMs are scarce. [73, 74]

Outline and aims thesis

This thesis consists of three main parts. In **Part II** the classification and quality of data on major trauma patients included in the Dutch National Trauma Registry from a regional network perspective was studied, resulting in three chapters. In **chapter 2** the prevalence and characteristics of missed registrations in a Dutch regional trauma registry was evaluated. In **chapter 3** the injury severity of traumatic brain injuries as coded by AIS with or without the

use of a standardised radiologic template was analysed. In **chapter 4** the effect of different AIS revisions on clinical outcome measures was described.

Part III described the evaluation of clinical and fatal outcome measures of major trauma patients in networks. First, two literature studies were conducted. **Chapter 5** aimed to assess the association between level of trauma care and fatal and non-fatal outcome measures for general and major trauma populations. **Chapter 6** assessed associations of level of trauma care with patient outcomes for populations with specific severe injuries. Second, two chapters looked at external validation of Chapter 4 and 5 in the registry data from trauma region Southwest Netherlands. **Chapter 7** investigated the association between mortality and primary admission and secondary transfer of patients to level I and II trauma centres, and tried to identify predictors of primary and secondary admission to a designated level I trauma centre. **Chapter 8** studies subgroups of severely injured patients potentially benefiting on in-hospital mortality and non-fatal clinical outcome measures for a specific level of trauma care.

In **Part IV,** health status was assessed with patient-reported outcome measures of major trauma patients in a network. **Chapter 9** reported on return to work and health-related quality of life one year after major trauma from a region perspective. In **chapter 10,** a comparison of health-related quality of life, and separate health dimensions, across different levels of care in a network for major trauma patients up to two years after the traumatic event was made. Additionally, **chapter 11** compared psychological health status two years after major trauma across different levels of care in a network.

In **chapter 12**, a general discussion and future perspectives were outlined. In **chapter 13**, a summary will be found.

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1

PART II

REGISTRY VALIDATION AND INJURY CLASSIFICATION

CHAPTER 2

2

Missing patients in a Dutch regional trauma registry: prevalence and epidemiology

Highlights

- *Registrations not appearing on automated lists in electronic health records were marked as missing in retrospect.*
- *Missing registrations are common, and the amount differed greatly across hospitals.*
- *Missed registrations can be time consuming because automated lists need a human touch to be complete.*

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Abstract

Introduction Health care patient records have been digitalised the past twenty years, and registries have been automated. Missing registrations are common, and can result in selection bias.

Objective To assess the prevalence and characteristics of missed registrations in a Dutch regional trauma registry.

Methods An automatically generated trauma registry export was done for ten out of eleven hospitals in trauma region Southwest Netherlands, between June 1 and August 31, 2020. Second, lists were checked for being falsely flagged as 'non-trauma'. Finally, a list was generated with trauma tick box flagged as 'trauma' but were not automatically in the export due to administrative errors. Automated and missed registration datasets were compared on patient characteristics and logistic regression models were run with random intercepts and missed registration as outcome variable on the complete dataset.

Results A total of 2,230 automated registrations and 175 (7.3 %) missed registrations were included for the Dutch National Trauma Registry, ranging from 1 to 14 % between participating hospitals. Patients of the missed registration dataset had characteristics of a higher level of care, compared with patients of automated registrations. Level of trauma care (level II OR 0.464 95 % CI 0.328–0.666, $p < 0.001$; level III OR 0.179 95 % CI 0.092–0.325, $p < 0.001$), major trauma (OR 2.928 95 % CI 1.792–4.65, $p < 0.001$), ICU admission (OR 2.337 95 % CI 1.792–4.650, $p < 0.001$), and surgery (OR 1.871 95 % CI 1.371–2.570, $p < 0.001$) were potential predictors for missed registrations in multivariable logistic regression analysis.

Conclusion Missed registrations occur frequently and the rate of missed registrations differs greatly between hospitals. Automated and missed registration datasets display differences related to patients requiring more intensive care, which held for the major trauma subset. Checking for missed registrations is time consuming, automated registration lists need a human touch for validation and to be complete.

Background

Trauma registries are useful for describing the burden of trauma with epidemiological research, quality indicators, and benchmarking [1, 2]. Many countries utilise a national trauma register with a core of hospital data, such as the Trauma Audit and Research Network (TARN) in England and the Japan Trauma Data Bank (JTDB) in Japan, among many others. Administrative hospital data have large amount of omissions or are not specific enough for trauma care evaluation [3]. In general, when registries and hospital administrations are complete, they are mutually beneficial for managing finances as well.

Data of trauma registries are optimally as complete as possible. However, missing registrations and missing values are common [4], reliability of data validation [5, 6] and injury coding [7-9] can be questionable, and are a potential source of information bias [10, 11]. Imputation methods that replaces missing information with substituted values, could be a reliable method to fill the gaps if quality of data is good [12].

Epidemiological studies can also suffer from an ecological fallacy when looking at the total burden of acute trauma care, if certain subgroups are excluded [13, 14]. An inclusive population based trauma registry in a trauma network, including all types of injuries in all hospitals, creates an ideal situation for data analysis. However, missing registrations do occur, and could introduce a selection or exclusion bias [15, 16].

In the Netherland all hospitals are required to participate in the Dutch National Trauma registry (DNTR) by law.[13] The DNTR captures data of patients in the acute trauma care chain from the prehospital setting to clinical discharge. Hospitals participating in the DNTR have been implementing electronic health records (EHR) the past 25 years. Such software heavily relies on information recorded by users of the specific EHR. Each piece of information is ideally uniform and follows agreement over content. If the workflow is flawless, automatically generated inclusion lists from EHR should be complete. At several points in the trauma registry workflow, registrations can be missed. First, a patient needs to be marked as trauma or non-trauma at presentation or admission (patients that are incorrectly excluded should be minimised). Second, administrative exchanges can interfere with the completeness of the administration of a trauma patient.

The aim of this study was to assess the prevalence and characteristics of missed registrations in a Dutch regional trauma registry.

Methods

Following review of the protocol, the local Medical Research Ethics Committee concluded this study was not subject of the Medical Research Involving Human Subjects Act (MEC-2023-0279). Data are reported in line with strengthening the reporting of observational studies in epidemiology (STROBE) [17, 18].

General setting

Trauma region Southwest Netherlands is a large and inclusive trauma region, with one level I trauma centre, nine level II/III facilities, and a Burn Centre. The catchment area consists of

rural, remote, industrial, urban, and touristic areas with a dense infrastructure inhabited by 2.5 million people, and has the availability of Helicopter Emergency Medical Services (HEMS). Trauma region Southwest participates in the Dutch National Trauma Registry (DNTR), all hospitals in this trauma region participate[13]. All included trauma patients admitted to an emergency department within 48 hours after trauma followed by either hospital admission, secondary transfer or death were included, excluding death on arrival. Trauma registrations of patients transferred between emergency departments were excluded considering the primary admission, due to missing clinical outcome measures. Injuries were coded with Abbreviated Injury Scale revision 2005 update 2008 (AIS08) [19]. All hospitals in trauma region Southwest Netherlands use the same software (HiX 6.1-6.3, Chipsoft, Amsterdam) for their EHR.

Data collection

The study period ran from June 1 to August 31, 2020, for ten out of eleven hospitals in trauma region Southwest. For one hospital it was not possible to run the same list, and was excluded based on different working procedure. Trauma registry record lists were generated by all patient records with a trauma tick box set to 'yes' (automated registrations). This tick box is checked by administrative employees at the emergency department based on pre-announcement by (helicopter) emergency medical services or while the patient is being admitted. This pre-announcement is accompanied with a few words on the main presenting complaints as a reason for emergency department admission, and shown in a list that can be generated per time period. Missed registrations were administered as follows: First, potential missed registrations were searched based on presenting complaints in lists of emergency department admissions with the trauma tick box set to 'no', and were consecutively set to 'yes' if inclusion criteria were met. Second, a generator of all patient records with the trauma tick box set to 'yes', that were eligible for DNTR inclusion was run, and administrative errors were repaired. Third, the final trauma registry record list was generated (complete dataset). The automated registrations added with the missing registrations was considered to be the complete dataset.

The following variables of the participating hospitals were extracted from the DNTR: gender, age, cause, place of origin, type of injuries, type of transport, transfer between emergency departments (ED), hospital length of stay (HLOS), intensive care stay (ICU LOS), mechanical ventilation duration, discharge destination, probability of survival, in-hospital mortality, injury severity score (ISS), injury severity per body region (MAIS), and level of trauma care. Major trauma was defined as ISS > 15. Additionally, a dichotomous 'missed registration variable' was created based on found missed registrations.

Data analysis

Data were analysed using R Software Environment (version 4.1.1, release date 2022-09-06, the R Foundation for Statistical Computing, Vienna Austria). The automated registrations dataset was compared with the missed registrations. The automated registrations dataset and missed registrations dataset combined was considered the complete dataset.

Normality of continuous variables was tested using the Shapiro-Wilk test. All continuous variables were non-normally distributed. Descriptive data are presented as median with 25th

and 75th percentiles (P_{25}-P_{75}) for continuous variables and number (frequency, %) for categorical variables.

A Mann-Whitney-test was used for comparing two groups. A Kruskal-Wallis-test was used for multiple groups. For categorical variables a χ^2test or Fisher's exact test was used, as applicable. All statistical tests were two-sided. A p-value of <0.05 was considered significant.

Univariate and multivariable logistic mixed models with random intercepts for subject and hospital were performed on CD with level of trauma care, gender, age, type of injuries, transfer between ED's, intensive care stay, in-hospital mortality, and ISS > 15 as covariates, and missed registrations as outcome variable. The following reference categories were taken for categorical covariates: Sex (male), systemic comorbidities (no), surgery (no), ICU admittance (no), discharge home (no), ISS (1-8), trauma care level (I), transfer between ED's (yes). Estimates per covariate were reported with Odds ratio's (OR), 95% confidence interval (CI), and p-value.

Sensitivity and specificity of the current registration workflow were determined and reported with 95% CI, based on a 2x2 table.

Besides the level I trauma centre, all hospitals were anonymised in descriptive analysis.

Results

Based on trauma registrations of three months, a total of 2,358 patients were included in the automated registrations dataset, 182 were identified as missed registrations, creating a complete dataset of 2,540 patient records. After excluding 135 patients with a transfer from an emergency department of one hospital to another hospital, the dataset to be studied comprised 2,405 records (n=2,230 automated registrations and n=175 missed registrations, Figure 1). Of the ten participating hospitals, the missed registrations rate varied from a minimum of 1.1% (n=2) to a maximum of 14.0% (n=51) (Table 1). The level I trauma centre had the most missed registrations.

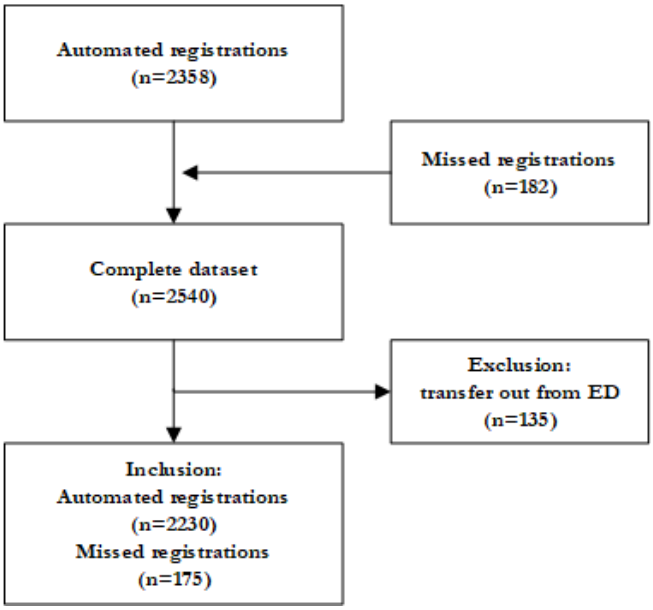

Figure 1. Flow chart selection for DNTR trauma region Southwest.

Table 1. Complete dataset, automated registrations, and missed registrations in the DNTR for trauma region Southwest from June 1 – August 31, 2020 per hospital.

Hospital (n=10)	Complete dataset (n=2,405)	Automated registrations (n=2,230; 92.7%)	Missed registrations (n=175; 7.3%)
1	365	314 (86.0%)	51 (14.0%)
2	339	310 (91.4%)	29 (8.6%)
3	374	344 (92.0%)	30 (8.0%)
4	301	279 (92.7%)	22 (7.3%)
5	334	314 (94.0%)	20 (6.0%)
6	20	19 (95.0%)	1 (5.0%)
7	125	119 (95.2%)	6 (4.8%)
8	233	223 (95.7%)	10 (4.3%)
9	140	136 (97.1%)	4 (2.9%)
10	174	172 (98.9%)	2 (1.1%)

When comparing the automated registrations with the missed registrations, patients with a missed registration had more penetrating injuries (n=18, 10.3%, $p < 0.001$), more surgeries (n=105, 60.0%, $p < 0.001$), a longer hospital length of stay (4 (P_{25}-P_{75} 2-8), $p = 0.035$), were more ICU admitted (n = 24, 13.7%, $p < 0.001$), were more frequently mechanically ventilated (n=19, 10.9%, $p < 0.001$), and had more often neck injuries (n=5, 2.9%, $p = 0.030$; Tables 2 and 3).

Table 2. Demographics and clinical outcome measures of the complete dataset, automated registrations, and missed registrations.

		Complete dataset (n=2,405)	Automated registrations (n=2,230)	Missed registrations (n=175)	p-value
Age (year)		59.8 (18.7-80.4)	60.0 (18.6-80.7)	53.0 (21.0-77.2)	0.366
Sex (female)		1136 (47.2%)	1047 (47.0%)	89 (50.9%)	0.319
Comorbidity	**Healthy**	938 (39.1%)	862 (38.8%)	76 (43.4%)	0.6367
	Mild	966 (40.3%)	900 (40.5%)	66 (37.7%)	
	Severe	460 (19.2%)	430 (19.3%)	30 (17.1%)	
	Unstable	35 (1.5%)	32 (1.4%)	3 (1.7%)	
Penetrating injury		116 (4.8%)	98 (4.4%)	18 (10.3%)	<0.001
Surgery		1097 (45.6%)	992 (44.5%)	105 (60.0%)	0.0001
HLOS (days)		3 (2-6)	3 (2-6)	4 (2-8)	0.035
ICU admission		166 (6.9%)	142 (6.4%)	24 (13.7%)	<0.0001
Mechanical Ventilation		77 (3.2%)	58 (2.6%)	19 (10.9%)	<0.001
Level of trauma care	**I**	365 (15.2%)	314 (14.1%)	51 (29.1%)	<0.001
	II	1581 (65.7%)	1470 (65.9%)	111 (63.4%)	
	III	459 (19.1%)	446 (20.0%)	13 (7.4%)	
Discharged home		1578 (65.6%)	1472 (66.0%)	106 (60.6%)	0.1425
Mortality		73 (3.0%)	67 (3.0%)	6 (3.4%)	0.753
Transfer out		182 (7.6%)	166 (7.5%)	16 (9.2%)	0.412
Trauma causes	**Violence**	94 (3.9%)	84 (3.8%)	10 (5.7%)	0.182
	Traffic	523 (21.8%)	487 (21.9%)	36 (20.6%)	
	Work	90 (3.7%)	82 (3.7%)	8 (4.6%)	
	Home/leisure	1513 (62.9%)	1406 (63.1%)	107 (61.1%)	
	Sport	157 (6.5%)	148 (6.6%)	9 (5.1%)	
	Self-harm	25 (1.0%)	20 (0.9%)	5 (2.9%)	

Data are shown as median (P_{25}-P_{75}) or as n (%). HLOS, Hospital Length of Stay; ICU, Intensive Care Unit.

In the major trauma subset, differences were also related to more intense care. Patients with missed registrations were younger (38 (P_{25}-P_{75} 26-60), p = 0.044), more severely injured (26 (P_{25}-P_{75} 25-35), p = 0.006), had more often penetrating injuries (n=4, 15.4%, p =0.030), a longer HLOS (20 (P_{25}-P_{75} 4.3-46.8), p = 0.015), were more frequently ICU admitted (n=20, 76.9%, p = 0.019), and were more frequently mechanically ventilated (n=17, 65.4%, p = 0.007; Table 4).

Table 3. Injuries coding for the complete dataset, automated registrations, and missed registrations.

		Complete dataset (n=2,405)	Automated registrations (n=2,230)	Missed registrations (n=175)	p-value
ISS		5 (4-9)	5 (4-9)	9 (4-9)	0.050
ISS category	**1-8**	1345 (55.9%)	1262 (57.7%)	83 (47.4%)	<0.001
	9-14	857 (35.6%)	791 (36.2%)	66 (37.7%)	
	> 15	161 (6.7%)	135 (6.1%)	26 (14.9%)	
MAIS ≥ 3	**Head**	772 (32.1%)	710 (31.8%)	62 (35.4%)	0.327
	Neck	28 (1.2%)	23 (1.0%)	5 (2.9%)	0.030
	Face	573 (23.8%)	539 (24.2%)	34 (19.4%)	0.156
	Chest	305 (12.7%)	280 (12.6%)	25 (14.3%)	0.508
	Abdomen	99 (4.1%)	88 (4.0%)	11 (6.3%)	0.134
	Spine	150 (6.2%)	143 (6.4%)	7 (4.0%)	0.204
	Arm	750 (31.2%)	705 (31.6%)	45 (25.7%)	0.105
	Leg	1141 (47.4%)	1056 (47.4%)	85 (48.6%)	0.756
	External	143 (6.0%)	129 (5.8%)	14 (8.0%)	0.233

Data are shown as median (P_{25}-P_{75}) or as n (%). ISS, Injury Severity Score; MAIS, Maximum Abbreviated Injury Scale.

Covariates potentially predicting missed registrations in univariate analysis were surgery (OR 1.871 95% CI 1.371-2.570, p < 0.001), admitted to ICU (OR 2.337 95% CI 1.440-3.650, p < 0.001), major trauma (OR 2.928 95% CI 1.792-4.650, p < 0.001), and level of trauma care (level II OR 0.464 95% CI 0.328-0.666, p < 0.001; level III OR 0.179 95% CI 1.792-4.650, p < 0.001; Table 5). In multivariable analysis surgery (OR 1.821 95% CI 1.294-2.573, p , 0.001) and level of trauma care (level II OR 0.509 95% CI 0.336-0.781, p = 0.001; level III OR 0.190 95% CI 0.093-0.365, p < 0.001) remained significant, as a potential predictor for missed registrations in the trauma registry.

Discussion

The missed registration rate in a time period of three months was 7.3% (n=175). There was a large range in the rate of missed registrations per hospital (1.1%–14.0%; n=2-51). The level I trauma centre had the highest percentage missed registrations (n= 51, 14,0%). In the general trauma population, elements indicative for a patient record missing in the trauma registry were the need for surgery during admission, ICU admittance, major trauma, and level of trauma care. These covariates were most likely related to the high percentages of missed registrations in the level I trauma centre. In addition, clinical outcome measures that were related to the major trauma population (admitted to level I, more penetrating injuries, ICU admittance, longer HLOS, and higher ISS) differed significantly between missed and automated registrations.

Table 4. Demographics and clinical outcome measures of the complete dataset, automated registrations, and missed registrations of major trauma patients.

		Complete dataset (n=161)	Automated registrations (n=135; 83.%)	Missed registrations (n=26; 16.1%)	p-value
Age		53.6 (28.0-72.9)	56.2 (29.0-74.5)	38.0 (26.4-60.1)	0.044
Sex (female)		51 (31.7%)	42 (31.1%)	9 (34.6%)	0.903
Comorbidity	Healthy	61 (38.1%)	48 (35.8%)	13 (50.0%)	0.482
	Mild	76 (47.5%)	66 (49.3%)	10 (38.5%)	
	Severe	19 (11.9%)	16 (11.9%)	3 (11.5%)	
	Unstable	4 (2.5%)	4 (3.0%)	-	
ISS		25 (17-29)	22 (17-29)	26 (25-35)	0.006
Penetrating		8 (5.0%)	4 (3.0%)	4 (15.4%)	0.030
Surgery		81 (50.3%)	64 (47.4%)	17 (65.4%)	0.143
HLOS		6 (3.0-20.0)	6.0 (3.0-15.5)	20.0 (4.3-46.8)	0.015
ICU admittance		87 (54.0%)	67 (49.6%)	20 (76.9%)	0.019
MV		64 (39.8%)	47 (34.8%)	17 (65.4%)	0.007
Level of care	I	114 (70.8%)	91 (67.4%)	23 (88.5%)	0.089
	II	42 (26.1%)	39 (28.9%)	3 (11.5%)	
	II	5 (3.1%)	5 (3.7%)	-	
Discharge (home)		60 (37.3%)	52 (38.5%)	8 (30.8%)	0.598
Mortality		38 (23.6%)	32 (23.7%)	6 (23.1%)	1.000
Transfer in		26 (16.2%)	21 (15.6%)	5 (19.2%)	0.861

Data are shown as median (P_{25}-P_{75}) or as n (%). HLOS, Hospital Length of Stay; ICU, Intensive Care Unit; MVD, Mechanical Ventilation.

Adherence to inclusion criteria of the DNTR Southwest overall were smaller than reported in previous studies [3, 15, 16]. In that way, the trauma registry used for this study has gained adequate attention and has become more complete. Analyses on automated registrations datasets are likely to be valid, however volume outcome measures and quality indicators might be biased for certain subgroups, such as major trauma. Missing patients in a registry might also be problematic for administration of finances, in-house trauma management, and integral health care packages. It would be of great value if a mutual and automated linkage could be implemented between the emergency department trauma tick box and International Classification of Diseases (ICD) trauma codes. With a linkage between admission and discharge with financial closure, a feedback loop would support completeness of the trauma registry. Some cautiousness is appropriate, since many patients receive minor trauma care secondary to other illnesses for which they are admitted.

Table 5. Univariate and multivariable logistic regression for outcome 'missed registrations'.

		Univariate		Multivariable	
		OR (95% CI)	***p-value***	**OR (95% CI)**	***p-value***
Intercept		-	-	0.115 (0.057-0.227)	*<0.001*
Sex (female)		1.169 (0.859-1.591)	*0.319*	1.377 (0.986-1.925)	*0.060*
Age (year)		0.997 (0.993-1.002)	*0.382*	0.998 (0.990-1.007)	*0.801*
Comorbidity	Mild	0.831 (0.589-1.171)	*0.292*	0.788 (0.494-1.251)	*0.315*
	Severe	0.791 (0.503-1.213)	*0.295*	0.753 (0.401-1.403)	*0.374*
	Unstable	1.063 (0.251-3.060)	*0.920*	1.004 (0.222-3.242)	*0.994*
Surgery		1.871 (1.371-2.570)	*<0.001*	1.821 (1.294-2.573)	*<0.001*
ICU admittance		2.337 (1.440-3.650)	*<0.001*	1.557 (0.824-2.847)	*0.160*
Discharge (home)		0.790 (0.577-1.086)	*0.143*	0.921 (0.598-1.416)	*0.711*
ISS	9-14	1.268 (0.905-1.771)	*0.164*	1.060 (0.697-1.607)	*0.782*
	>15	2.928 (1.792-4.650)	*<0.001*	1.229 (0.604-2.430)	*0.559*
Level of care	II	0.464 (0.328-0.666)	*<0.001*	0.509 (0.336-0.781)	*0.001*
	III	0.179 (0.092-0.325)	*<0.001*	0.190 (0.093-0.365)	*<0.001*
Transfer in		1.251 (0.704-2.081)	*0.413*	0.950 (0.526-1.610)	*0.856*

ICU, Intesive Care Unit; ISS, Injury Severity Score.

Timing is essential for the extraction of a data set. Administrative workflows take time, so extracting data while patient care is not completed yet is not optimal, and will likely result in unnecessary missed registrations and inefficiency of making sure all records are included. Waiting for a longer period of time, without checking on missed registrations, will not result in complete data either. Besides, checking on larger databases can be frustrating and time consuming. The process of checking on missed registrations should be done continuously in orderly amounts for an optimal efficient and extracting a complete data set without missing registrations.

Limitations

While searching for missed registrations this study solely focused on inclusion criteria. During work on the DNTR Southwest, there is also a lot of attention for excluding records with a false checked tick box, or when inclusion criteria are not met (*e.g.*, admission to the ED > 48 hours after trauma, or only ward monitoring without injuries). During the work process of the DNTR in the studied trauma region, many records are excluded, however were not monitored structurally. This would have created a more profound overview of the working process of the trauma registry and the effect of records either missing or incorrectly included in databases. We did get some insight in the diagnostic value for identifying patients that fulfill the inclusion criteria of the DNTR; For the level I trauma centre the sensitivity and specificity were 97.7% and 84.0%, respectively, and this was 99.2% and 86.7% for a large level II trauma facility. This shows that focus on falsely ticked trauma patients can also be time consuming, and in order to reduce this inefficiency, requires a feedback loop on the selection workflow.

The study period was between the first and second pandemic outbreak of SARS-CoV-2. In this period, social restrictions were abolished in the Netherlands, which led to an increase in minor injuries and major trauma. There was also an increase in minor self-harm injuries and violence related major injuries in the Netherlands [20]. In addition, outside the study period, during the first and second wave, hospital length of stay was shortened and patient with moderate traumatic brain injuries were less frequently admitted to an ICU [21]. In sum, Dutch trauma etiology was different from reference years in the study period, which might have biased our results.

Strengths

This study was able to validate completeness of the DNTR Southwest for all but one hospital in trauma region Southwest Netherlands. All hospitals used the same software for their electronic health records, thereby creating an uniform image of administrative working processes. Despite uniform software, the range of missing registrations was large between the participating hospitals, opting for custom attention per hospital. A first anchor of improvement could be to remain in close contact with employees who register the patients in the emergency department at first on inclusion criteria. A primary physician could also be involved in this process. This will not be enough for a zero percent missing registrations, since many administrative errors occur during admission. Therefore, a most thorough measurement would be to link automated trauma list to ICD-codes. ICD-codes being linked to financial administration might be a useful tool, and finances are an incentive for a complete administration, at least more than other administrative purposes. Automated list should also have more update possibilities and filter options, in order to include and exclude more easy. Previous measurements also indicate that close contact with software companies that provide electronic patient health records is, is beneficial for future perspectives. Finally, usage of text mining, registration bots, and other forms of artificial intelligence should be explored in order to keep registration loads as low as possible.

Conclusion

Missed registrations occur frequently and the rate of missed registrations differ greatly between hospitals. Automated and missed registration datasets display differences related to patients requiring more intensive care, which also held for the major trauma subset. Checking for missed registrations is time consuming, automated registration lists need a human touch for validation and to be complete.

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2

CHAPTER 3

3

Coding traumatic brain injury with the abbreviated injury scale following a standardised radiologic template will improve classification of trauma populations

Highlights

- *Radiologic reports are an important source for injury coding with the abbreviated injury scale (AIS), and are often not specific enough.*
- *An AIS based standardised radiologic template for reporting resulted in more detailed AIS head codes and more patients classified as major trauma.*
- *Injury coding with the AIS based on a standardised radiologic template will improve exchanging medical information in the acute health care setting and classification of trauma populations.*

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Abstract

Introduction Injury coding with the Abbreviated Injury Scale (AIS) is an important element for benchmarking, trauma registries and research.

Objective To compare the severity of traumatic brain injury (TBI) coding derived from the AIS with or without the use of a standardised radiologic template.

Methods A retrospective two-centre cohort study including patients aged ≥ 18 years with isolated TBI admitted to an intensive care between 2011 and 2016 was conducted. TBI was re-coded conform the AIS by coders, and CT-brain imaging was reassessed by neuro-radiologist following a standardised radiologic template from which AIS-codes were derived.

Results A total of 560 patients were included (median age 57, 37% female). The percentage of MAIS ≥ 4 and major trauma was higher when AIS coding for TBI was derived from a standardised radiologic template vs. coding without (n=456 (81.4%) and n=374 (66.8%), $p < 0.001$; n=441 (78.8%) and n=352 (62.9%), $p < 0.001$, respectively). There was an inter-centre difference in the proportion of MAIS ≥ 4 re-coded without a standardised radiologic template (n=212 (68.2%) and n=140 (56.2%), $p = 0.004$), and no difference when re-coded with the template (n=251 (807%) and n=190 (76.3%), $p = 0.206$).

Conclusion Coding TBI with AIS based on a standardised radiologic template results in fewer missed AIS head codes, more detailed AIS head codes, and more patients classified as 'major trauma'.

Clinical relevance Injury coding based on a standardised radiologic template will improve exchanging medical information in the acute health care setting and classification of trauma populations.

Keywords 'Injury Scale, Abbreviated', 'Coding, Clinical', 'Injury', 'Radiology', 'Registries', 'Improvement, Quality'

Introduction

Injury coding is an important element for quality benchmarking of trauma care and identification and selection patient groups within trauma registries [1-5]. Injury coding is mostly done retrospectively by coders based on extensive information in electronic health records (EHR), that built up throughout the acute health care chain. Much information – such as blood loss, open fractures, or coma - is estimated semi-quantitatively or qualitatively described in electronic health records (EHR). The written clinical and radiological information are the main sources for injury coders. However, a correct interpretation may require expertise. To facilitate an efficient coding process and optimise reliability of the codes registered, missing relevant information in EHRs about injuries should be avoided.

The Abbreviated Injury Scale (AIS) details and classifies traumatic injuries according to a very specific code structure [6-8]. Each AIS injury code is assigned a suffix, reflecting the severity of a specific injury, from minor severity to untreatable. These discrete severity levels we developed in the context of 30-days mortality – not permanent disability. Because medical care and treatment opportunities improve over time, mortality decreases in general. Therefore these severity levels are periodically recalculated for specific AIS codes [9-13]. The associated Injury Severity Score (ISS) is derived from the AIS coded injuries in the various body areas within a single individual. An ISS > 15 is considered to be a threshold for 'major trauma' worldwide [14-16]. Although the AIS and subsequent ISS are used in individual patients to assess the a priori risk to die and on a population level to measure quality of trauma care, both tools are subject to methodological and practical limitations [17]. The main causes of death after trauma nowadays – at least in the western world - are major bleeding and traumatic brain injury.

Uniform injury coding is essential to achieve reliable source data, not only to compare individual patients but also to correct for case-mix when comparing quality of care between trauma centres. The educational background of coders is diverse, ranging from administrative medical personnel to experienced doctors. Interpretation of extensive medical information on injuries is mostly reserved for clinicians with medical experience [18-21]. Various studies have shown variability between injury coders and between trauma facilities in injury coding with the AIS from its developing years on [19, 22-24]. Especially injury coding of TBI has shown significant variability.[19, 25]

The abovementioned raises questions on correctness of benchmarking, quality indicators, and (sub)population analysis that are based on certain injuries or classified with an specific ISS threshold. Radiologic reports are an important source for injury coding. An important element that could attribute to quality improvement is to minimise the number of inconclusive radiology reports. Inconclusive radiologic reports are those in which the reporting is not specific enough for accurate AIS coding, leading to an over-reliance on unsubstantiated or conservative injury coding. Additional modalities in radiologic reporting could potentially positively impact injury coding, thus classification of trauma populations following their injuries, and improve registry data analysis.
A standardised radiologic reporting template for Computed Tomography (CT) scans on head compatible with the AIS was developed, with the intention of streamlining clinical injury coding. Lacking uniformity of injury reporting in electronic health records was hypothesised to

negatively impact classifying trauma populations by injury severity according to the AIS. This study aimed to measure to what extent a standardised radiologic template influences AIS coding and severity assessment of traumatic brain injuries.

Methods

The local Medical Research Ethics Committee concluded this study was not subject of the Medical Research Involving Human Subjects Act (MEC-2022-0779), and provided a waiver of consent. Data are reported in line with strengthening the reporting of observational studies in epidemiology (STROBE).[26]

Study setting

Both participating level I trauma centres are located in urbanised and industrialised areas. These centres have a regional role in the admission of major trauma patients from their respective trauma regions, and both have neurosurgical facilities around the clock. Serving multiple emergency medical services and having the availability of a physician staffed helicopter, their combined catchment area consist 3.5 million inhabitants.

Study design

This two-centre retrospective cohort study was conducted on a previous collected dataset, and inclusion and exclusion criteria were taken from the corresponding study.[27]Only ICU patients were selected to definitively exclude cases of minor TBI, to address potential issues of over-triage or overestimation of the AIS score, and to partially mitigate the impact of inter-observer variability. Trauma patients aged ≥18 years, who sustained moderate-to-severe TBI with a maximum AIS (MAIS) of the head ≥ 3, and MAIS ≤ 2 in other anatomical regions admitted to an intensive care unit via the emergency room (ER) from January 1, 2011 until December 31, 2016 were included. Patients were excluded when admitted with either an isolated cervical spinal injury, with the presence of a non-traumatic intracranial hematoma, or when secondary brain damage was caused due to asphyxia.

Data collection – Baseline

Patients were selected from the Dutch Nationwide Trauma Registry (DNTR) of the two participating level I trauma centres [28]. Demographics, clinical outcome measures and in-hospital mortality data were extracted from the DNTR of both centres in December 2017 (age, sex, hospital and ICU length of stay, trauma mechanism, AIS with derived MAIS and ISS, and in-hospital mortality).

Data collection – Image reporting

A standardised radiologic template for reporting traumatic brain injuries was developed. This template was based on most elements of the AIS revision 2005 (update 2008) head section (type of vault/base fracture and clinical elements were left out of the template), the Marshall classification of TBI, and the Rotterdam score [6, 29, 30]. The following elements were represented in the template:: skull base fracture, skull vault fracture, pneumocephalus, subarachnoid bleeding, epidural bleeding (mm./cc.), subdural bleeding (mm./cc.), cerebral

contusion (mm.), petechial bleeding, midline shift (mm.), herniation, compressed basal cisterns, third ventricle compression, and remarks (Supplemental Figure 1).

All acute phase CT-brain imaging was reassessed by two neuro-radiologist in each respective centre in July 2019. All four radiologist (JDK, JWD, MVH, LC) were fellow and had five to six years of experience in reporting CT scans. Reassessments were conducted using a standardised radiologic template.

Data collection –Injury coding

From the reassessment of the radiologists each TBI patient was AIS coded, the severity per injury (MAIS head) was derived, and ISS was calculated, termed "template coding".

Each participating centre provided a person who assigned injury codes to each TBI patient, i.e. a coder for re-coding. In April 2021, traumatic brain injuries were re-coded, alternating by the coder of the other centre using the AIS revision 2005 (update 2008).[6] Both coders (BS, JVD) had 10 years of experience with AIS injury coding. In the country where the study took place, all radiologic (TBI) reports are supervised by a senior (neuro-)radiologist. For each TBI patient MAIS head was derived from AIS codes, and the ISS was calculated. In addition, the number of 'not further specified' AIS codes were determined. Not further specified AIS codes occur when detailed information is lacking on the type of injury or the severity of an injury.

Figure 1a and Figure 1b combined illustrate how AIS codes were assigned to a TBI patient by radiologic reports without and with a standardised radiologic template. In Figure 1a, four images from the same CT-scan taken from a TBI patient are displayed. In Figure 1b, a radiologic reports without the template is shown (left), and a radiologic report with the template is shown (right), as well as AIS codes, derived MAIS head, and calculated ISS based on each radiologic report.

Data collection - outcome

Severity of TBI was defined per MAIS, and maximum AIS was dichotomised in MAIS = 3 and MAIS ≥ 4. 'Major trauma' was defined as ISS > 15. The number of 'Not further specified' (NFS) AIS head codes were derived per patient.

Statistical analysis

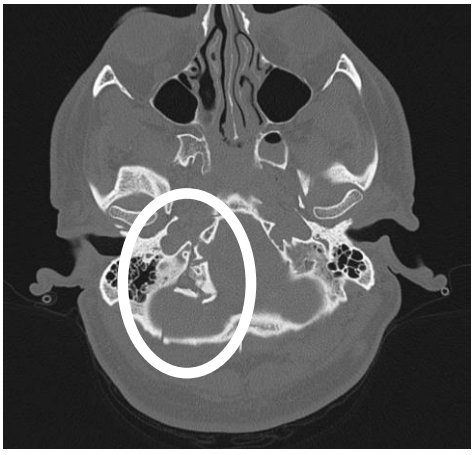
Statistical analyses were done with Statistical Package for Social Sciences version 25.0 (SPSS, Chicago, IL).

Frequencies and percentages are given for categorical variables and continuous variables are displayed as median (P_{25}-P_{75}), since continuous data were non-parametric based on the Shapiro-Wilk test. Differences in baseline characteristics between the two participating centres were tested using Mann–Whitney U-tests for comparing two groups, and for categorical variables χ^2-tests were done.

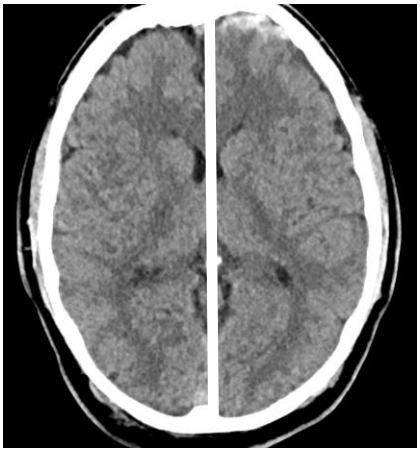
Figure 1a. Example of radiologic images made of a person with traumatic brain injuries.

Bilateral extra-axial hematoma coronal-plain (22.7 mm.).

Hemorrhagic contusion left temporal lobe (8 mm.).



Fracture right occipital bone, extending into skull base.



Absence of a midline shift.

For comparing dichotomised MAIS head between re-coding without and with a standardised radiologic template, the false positive rates and false negative rates were calculated and McNemar tests were done. The false positive rate was defined as an overestimation of the injury severity by the (re)coders, and the false negative rate was defined as an under-estimation of the injury severity by the (re)coders, both relative to the injury severity coded based on the standardised radiologic template. The true positive rate, or sensitivity, was defined as the proportion classified as MAIS < 4 by re-coding without a standardised radiologic template of the group classified as MAIS < 4 re-coded with a standardised radiologic template. The true negative rate, or specificity, was defined as the proportion classified as MAIS ≥ 4 by re-coding without a standardised radiologic template of the group classified as MAIS ≥ 4 re-coded with a standardised radiologic template. A comparison between ISS derived from regular AIS coding and ISS derived from AIS coding by template was done with the intraclass correlation

coefficient (ICC). The same was done for the comparison between ISS extracted from the DNTR and ISS derived from AIS coding by template, as a sensitivity analysis, and only done for period 2015-2016, since the ISS extracted from the DNTR was derived from AIS98 until 2014 and from AIS08 in 2015 and 2016.

Figure 1b. Example of AIS injury coding without and with a standardised radiologic template based on images of figure 1a.

Radiologic report – without template	**Radiologic report – with template**
CT skull blank. No previous comparative examinations. Traumatic subdural hematoma bifrontal, most prominent on the left side (series 2, image 22). Possible hemorrhagic contusion peripherical in the temporal lobe on the left side (series 2, image 13). Veil-like sphenoid sinus, as well as some ethmoid cells. Fracture occipital bone at the right side, extending into the skull base, through the carotic canal and the vertebral canal at the right side. Blood in the sphenoid sinus. Possible lateral wall fracture. **Summary:** Right-sided skull base fracture involving the occipital bone. Subdural hematoma bifrontal and possible hemorrhagic contusion left.	**Comparative previous examinations: [None]** **Description:** **-Protocol: [NECT Brain]** **-Extracranial injuries: [None]** **-Base fracture: [**Fracture of the right occipital bone extending into the skull base, involving the carotid canal and vertebral canal on the right side. Possible lateral wall fracture on the right**]** **-Vault fracture: [**Fracture of the right occipital bone extending into the skull base **]** **-Panfacial fracture: [**fluid or blood in the sphenoid sinus and ethmoid cells. Blood in the sphenoid sinus**]** **-Pneumocephalus: [No]** **-Subarachnoid hemorrhage: [No]** **-Extra-axial hematoma (including coronal-plain max. diameter in mm.): [**Subdural hematoma bifrontal, more prominent on the left side, 23 mm**]** **-Intracerebral hematoma, including contusion (max. length in mm.): [**Hemorrhagic contusion in the left temporal lobe, 8 mm**]** **-Petechial hemorrhage(s): [No]** **-Midline shift (mm.): [0]** **-Herniation: [No]** **-Ventricle(s): [Normal]** **-Compressed brain stem cisterns: [No]** **-Other findings: [No]** **Summary:** - Right-sided skull base fracture involving the occipital bone, extending to the carotid canal and vertebral canal. - Bifrontal subdural hematoma, more pronounced on the left. - Hemorrhagic contusion in the left temporal lobe. - Fluid or blood observed in the sphenoid sinus and ethmoid cells.

AIS, MAIS and ISS – without template		**AIS, MAIS and ISS – with template**	
Base fracture (basilar) NFS	150200.3	**Base fracture (basilar) NFS**	150200.3
Cerebrum – hematoma – subdural NFS	140650.3	**Cerebrum – hematoma – subdural – large - bilateral - > 1 cm.**	140655.5
		Cerebrum – contusion – tiny; <1 cm	140605.2
MAIS head	3	**MAIS head**	5
Injury Severity Score	9	**Injury Severity Score**	25

The ICC ranges from 0 (no reliability) to 1 (perfect reliability). The ICC absolute agreement for injury severity classification with and without a structured radiologic template was tested and presented with Pearson's r and a 95% confidence interval (CI). A two-way mixed model was chosen because the coders and radiologists were non-randomly assigned to a sample. The classification of Landis and Koch was used to classify agreement between ISS derived from re-

coded AIS without and with a standardised radiologic template (0.00–0.20, Slight, 0.20–0.40, Fair 0.40–0.60, Moderate 0.61–0.80, Substantial, 0.81–1.00 Almost perfect). In addition, Bland-Altman plots were created, plotting the differences between the ISS calculated following two methods (re-coding and radiologic template, or DNTR extracted ISS and radiologic template on the y-axis and the mean of the two methods on the x-axis [31]. Data are shown for the total cohort and for the individual hospitals. All statistical tests were two-sided. A p-value of <0.05 was considered significant.

Results

A total of 596 patients were selected, of whom 36 were excluded because of either an isolated cervical spinal injury, the presence of a non-traumatic intracranial hematoma, or when secondary brain damage was caused due to asphyxia., remaining with a final dataset of 560 included patient records; Hospital I included 311 (53%) patients and hospital II included 249 (47%) patients (Figure 2).

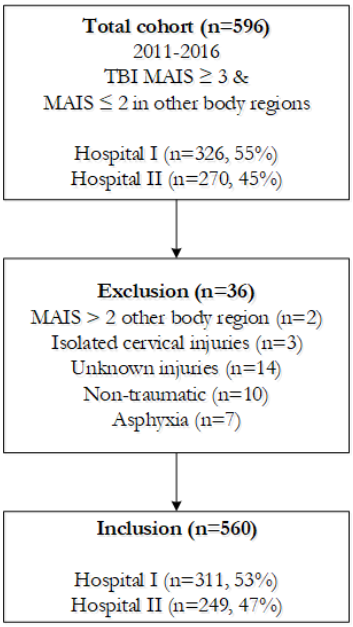


Figure 2. Study flow chart.

Study population

The study populations across the hospitals did not differ significantly in terms of age, sex, hospital stay, ICU admission, nor mortality (Table 1). There was a significant difference in ISS (25 P_{25}-P_{75} 20-27 vs. 21 P_{25}-P_{75} 17-26, $P < 0.001$) and mechanisms of injury ($P < 0.001$) between both populations. Hospital I had more high energy falls and non-accidental trauma (n=46, 14.8% and n=33, 10.6%, respectively), while hospital II had more falls from stairs and road traffic accidents (n=57 (18.3%) and n=128 (41.2%), respectively).

Table 1. Characteristics of the total cohort and epidemiological comparison between both participating hospitals.

	Total cohort (n=560)	Hospital I (n=311)	Hospital II (n=249)	p-value
Age	57 (38-71)	57 (37-71)	58 (38.5-70)	0.588
Females	207 (37%)	108 (34.7%)	99 (39.8%)	0.220
Mechanism of Injury				
Road Traffic Accident	246 (43.9%)	128 (41.2%)	118 (47.4%)	< 0.001
Fall From Stairs	112 (20.0%)	57 (18.3%)	55 (22.1%)	
High Energy Fall	62 (11.1%)	46 (14.8%)	16 (6.4%)	
Low Energy Fall	52 (9.3%)	27 (8.7%)	25 (10.0%)	
Non-Accidental Trauma	44 (7.9%)	33 (10.6%)	11 (4.4%)	
Collapse	23 (4.1%)	14 (4.5%)	9 (3.6%)	
Other	21 (3.8%)	6 (1.9%)	15 (6.0%)	
ISS	24 (17-24)	25 (20-27)	21 (17-26)	< 0.001
Hospital LOS	12 (5-24)	11 (5-22)	13 (6-26)	0.154
ICU LOS	4 (2-9)	4 (2-11)	4 (2-8)	0.305
In-hospital mortality	158 (28.2%)	86 (27.7%)	72 (28.9%)	0.741

Data are shown as median (P_{25}-P_{75}) or as n (%). ICU, Intensive Care Unit; ISS, Injury Severity Score; LOS, Length Of Stay.

Injury coding

The percentage of MAIS ≥ 4 and major trauma (ISS > 15) was higher when TBI was AIS codes were derived from the radiologic template compared with re-coded without the template (n=456 (81.4%) and n=374 (66.8%), $p < 0.001$; n=441 (78.8%) and n=352 (62.9%), $p < 0.001$, respectively). The derived ISS was not significantly different when TBI was AIS coded based on the radiologic template compared with re-coding without the template (21 P_{25}-P_{75} 14-26 and 21 P_{25}-P_{75} 17-26). There was a significant inter-centre difference regarding injury coding of MAIS head ≥ 4 when injuries were re-coded without a template compared with coding based on the radiologic template (n=212 (68.2%) and n=140 (56.2%); $p = 0.004$; Table 2). This difference was not significant when injuries were coded according to the radiologic template (n=251 (80.7%) and n=190 (76.3%); $p = 0.206$).

The ISS remained significantly different between centres when derived from re-coded AIS TBI codes(24 P_{25}-P_{75} 16-26 and 17 P_{25}-P_{75} 12-26; $p < 0.001$) compared with derived from coded injuries based on the radiologic template (24 P_{25}-P_{75} 17-26 and 20 P_{25}-P_{75} 16-26; $p = 0.011$) as shown in Table 2.

The coding variability did not affect the frequency of major trauma patients (ISS>15) based on AIS head re-coding by coders (n=218 (70.1%) vs. n=156 (62.7%); p=0.063) or based on the radiologic template (n=257 (82.6%) vs. 199 (79.9%); p=0.411) between hospitals (Table 2). However, the number of major trauma patients was higher with the radiologic template than without it for the total cohort (n=456 (81.4%) vs. n=374 (66.8%), p-value < 0.001) and for both hospitals separately (n=257 (82.6%) vs. n=218 (70.1%), p-value < 0.001; n=199 (79.9%) vs. n=156 (62.7%), p-value < 0.001).

Table 2. Differences in injury coding following the AIS by recoders and according to a standardised radiologic template, for the total cohort and both participating hospitals.

	Injury coding	Total cohort (n=560)	Hospital I (n=311)	Hospital II (n=249)	p-value
MAIS ≥ 4	Recoding	352 (62.9%)	212 (68.2%)	140 (56.2%)	0.004
	Template	441 (78.8%)	251(80.7%)	190 (76,3%)	0.206
ISS	Recoding	21 (14-26)	24 (16-26)	17 (12-26)	< 0.001
	Template	21 (17-26)	24 (17-26)	20 (16-26)	0.011
MT	Recoding	374 (66.8%)	218 (70.1%)	156 (62.7%)	0.063
	Template	456 (81.4%)	257 (82.6%)	199 (79.9%)	0.411
AIS (n)	Recoding	5 (3-6)	5 (4-7)	4 (3-5)	< 0.001
	Template	5 (3-7)	5 (4-7)	5 (3-7)	0.906
NFS no.	Recoding	0 (0-1)	0 (0-0)	1 (0-2)	< 0.001

Data shown as median (P_{25}-P_{75}) or as n (%). AIS, Abbreviated Injury Scale; ISS, Injury Severity Score; MAIS, Maximum Abbreviated Injury Scale; MT, Major Trauma; NFS, Not Further Specified.

The frequency of AIS codes per patient based on re-coding AIS head without the radiologic template differed significantly between the two centres (5 P_{25}-P_{75} 4-7 and 4 P_{25}-P_{75} 3-5; p=< 0.001). This was however not significantly different when injuries were re-coded according to the radiologic template (5 P_{25}-P_{75} 4-7 and 5 P_{25}-P_{75} 3-7; p = 0.906; Table 2). Finally, the number of 'not further specified' codes were significantly different between the two participating centres (0 P_{25}-P_{75} 0-0 and 1 P_{25}-P_{75} 0-2; p=< 0.001; Table 2).

Reliability

Contingency tables of MAIS < 4 and MAIS ≥ 4 displayed a true positive rate of 67% and a true negative rate of 71%. The false positive rate and false negative rate were 33% and 29%, respectively, resulting in a significant difference according to McNemar's test for the total cohort (p<0.001, Table 3). The true positive rate and true negative rate were 65% and 76% for hospital I and 69% and 64% for hospital II, respectively. The false positive rate and false negative rate were respectively 35% and 24% for hospital I, and 31% and 36% for hospital II, resulting in a significant difference for both hospitals according to McNemar's test (p<0.001).

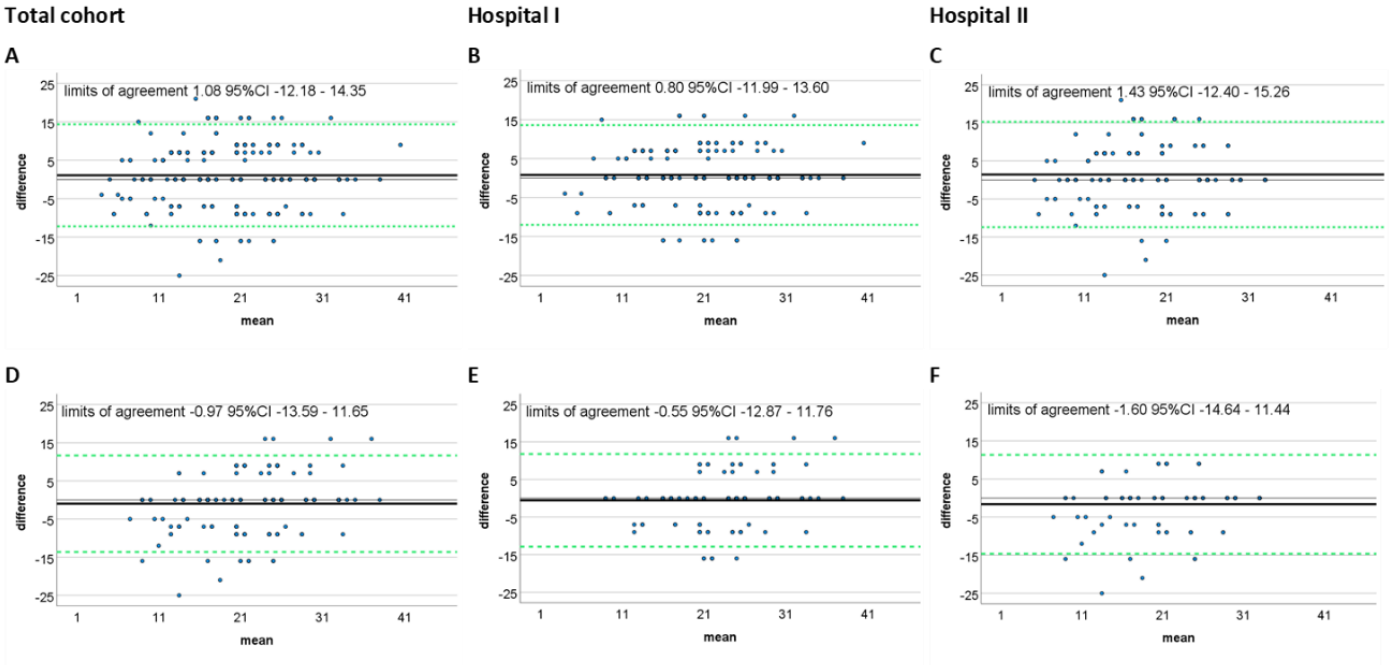
The Intraclass Correlation Coefficient (ICC) of the ISS derived from the re-coding process compared with ISS derived from the radiology template was moderate for the total cohort and for both hospitals (0.73 95% CI 0.68-0.77; 0.73 95% CI 0.66-0.78; 0.77 95% CI 0.64-0.78, respectively, Figure 3). The Bland-Altman plots indicate there is no systematic difference between the two coding methods (Figure 3).

Table 3. Contingency tables of MAIS 3 and MAIS ≥ 4 following AIS coding by recoding without and with a radiologic template, for the total cohort and both participating hospitals.

total cohort		**template**					
		MAIS = 3	**MAIS ≥ 4**	**total**	**FPR**	**FNR**	**McNemar**
recoding	**MAIS = 3**	80 (14.3%)	128 (22.9%)	208 (37.1%)	33%	29%	< 0.001
	MAIS ≥ 4	39 (7.0%)	313 (55.9%)	352 (62.9%)			
	total	119 (21.2%)	441 (78.8%)	560			
hospital I		**template**					
		MAIS = 3	**MAIS ≥ 4**	**total**	**FPR**	**FNR**	**McNemar**
recoding	**MAIS = 3**	39 (12.5%)	60 (19.3%)	99 (31.8%)	35%	24%	< 0.001
	MAIS ≥ 4	21 (6.8%)	191 (61.4%)	212 (68.2%)			
	total	60 (19.3%)	251 (80.7%)	311			
hospital II		**template**					
		MAIS = 3	**MAIS ≥ 4**	**total**	**FPR**	**FNR**	**McNemar**
recoding	**MAIS = 3**	41 (16.5%)	68 (27.3%)	109 (43.8%)	31%	36%	< 0.001
	MAIS ≥ 4	18 (7.2%)	122 (49.0%)	140 (56.2%)			
	total	59 (23.7%)	190 (76.3%)	249			

FNR, False Negative Rate; FPR, False Positive Rate; MAIS, Maximum Abbreviated Injury Scale.

Figure 3. Bland-Altman plots comparing ISS based on TBI recoding without and with a radiologic template, and recoding with a radiologic template compared with DNTR extracted TBI codes, for the total cohort and both hospitals separately. The first row of panels (A-C) are a comparison of injury coding based on a standardized radiologic template and injury coding without a standardised radiologic template. The second row of panels (D-F) are a comparison of injury coding based on a standardized radiologic template and injury coding extracted from the DNTR. The black line represents the mean difference between the two displayed ISS calculations following a two specific method of injury coding. The green lines represents the 95% CI limits of agreement from the mean differences.



Discussion

This two-centre retrospective cohort study assessed the impact of the standardised radiologic template on the injury severity assessment and classification of TBI according to the AIS of the head in two major level 1 trauma centres. The use of the radiologic template changed the classification of traumatic brain injury severity in 30% of the cases. Using the template reduced the number of missed TBI, more detailed injury codes, increased the number of cases classified as 'major trauma', and increased the inter-centre coding consistency. Coders differed across centres in TBI severity, major trauma classification, and number of TBI and non-specified TBI codes. Using a standardised radiologic template for injury coding evened these differences out.

Prior studies showed that injury coding with AIS is not flawless. Classifying major trauma seems to be difficult for benchmarking due to unreliable injury coding, since certified coders can miss up to 30% of the injuries of which TBI are mostly missed [19]. However, a comparative study has shown a high rate of inter-observer reliability in a group of coders who are employees of the same institution [21]. In addition, an international study on injury coding showed high reliability within a trauma centre, but significant variability between trauma centres from different countries [25]. Previously mentioned studies show that inter-observer agreement is high when the coding process is either done by clinicians or by qualified personnel as long as the information is recorded with sufficient detail [24]. Radiologists code more consistently across trauma populations, since they are trained to interpret diagnostic images. Radiologist are also used to report uniformly, therefore a radiologic template can help to make a translation to injury coding by coders. Even though Figure 1 displays ostensibly that a standardised radiologic report is longer, word counts of the written parts of the two reports are nearly the same. However, the summary is longer and more specific with a standardised radiologic template compared with the summary that was not based on a standardised template. The current study shows that a standardised radiologic template is a very efficient way of creating disambiguate injury reporting, which can also be implemented across different facilities. This may improve injury coding quality for both patients and populations, resulting in more reliable research and benchmarking data.

Hospital I coded the independent injuries of patients admitted to hospital II less severely, with more NFS codes and a lower ISS, than the original coders of hospital II. This is indicative for a more conservative injury coding by hospital I. This is also affirmed by the frequency of patients classified as major trauma, when comparing injury coding following the radiologic template than re-coding without. With the standardised radiologic template as leading method for TBI coding, the total cohort would have been classified with 22.9% more MAIS head ≥ 4 and 7.0% less MAIS head ≥ 4, resulting in 14.6% more patients classified as 'major trauma'. This would have been 19.3% and 6.8% for hospital I, and 27.3% and 7.2% for hospital II, resulting in 12.5% and 17.2% more patients classified as major trauma, respectively. The percentage of MAIS head downgraded from MAIS ≥ 4 to MAIS head 3 is lower and similar between participating hospitals, compared with the percentage MAIS head 3 that was upgraded to MAIS head ≥ 4, which is higher in the study cohort admitted to hospital II. With major trauma quality indicators in the Netherlands currently focusing on volume and

percentage directly admitted to a regional level I trauma centre, the results in this study could place the status quo of these indicators in new light.

Limitations & Strength

A previous study showed case mix differences between trauma populations of two hospitals [25]. AIS coding differences between the original coders might have also been present. The current study did not compensate for these differences in the analysis. Despite these differences, injury severity based on the radiologic standardised template was stable between the two hospitals. Case-mix differences across hospitals can be dependent on the local health care context, therefore extrapolating the current result (internationally) should be taken with caution.

Reassessments of injury reporting with the standardised radiologic template by the radiologists were done without time pressure, unlike the original radiologic reports without the standardised radiologic template in the acute health care setting. Also, the radiologist could focus on TBI reporting only, unlike the acute health care setting during which more variation of diseases and injury coding takes place. The radiologists were very aware of the task the had to deliver. This might have influenced the results towards a larger difference between the two type of TBI coding assessments. On the other hand, the two coders were very experienced, which does not explain the large difference between the two type of TBI coding assessments, and especially the inter-centre difference between the participating centres.

There are two factors that likely underestimate the positive effect of introducing a radiologic template for TBI coding. Firstly, only level I trauma centres participated in this study, which are also 24/7 neurosurgical facilities. Although less frequently, due to undertriage, major trauma patients are also admitted to non-level I trauma centres, and a large proportion of these patients suffer from TBI [32]. Secondly, some specific brain injuries influencing the injury severity that are partially AIS coded by clinical symptoms were not part of the standardised radiologic template (diffuse axonal injuries and coma). Moreover, the severity of base and vault fractures could not be specified in the radiologic template. With these missing injury coding elements, coding has been relatively conservative following the standardised radiologic template, and the severity of TBI would have been higher in certain cases when such information would have been reported [27].

Future perspectives

For an optimal effect of implementing a radiologic template some elements need to be in place; In the first place, perseverance is needed for the whole radiologic team consistently reporting CT-scans according to the template. Each medical discipline that use radiologic reports based on a standardised template should keep their motivation high on demanding consistent reporting. Second, the template and AIS should be implemented in a curriculum framework for medical students. Thirdly, the template can be used as a basis for artificial intelligence techniques deriving AIS code from radiologic images and accessory reports. Fourth, a standardised template for other (complex) body regions might be complementary to the TBI template. Especially traumatic spine injuries , and solid organ injuries (thoracic and abdominal) have severe consequences for trauma patients, resulting in a high a priori mortality

risk. Experience by implementing a template used for this study will much likely result in improved revisions. Templates for other body regions will also profit from these experiences. Finally, once a template is implemented, and coders will code injuries more uniformly, high quality injury coding will lead to registrations with optimal classification of trauma populations following their injuries. Benchmarking and financial administration can benefit from such development.

Other medical disciplines will mostly likely also benefit from clear communication between radiologic reports implementing reports based on specific disease classifications in specific acute health care domains. Patient outcome measures, decision making on interventions, and a minimisation of redundant financial costs could also be part of a beneficial effect that radiologic reports adapted to specific disease or injury classifications have.

Conclusion

Coding traumatic brain injuries with the Abbreviated Injury Scale based on a structured radiologic template results in fewer missed traumatic brain injury codes, a reduction of non-specified traumatic brain injuries codes, more patients classified as major trauma, and an increase of inter-centre uniformity in coding traumatic brain injuries. A template for radiologic reporting traumatic brain injuries may positively contribute to the quality of injury coding, inter-observer reliability, less registration load, benchmarking, and financial administration. This could ultimately lead to increased accuracy in patient selection and subset outcome analysis in trauma populations. High quality injury coding will improve classification of trauma populations following their injuries.

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Clinical data

Examination question:

Comparative previous examinations: [...]

Description:
-Protocol

-Extracranial injuries: [...]
-Base fracture: [...]
-Vault fracture: [...]
-Panfacial fracture: [...]
-Pneumocephalus: [...]
-Subarachnoid hemorrhage: [...]
-Extra-axial hematoma (including coronal-plain max. diameter in mm.): [...]
-Intracerebral hematoma, including contusion (max. length in mm.): [...]
-Petechial hemorrhage(s): [...]
-Midline shift (mm.): [...]
-Herniation: [...]
-Ventricle(s): [...]
-Compressed brain stem cisterns: [...]
-Other findings: [...]

Summary:

Conclusion discussed with [...] at [...] on [...]

Supplemental Figure 1. Standardised radiologic template.

3

CHAPTER 4

The definition of major trauma using different revisions of the abbreviated injury scale

Highlights

- *The effect of revising the Abbreviated Injury Scale for injury coding on clinical outcome measures was determined.*
- *For ICU-admission and in-hospital mortality the injury severity threshold was lower when coding with AIS 2008 or AIS 2015 compared with AIS 1998.*
- *These results on entry data confirm studies evaluating mapped datasets.*

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Abstract

Background A threshold Injury Severity Score (ISS) ≥ 16 is common in classifying major trauma (MT), although the Abbreviated Injury Scale (AIS) has been extensively revised over time. The aim of this study was to determine effects of different AIS revisions (1998, 2008 and 2015) on clinical outcome measures.

Methods A retrospective observational cohort study including all primary admitted trauma patients was performed (in 2013-2014 AIS98 was used, in 2015-2016 AIS08, AIS08 mapped to AIS15). Different ISS thresholds for MT and their corresponding observed mortality and ICU admission rates were compared between AIS98, AIS08, and AIS15 with Chi-square tests and logistic regression models.

Results 39,317 patients were included. Thresholds ISS08 ≥ 11 and ISS15 ≥ 12 were similar to a threshold ISS98 ≥ 16 for in-hospital mortality (12.9%, 12.9%, 13.1% respectively) and ICU admission (46.7%, 46.2%, 46.8% respectively). AIS98 and AIS08 differed significantly for in-hospital mortality in ISS 4-8 ($\chi^2 = 9.926$, $p = 0.007$), ISS 9-11 ($\chi^2 = 13.541$, $p = 0.001$), ISS 25-40 ($\chi^2 = 13.905$, $p = 0.001$) and ISS 41-75 ($\chi^2 = 7.217$, $p = 0.027$). Mortality risks did not differ significantly between AIS08 and AIS15.

Conclusion ISS08 ≥ 11 and ISS15 ≥ 12 perform similarly to a threshold ISS98 ≥ 16 for in-hospital mortality and ICU admission. This confirms studies evaluating mapped datasets, and is the first to present an evaluation of implementation of AIS15 on registry datasets. Defining MT using appropriate ISS thresholds is important for quality indicators, comparing datasets and adjusting for injury severity.

Background

The Abbreviated Injury Scale (AIS)[1-4] provides an anatomically-based, mortality-weighted code set used to classify injury severity. AIS coding, and AIS-derived scores such as the Injury Severity Score (ISS)[5, 6] are used to identify and classify injured patients within trauma systems, and can also be used as a component of risk adjustment and benchmarking using mortality prediction models.[7-11] Although based on expert opinion, the ISS has persevered for over 40 years as the 'gold standard'[8, 12] of injury scoring. The ISS is commonly used to define major trauma (MT) using an ISS ≥ 16. This threshold was adopted following evaluation of mortality rates in the North American Major Trauma Outcome Study in the 1980s[13, 14]. However, in recent years the focus on outcome measures in trauma care has shifted from fatal to nonfatal outcomes.[15-18] Also, the ISS has substantial limitations, including in the prediction of outcome after serious injury.[8, 10, 11, 19-21]

AIS code sets are periodically revised to better reflect contemporary performance of trauma systems. Not all trauma registries use the same AIS revision at any given time; worldwide, registries implement newer AIS revisions whenever considered necessary at a local level. However, differences in the classification of injury severity between AIS revisions can affect assessments of injury severity, both in individual patients and across populations. In turn, this can compromise assessments of quality of care, or of the level of performance of trauma systems.

In particular, changing from the widely used 1998 AIS update[3] (AIS98) to the 2008 update[2] (AIS08) profoundly affects descriptions of injury severity[22, 23] and outcome predictions.[4, 24] In AIS08, many injuries were re-assigned to higher or lower severity levels, although in practice more injuries decreased in severity.[25] As a result, the distribution of the ISS has down-shifted causing a 20 percent decrease in MT patients.[26] In addition, an increase in mortality rate, length of stay (LOS), need for intensive care (IC) and urgent surgery has been reported in (re-classified) MT populations due to this shift.[25, 27] This affects measurements of the performance of trauma care over time, or across registries using different AIS revisions. The effects of a subsequent AIS revision in 2015 (AIS2015)[4] on a trauma registry has not been evaluated in any published work.

Since AIS revisions can affect assessments of injury severity, it is of vital importance that the derived ISS is used to classify MT[27], particularly as other measures such as quality indicators rely heavily on such a classification.[28] The definition of MT becomes particularly relevant if a newer AIS revision is being implemented in a trauma registry, or if the time span of a study overlaps different AIS revisions. The present study aimed to assess the effects of different AIS revisions (and derived ISS) on clinical outcome measures and the volume of primary admitted MT patients to a designated regional level I trauma centre.

Methods

General setting

The Dutch National Trauma Registry (DNTR) is nationally coordinated through 11 trauma regions. Yearly around 80,000 incidents are registered, of which approximately five percent is considered as major trauma.[29] All patients admitted to the emergency department (ED) (within 48 hours after trauma), followed by either hospitalisation, transfer to other hospitals or death are included, excluding deaths on arrival. Trauma Region Southwest Netherlands (DTR SW) consists of urban, rural, industrial and tourist areas with a strong infrastructure, inhabited by 2.5 million people. Helicopter Emergency Medical Services (HEMS) are available. Each year around 10,000 inclusions are registered in the DTR SW, a region containing one level I trauma centre. The proportion of primary admitted MT patients to a regional designated level I trauma centre (TC) is currently regarded as a quality indicator in the Netherlands.

Population

Trauma patients were retrospectively selected from the DTR SW cohort between 2013 and 2016. AIS98 was used for injury coding until 2014, and from 2015 onward AIS08 was used. A wide variety of trauma settings and injuries are represented in the database, from traffic accidents or falls in private and leisure settings to burns, violence, drowning, asphyxia (hanging) and other forms of self-harm. The structure of the DTR SW trauma system did not change during the study period.

AIS Comparison

AIS98[3] was used for injury coding in 2013-2014; injuries from 2015-2016 were coded using AIS08[2]. For the latter period, AIS08 codes were mapped to AIS15 using the tables provided in the AIS15 revision.[4] ISS was calculated from AIS codes for all patients; these were termed ISS98, ISS08 and ISS15 depending on the AIS revision from which they were derived.

Comparison VSTR

For international comparison, and as a sensitivity analysis, the inclusion and exclusion criteria of the Victorian State Trauma Registry (VSTR) were fitted on the DTR SW database, as the DTR has more general inclusion criteria than the VSTR. The VSTR includes patients with an ISS ≥ 12, death in ED or after hospitalisation, patients in need of urgent surgery or ICU > 24 hours with mechanical ventilation, or a length of stay (LOS) greater than three days. Specific VSTR inclusion and exclusion criteria are available elsewhere.[30]

Data analysis

Patients who were transferred from one ED to another were identified, and records from the transferring hospital were excluded in order to avoid double-counting. Cumulative mortality rates above all possible ISS thresholds were calculated, and compared between AIS98, AIS08 and AIS15. The baseline mortality threshold for MT was set at the mortality rate of ISS98 ≥ 16. At the same threshold of ISS98 ≥ 16, the ICU admission rate was calculated. For the AIS08 and AIS15 revisions, new ISS thresholds were selected based on the mortality and ICU admission rates of ISS98 ≥16.[27, 31] For time periods 2013-2014 and 2015-2016, in which different AIS revisions (AIS98 and AIS08 respectively) were used for coding injuries, normality of distribution for continuous variables was tested using the Shapiro-Wilk test. All continuous variables were non-normally distributed. Descriptive statistics were reported as a median (P_{25}-P_{75}) for continuous variables and number (percentage) for categorical variables. A Mann-Whitney test was used when comparing two groups, and a Kruskal-Wallis test was used when comparing multiple groups. For nominal variables, a χ^2-test or Fisher's (two-sided) exact test was used as applicable. A p-value of 0.05 was considered significant.

Statistical differences in the distributions of ISS98 and ISS08, and ISS98 and ISS15 were calculated using a Mann-Whitney test, and the differences between ISS08 and ISS15 with a Wilcoxon Signed Rank test, as these measures were mapped and hence not independent. Statistical differences of in-hospital mortality within each ISS category between AIS revisions were tested with a χ^2-test. Logistic regression analysis was performed with in-hospital mortality as the outcome parameter, and the AIS revision and ISS considered as factors. Grouped ISS was checked for interaction with AIS revision. Odds ratios were calculated using logistic regression models (with 95% confidence intervals) for the association between MT (ISS ≥ 16) and in-hospital mortality, as well as for the new MT ISS thresholds and in-hospital mortality for AIS98 (2013-2014), AIS08 (2015-2016) and mapped AIS08 to AIS15 (2015-2016). Homogeneity of odds ratios, after stratifying for AIS revision, were tested with Breslow D statistics for AIS08 compared with AIS98 and AIS15 compared with AIS98. Statistical differences between OR's for AIS08 and AIS15 compared with AIS98 were calculated with a Cochran-Mantel-Haenszel test.

This study was exempted by a local Medical Research Ethics Committee after being assessed as not subject to the Medical Research Involving Human Subjects Act due to the use of retrospective data. Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines were followed. Statistical analyses were done with Statistical Package for Social Sciences version 24.0.0.0 (SPSS, Chicago, IL) and R software environment (version 3.2.2 or higher, the R Foundation for Statistical Computing, Vienna, Austria).

Results

Records of 39,317 patients with a total of 87,991 injuries between 2013 and 2016 were registered in the DTR SW in the period 2013-2016; after excluding transfers between ED's, 37,777 patients (84,185 injuries) were evaluated (Figure 1). The 19,383 patients initially coded using AIS08 sustained 43,335 injuries; all of these were mapped to AIS15.

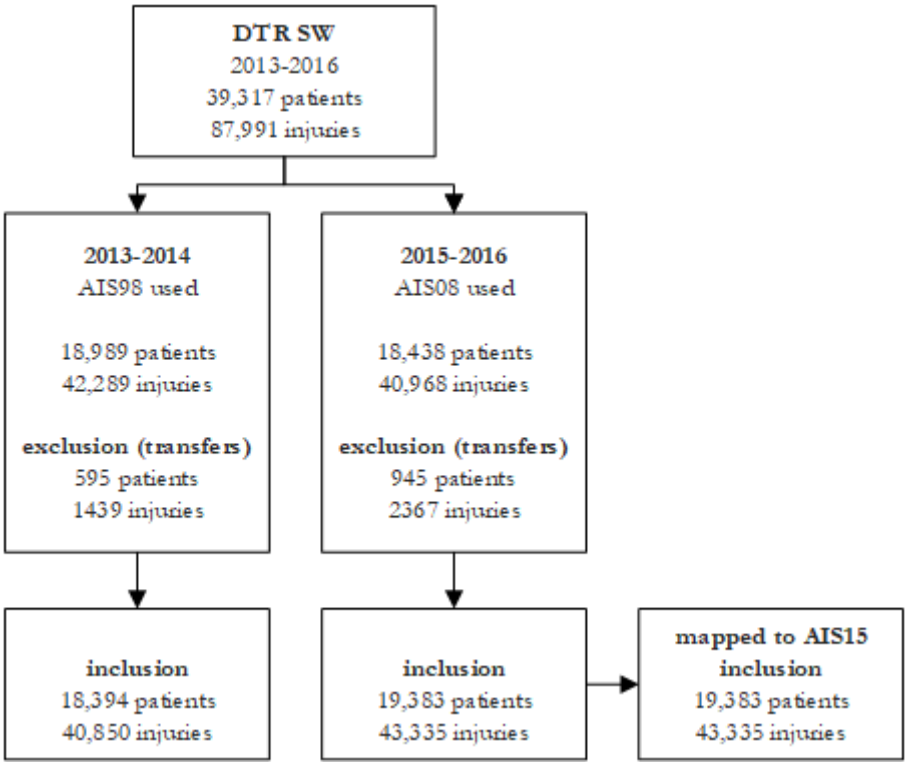

Figure 1. Inclusion flow chart.

Between the two time periods in which different AIS revisions were used, the trauma populations were comparable (Table 1). Gender, age, injury mechanism, hospital length of stay (LOS), days on intensive/high/medium care unit (LOS ICU/HCU/MCU) and number of mechanical ventilation days (LOS MV) did not differ significantly between the two time periods.

Medians (P_{25}-P_{75}) for ISS98, ISS08 and ISS15 were 9 (4-9), 5 (3-9) and 5 (4-9) respectively. There were significant differences between the distributions of ISS98, and both ISS08 (U = -31.011 , p < 0.0001) and ISS15 (U = -16.112 , p < 0.0001). A significant difference was also found between the distribution of the ISS15 compared to ISS08 (Z = -55.693, p < 0.0001). The modified DTR SW data fitted by VSTR criteria resulted in medians (P_{25}-P_{75}) of 9 (6-16), 9 (5-14) and 9 (6-14) for ISS98, ISS08 and ISS15 respectively.

Table 1. Epidemiological comparison between trauma populations of 2013-2014 and 2015-2016.

		2013-2014 AIS98 used (n=18,394)	2015-2016 AIS08 used (n=19,383)	p-value
Gender	**(male)**	9123 (49.6%)	9630 (49.7%)	0.869
Age	**(years)**	60.9 (33.6-88.8)	61.2 (33.1-89.2)	0.238
LOS	**(days)**	3 (1-6)	3 (1-6)	0.086
LOS ICU/HCU/MCU	**(days)**	2 (1-4)	2 (1-4)	0.054
LOS MV	**(days)**	3 (1-8)	3 (1-8)	0.708
Cause*	**Violence**	299 (3.2%)	631 (3.3%)	0.752
	Traffic	1896 (20.2%)	3831 (19.9%)	0.388
	Work	378 (4.0%)	783 (4.1%)	0.959
	Home/Leisure	6122 (65.2%)	12,700 (65.6)	0.612
	Sport	567 (6.0%)	1103 (5.7%)	0.0234
	self-harm	89 (0.9%)	233 (1.2%)	0.055
	Other	15 (0.2%)	16 (0.1%)	0.061

*Cause was registered from 2014 onwards (9351 of 18,394 patients in 2013-2014). Statistical comparison is between 2014 (n=21, cause unknown) and 2015-2016 (n=86, cause unknown).

LOS, Length Of Stay; ICU, Intensive Care Unit; HCU, High Care Unit; MCU, Medium Care Unit; MV, Mechanical Ventilation.

Cumulative mortality levels at ISS ≥ 16 coded with AIS98, AIS08 and AIS15 were 13.1%, 20.0% and 19.7% respectively (Figure 2). The use of an ISS08 ≥ 11 and ISS15 ≥ 12 provided an equivalent mortality risk. These differences between AIS revisions were also seen for the DTR SW population with the use of VSTR in- and exclusion criteria.

Dichotomised mortality levels and ICU admission rates are presented in Table 2. Mortality rates with MT thresholds using an ISS ≥ 16 for all AIS revisions differed substantially. When an ISS ≥ 16 was used for all three AIS revisions, there was significant heterogeneity between revisions in terms of mortality risk (Breslow-D, p = 0.025, Table S1). However, when odds ratios were compared with alternative MT thresholds across the three AIS revisions, Breslow-D statistics were non-significant, demonstrating homogeneity for comparisons between AIS98 and both AIS08 and AIS15. When adjusted MT thresholds were applied to the need for ICU, similar patient proportions were seen (Table 2).

Increasing ISS category resulted in an increased likelihood of death (Figure 3 and Table S2). Logistic regression with AIS revision and ISS category as factors, and in-hospital mortality as

an outcome resulted in a crude OR of 1.26 *(95% CI 1.096-1.441)* for AIS08. Significant mortality differences between AIS revisions were seen for ISS 4-8 ($\chi^2 = 9.926$, $p = 0.007$), ISS 9-11 ($\chi^2 = 13.541$, $p = 0.001$), ISS 25-40 ($\chi^2 = 13.905$, $p = 0.001$) and ISS 41-75 ($\chi^2 = 7.217$, $p = 0.027$). No significant differences in mortality risk were reported for any ISS category when comparing ISS calculated using AIS08 and AIS15.

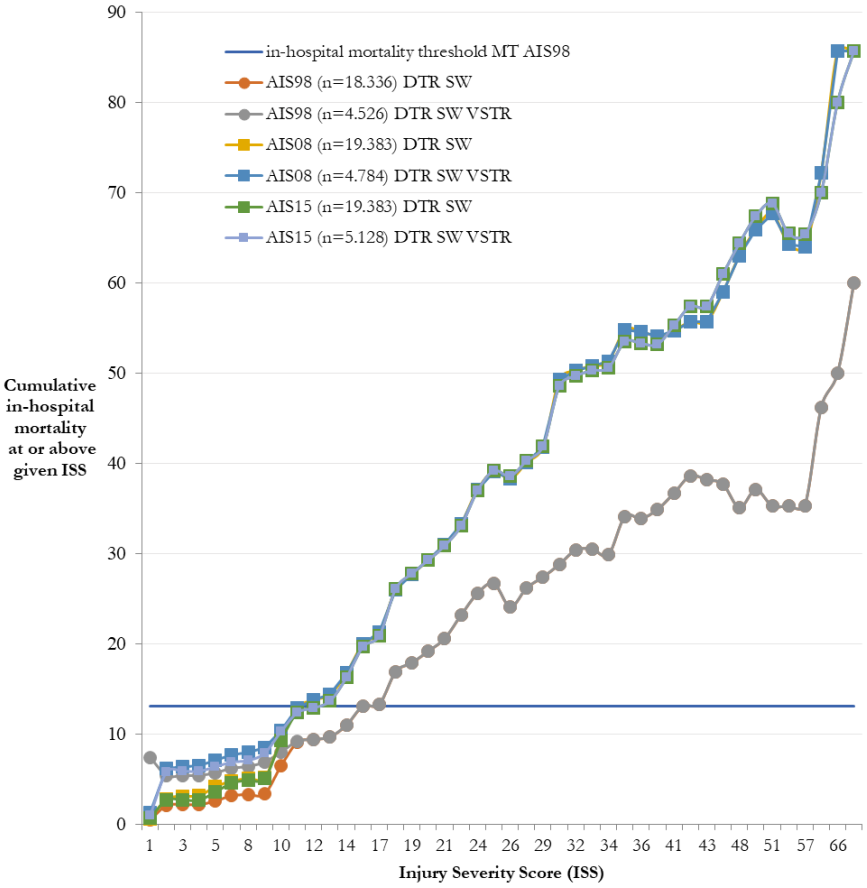

Figure 2. Cumulative in-hospital mortality for each ISS in the DTR SW and DTR SW with inclusion criteria of the VSTR, using AIS98, AIS08 and AIS15. For reference, the mortality level of MT coded with AIS98 during 2013-2014 (13.1%) is indicated by the horizontal solid line.

Using an ISS98 ≥ 16 threshold				Using an ISS08 ≥ 16 threshold				Using a ISS15 ≥ 16 threshold			
	Died	**Survived**	**Total**		**Died**	**Survived**	**Total**		**Died**	**Survived**	**Total**
ISS < 16	208	16,912	17,120	**ISS < 16**	266	18,024	18,290	**ISS < 16**	267	18,009	18,276
	1.20%	*98.80%*			*1.50%*	*98.50%*			*1.50%*	*98.50%*	
ISS ≥ 16	159	1,057	1,216	**ISS ≥ 16**	219	874	1,093	**ISS ≥ 16**	218	889	1,107
	13.10%	*86.90%*			*20.00%*	*80.00%*			*19.70%*	*80.30%*	
Total	367	17,969	18,336	**Total**	485	18,898	19,383	**Total**	485	18,898	19,383
				ISS08 < 11	258	17,363	17,621	**ISS15 < 12**	259	17,375	17,634
					1.50%	*98.50%*			*1.50%*	*98.50%*	
				ISS08 ≥ 11	227	1,535	1,762	**ISS15 ≥ 12**	226	1,523	1,749
					12.90%	*87.10%*			*12.90%*	*87.10%*	
				Total	485	18,898	19,383	**Total**	485	18,898	19,383
Using an ISS98 ≥ 16 threshold				**Using an ISS08 ≥ 16 threshold**				**Using a ISS15 ≥ 16 threshold**			
	ICU	**No ICU**	**Total**		**ICU**	**No ICU**	**Total**		**ICU**	**No ICU**	**Total**
ISS < 16	1,008	16,112	17,120	**ISS08 < 11**	1,067	16,554	17,621	**ISS15 < 12**	1,083	16,551	17,634
	5.90%	*94.10%*			*6.10%*	*93.90%*			*6.10%*	*93.90%*	
ISS ≥ 16	568	648	1,216	**ISS08 ≥ 11**	824	938	1,762	**ISS15 ≥ 12**	808	941	1,749
	46.70%	*53.30%*			*46.80%*	*53.20%*			*46.20%*	*53.80%*	
Total	1.576	16,760	18,336	**Total**	1,891	17,492	19,383	**Total**	1,891	17,492	19,383

Table 2. Contingency tables of in-hospital mortality and need for ICU for MT patients for AIS98, AIS08 and AIS15. MT is considered ISS ≥ 16 in the upper three contingency tables, the lower two rows of contingency tables utilize alternative ISS thresholds for MT (AIS08 ≥ 11, AIS15 ≥ 12). Percentages are row orientated. ICU, Intensive care unit; HCU, High Care Unit; MCU,

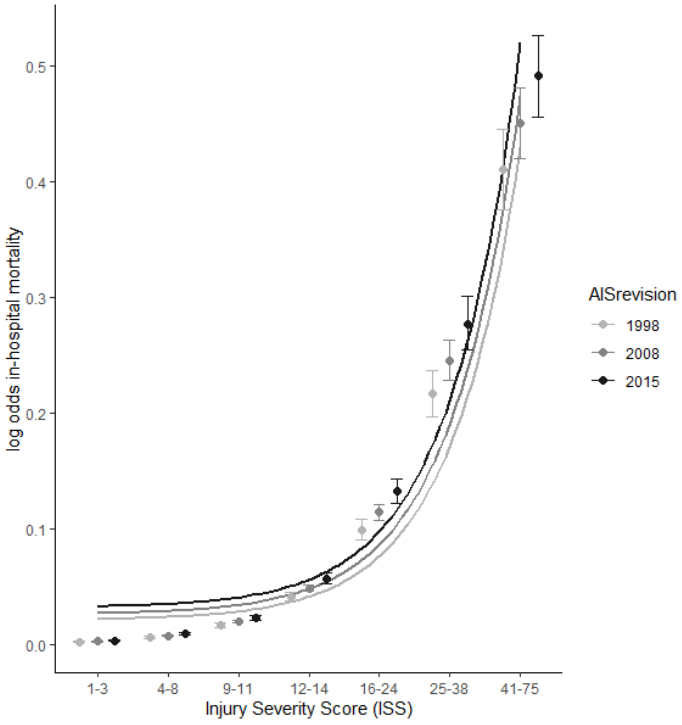

Figure 3. In-hospital mortality likelihood logistic regression for ISS categories and AIS revision. 95% confidence intervals for log odds are shown for each ISS category.

Significant mortality differences between AIS revisions were seen for ISS 4-8 ($\chi^2 = 9.926$, $p = 0.007$), ISS 9-11 ($\chi^2 = 13.541$, $p = 0.001$), ISS 25-40 ($\chi^2 = 13.905$, $p = 0.001$) and ISS 41-75 ($\chi^2 = 7.217$, $p = 0.027$). No significant differences in mortality risk were reported for any ISS category when comparing ISS calculated using AIS08 and AIS15.

Figure 4 shows the proportions of primary admitted MT patients for DTR SW; 56% of MT in 2013-2014, and 70% in 2015-2016 arrived directly to the level 1 trauma centre. With a threshold for MT at ISS08 ≥ 11 coded with AIS08, this percentage decreased to 54% in 2015-2016. Using a threshold for MT at ISS ≥ 12 with AIS15, the proportion of primary admitted MT patients remained at 54% in 2015-2016.

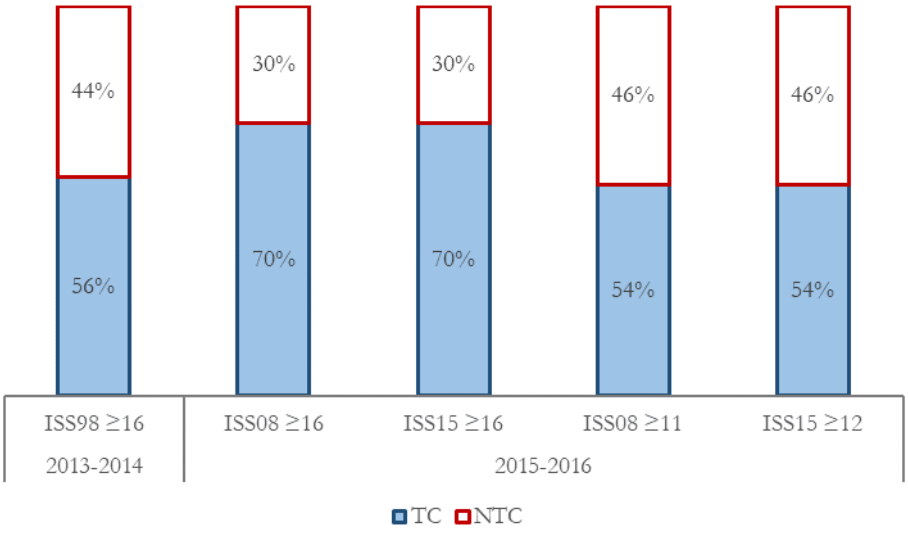

Figure 4. Allocation of MT patients in 2013-2016 in trauma region Southwest Netherlands (DTR SW), showing the proportions of MT patients taken directly to the designated TC (level I) or to NTC (non-level I). MT is considered to be ISS ≥ 16; alternative MT thresholds are shown for AIS08 (ISS ≥ 11) and AIS15 (ISS ≥ 12).

Discussion

This is the first study in the world to report on the potential effects of adopting AIS15 on an existing trauma registry. The code set differences between AIS08 and AIS15 were known to be comparatively minor, compared with those between AIS98 and AIS08.[31] However, changes in real-world datasets often differ in type and extent to those seen between AIS revisions, as there is considerable variation in the incidence of particular codes.[26] As such, it is notable that there were no significant differences in mortality between AIS08-based and AIS15-based ISS when grouped into categories (Table S2), and very little difference across each individual ISS (Figure 2). Although a slightly different ISS threshold (ISS08 ≥ 11 and ISS15 ≥ 12) provided the best comparability with an AIS98-based ISS ≥ 16 threshold, in practice this only affected 31 patients, and changed the number of patients classified as major trauma by less than 1%.

Defining major trauma using an ISS ≥ 16 has been regarded as standard since the 1980s.[13, 14] This study demonstrated that in-hospital mortality rates as well as ICU admission rates differ significantly and substantially when using the ISS ≥ 16 threshold across different AIS revisions. Comparing a threshold of ISS98 ≥16 with thresholds of ISS08 ≥ 11 and ISS15 ≥ 12 results in equivalent mortality and ICU admission rates (Table 2). This is in line with the findings of Palmer et al,[32] who used a validated mapping tool converting AIS98 to AIS08. The present study externally validates their findings using manually coded injuries. Both trauma registries are in high income countries with a relatively low percentage of penetrating injuries, which renders them comparable in terms of epidemiology.

VSTR criteria fitted on DTR SW data resulted in higher medians and broader quartiles for ISS98, ISS08 and ISS15. The two registries have different inclusion criteria; the VSTR excludes specific isolated injuries such as isolated hip fractures, closed limb fractures, facial injuries and smaller burn injuries. The inclusion criteria of the DTR are more general; trauma < 48 hours prior to admission to the ED and subsequent hospital admission, transfer to a different hospital or death (excluding death on arrival).[29] Both registries are therefore especially comparable for the higher segments of injury severity, and showed virtually no differences in mortality risk above an ISS of 11 (Figure 2).

Injuries due to hypothermia, asphyxia (suffocation), (near) drowning, electrical injuries and whole body (explosion-type) injuries are not codable using AIS98, but were collected in the whole study period by the DTR SW. These injury codes were added to the AIS in revisions after AIS98. This has resulted in a selection bias. In the population of the current study coded with AIS98, 62 patients had missing ISS values in the study period during which AIS98 was used, due to sustaining injuries only in these injury categories. Other patients had an ISS98 in combination with the added injury categories (n = 41), resulting in an ISS that was too low. Patients without an ISS were excluded from the main analysis, and the patients with a misclassified ISS were included in the main analysis. Adding and upgrading the ISS98 for these registries to make sure these subgroups were fully represented in both study periods, resulted in a larger in-hospital mortality rate for MT. When comparing AIS08 and AIS15 with AIS98, the Breslow-D statistic displayed no homogeneity (Table S1). When adding the additional subgroups, homogeneity of OR's was present. By adding the injury categories the alternative thresholds for MT increased to an ISS ≥ 13 for both AIS08 and AIS15, compared to an ISS threshold of ≥ 11 and ≥ 12 respectively without the additional injury categories.

Adjusted ISS thresholds for MT populations determined for use with AIS08- and AIS15-coded data provide ongoing comparability within trauma registries which have previously used AIS98, or across trauma registries using different AIS revisions. This assumes that the ISS remains an objective 'gold standard', instead of the de facto standard for measuring injury severity, assessing mortality risk and providing quality indicators for measuring trauma network performance. However, this is not the case. Other studies have included other anatomical summary scores,[11] or added physiological parameters and biomarkers[33] to national trauma registries to better define MT populations or risk-adjust when evaluating outcomes.[34] Modifying ISS thresholds for defining MT should be seen as an important, but temporary measure when comparing data collected across more than one AIS revision. In addition, growing interest in non-fatal functional outcomes like health-related quality of life and the evaluation of regionalisation of trauma care, makes the definition of major trauma more complex and may give new insights the coming years.

Strengths and Limitations

Unlike other studies comparing the effects of different AIS revisions, the present study utilised AIS98 in one two-year period, and AIS08 (mapped to AIS15) in a second two-year period. An advantage of this methodology was that time-consuming double-coding, or potentially inaccurate mapping were avoided, making the study more easily replicable. Although the time periods used were epidemiologically similar (Table 1), some differences may have remained. For example, within the DTR SW, patients primarily admitted to TC's are known to have

higher mortality rates than patients admitted to non-trauma centres (NTC) with the same ISS. Consequently, the level of care could be a confounding variable for outcome due to case mix. This study only looked at the impact of a different AIS revisions from a regional point of view. Also, if patients were transferred between hospitals, primary registries of the referring hospital were excluded. Transfers to hospitals outside the DTR SW trauma region were not registered and not available for analysis. In spite of the similar proportions of transfers to the TC observed, some biases may have been present, either due to referral patterns, or injury coding differences between hospitals. Transferred patients are a complex subgroup due to the local health care context.[35-37]

Conclusion

When coding injuries using AIS08 or AIS15, thresholds of ISS08 ≥ 11 and ISS15 ≥ 12 respectively, perform similarly to a threshold of ISS ≥ 16 in AIS98 in terms of in-hospital mortality and ICU admission. After adjusting for non-codable injuries in AIS98, this threshold is ISS ≥ 13 for AIS08 and AIS15. This confirms previous work evaluating AIS08 with mapped datasets, and is the first to present an evaluation of the effects of AIS15 on trauma registry datasets. Defining major trauma using an appropriate ISS threshold is important for quality indicators, comparing datasets and adjusting for injury severity, but should not replace efforts to develop more appropriate major trauma definitions.

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Supplemental Table S1. Odds ratios for in-hospital mortality in MT patients using different AIS versions (AIS98, AIS08 and AIS15) and using different MT ISS thresholds. Comparisons are of AIS08 or AIS15 with AIS98.

AIS Revision	MT threshold used	OR	95% CI	Breslow-D
AIS98	ISS ≥ 16	12.23	(9.86-15.17)	
AIS08	ISS ≥ 16	16.98	(14.02-20.56)	0.025●¥
AIS15	ISS ≥ 16	16.54	(13.66-20.02)	0.040●¥
AIS98	ISS ≥ 16	12.23	(9.86-15.17)	
AIS08	ISS ≥ 11	9.95	(8.26-11.99)	0.155Ø¥
AIS15	ISS ≥ 12	9.96	(8.27-11.99)	0.155Ø¥

●No homogeneity of OR. Ø Homogeneity of OR. ¥ Cochran-Mantel-Haenszel $p < 0.0001$.

ISS, Injury Severity Score.

Supplemental Table S2. Crude mortality numbers (rates) and odds ratios (with 95% CI) in ISS categories for AIS98, AIS08 and AIS15.

In-hospital mortality								
	AIS98	**AIS08**	**AIS15**	**AIS revision***	**AIS98 compared with AIS08**		**AIS08 compared with AIS15**	
ISS	**n** *(%)*	**n** *(%)*	**n** *(%)*	**X²** *(p)*	**X²** *(p)*	**OR** *(95% CI)* ^	**X²** *(p)*	**OR** *(95% CI)* °
1-3	10 *(0,5)*	24 *(0,5)*	12 *(0,5)*	0.237 *(0.888)*	0.095 *(0.758)*	0.890 *(0.425,1.865)*	0.206 *(0.650)*	1.174 *(0.586,2.353)*
4-8	24 *(0,3)*	50 *(0,7)*	57 *(0,6)*	9.926 *(0.007)*	9.885 *(0.002)*	2.147 *(1.318,3.498)*	0.884 *(0.347)*	0.833 *(0.569,1.220)*
9-11	169 *(2,1)*	188 *(2,9)*	190 *(2,8)*	13.541 *(0.001)*	10.904 *(0.001)*	*1.423 (1.153,1.756)*	0.038 *(0.845)*	*0.980 (0.798,1.202)*
12-14	5 *(0,9)*	4 *(0,7)*	8 *(1,2)*	0.708 *(0.702)*	0.105 *(0.746)*	*0.805 (0.215,3.013)*	0.665 *(0.415)*	*1.644 (0.492,5.489)*
16-24	42 *(5,0)*	37 *(5,5)*	37 *(5,3)*	0.165 *(0.921)*	0.155 *(0.694)*	1.096 *(0.695,1.727)*	0.014 *(0.906)*	0.972 *(0.608,1.555)*
25-40	88 *(21,3)*	135 *(32,1)*	134 *(32,1)*	13.905 *(0.001)*	10.944 *(0.001)*	1.710 *(1.243,2.354)*	0.000 *(0.983)*	0.997 *(0.740,1.342)*
41-75	29 *(35,4)*	47 *(53,4)*	47 *(54,0)*	7.217 *(0.027)*	5.335 *(0.021)*	2.078 *(1.113,3.878)*	0.007 *(0.933)*	1.026 *(0.562,1.875)*
Total	367 *(1,9)*	485 *(2,4)*	485 *(2,4)*	13.646 *(0.001)*	10.698 *(0.001)*	1.257 *(1.096,1.441)*	0.000 *(1.000)*	1.000 *(0.880,1.136)*

PART III

CLINICAL OUTCOME MEASURES IN A TRAUMA NETWORK

CHAPTER 5

The association between level of trauma care and clinical outcome measures: a systematic review and meta-analysis

Highlights

- *By implementing trauma systems, a level of trauma care classification was introduced, and linked to improvements in survival and other outcomes.*
- *The association between level of trauma care and in-hospital mortality is evident for major trauma populations.*
- *This association does not hold for general trauma populations.*

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Abstract

Background With implementation of trauma systems, a level of trauma care classification was introduced. Use of such a system has been linked to significant improvements in survival and other outcomes.

Objectives The aim of this study was assessing the association between level of trauma care and fatal and non-fatal outcome measures for general and major trauma populations.

Methods A systematic literature search was conducted using six electronic databases up to December 18, 2019. Studies comparing mortality or non-fatal outcomes between different levels of trauma care in general and major trauma populations (preferably Injury Severity Score >15) were included. Two independent reviewers performed selection of relevant studies, data extraction and a quality assessment of included articles. With a random-effects meta-analysis, adjusted and unadjusted pooled effect sizes were calculated for level I versus non-level I trauma centers.

Results Twenty-two studies were included. Quality of the included studies was good, however adjustment for comorbidity (32%) and inter-hospital transfer (38%) was performed less frequently. Nine (60%) of the fifteen studies analyzing in-hospital mortality in general trauma populations reported a survival benefit for level I trauma centers. Level I trauma centers were not associated with higher mortality than non-level I trauma centers (adjusted OR 0.97; CI 95% 0.61-1.52). Of the eleven studies reporting in-hospital mortality in major trauma populations, ten (91%) reported a survival benefit for level I trauma centers. Level I trauma centers were associated with lower mortality than non-level I trauma centers (adjusted OR 0.77; CI 95% 0.69-0.87).

Conclusion The association between level of trauma care and in-hospital mortality is evident for major trauma populations, however this does not hold for general trauma populations. Level I trauma centers produce improved survival in major trauma populations. This association could not be proven for non-fatal outcomes in general and major trauma populations due to inconsistencies in the body of evidence.

Background

Trauma is an important cause of morbidity and mortality worldwide. Injuries are the leading cause of death among people under 45 years old and men between the ages of 15 and 65 have the greatest burden of injury in total.[1] The economic impact due to trauma is high because of direct health care costs and productivity loss caused by work absenteeism.[2, 3]

With the implementation of regional trauma systems, significant improvements in survival and other outcomes have been documented.[4] In many countries a classification of the level of trauma care is linked with regional organization of trauma care. Globally, the level of trauma care is often classified numerical, with level I being the highest possible care. Other classifications like tertiary versus non-tertiary or (major) trauma center (TC) versus non-trauma centers (NTC) are also used.[5-9]

Part of the implementation and maturation of trauma networks is the optimal 'concentration and spread' of facilities and their resources. A central thought is that hospitals or individual trauma surgeons with high volume of specific patient categories are able to provide the best possible care and are effective concerning cost reduction.[10] Studies on outcome differences between levels of trauma care show inconsistent results.[4, 11] The underlying rationale seems complex due to case mix differences and the time factor of maturing trauma systems or the impact of implementing regional trauma systems. From a regional perspective trauma care is dynamical due to inter-hospital transfers, differences in transport of trauma patients and geographical characteristics of trauma regions. Because of inconsistent results and the complexity of trauma care, this study aimed to provide an overview, including a synthesis of data, of the association between level of trauma care and fatal and non-fatal outcome measures for general and major trauma populations.

Methods

This study was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA[12]) and was registered in the International Prospective Register of Systematic Reviews (PROSPERO[13]) under identification number CRD42019146647. Analyses were performed with Review Manager (RevMan, version 5 Copenhagen: the Nordic Cochrane Center, The Cochrane Collaboration, 2014).

Search strategy

Several search strategies were employed to find published literature assessing the trauma center level status association with in-hospital and patient-reported outcomes. The first strategy consisted of computerized database searches. On December 18, 2019 the search engines Embase, Medline Ovid, Web of science Core Collection, Cochrane Central registry of trials and Google scholar were searched to identify published studies that examined trauma patient outcomes in relation to trauma center level. There were no time restrictions and the search algorithm was restricted to English articles only. An experienced biomedical information specialist designed the search terms for the respective databases. The search algorithm included Medical Subject Headings (MeSH) terms and text words for trauma, injured patients, emergency medical services, level of trauma care, trauma center, mortality and

different non-fatal health outcomes like length of stay (LOS), intensive care unit (ICU) stay, discharge and functional outcome measures (Appendix A). The second strategy consisted of identifying relevant studies from the reference lists of studies all included studies.

Study selection

Studies were eligible for inclusion if they consisted of either randomized trials, cross-sectional studies or cohort studies and reported on level of trauma care in relation to fatal and non-fatal outcome measures. Studies were included if their study examined injuries of all causes and if their population consisted of general trauma (GT) or major trauma (MT, minimum Injury Severity Score (ISS) >15). The exclusion criteria consisted of studies focusing on specific subpopulations such as transferred patients, burn patients or pediatric patients. Studies that address trauma system implementation, transfers, geography and urbanization, economic evaluation, volume-outcome, prediction or general public health issues in relation with trauma care were also excluded. Studies that provided (duplicate) data from a conference, forum, panel discussion, or experience talk were also excluded.

Two reviewers (J.C.V.D. and C.R.L.V.D.D.) independently screened the titles and abstracts of the articles found by the search strategy to identify potentially eligible studies. The full text documents of these studies were retrieved and independently screened by the aforementioned reviewers to further narrow down the studies eligible for inclusion. In case of disagreement this was resolved through discussion or, if necessary, a third review author (C.A.S.) was consulted to reach consensus.

Data extraction and quality assessment of included studies

Two reviewers (J.C.V.D. and C.R.L.V.D.D.) independently performed data extraction from the included studies. Extracted information included a number of study characteristics (publication year, study design, country, study period, data source, and sample size), inclusion and exclusion criteria, type of trauma center level comparison (*e.g.*, tertiary versus non-tertiary, level I versus non-level I), study outcome measures, and key findings.

The Newcastle-Ottawa Scale (NOS) was scored for each study in order to create an international standardized comparability.[14] In addition, a quality assessment tool was created to assess quality, generalizability and risk of bias of the included studies. These quality elements were based on existing literature.[10, 15] Each included study was subjected to quality assessment by the reviewers. In case of disagreement this was resolved by assessing the study together. If necessary, a third review author (C.A.S.) was consulted to reach consensus. Funnel plots were used to address the risk of publication bias.[16]

Data analysis

A meta-analysis was performed to determine the relationship between trauma center level and in-hospital mortality as an outcome in general trauma populations. A subgroup analysis was performed for MT patients.

The main focus of the meta-analysis was a comparison of Level I and non-level I trauma care. If the level distinction was not numerical, the highest level of care was used to compare with

other levels of trauma care. Tertiary or academic trauma care and major trauma centers were considered the equivalent of level I. When studies compared level I with multiple other levels, all individual comparisons were included in the meta-analysis. The highest level of care was maintained as the reference group.

The main outcome parameter of the meta-analysis was in-hospital mortality. Unadjusted numbers and adjusted odds ratios (OR) with confidence intervals were extracted from the included studies. The 'number needed to treat for an additional beneficial outcome' (NNTB) was calculated as a comparative measure of effect for unadjusted OR's. Non-fatal outcomes were LOS, ICU LOS, discharge destination, functional outcomes and quality of life. In the case of absence of adjusted OR's, the crude mortality rates were used. If this was not possible studies were excluded from the quantitative analysis. The Mantel-Haenszel method provided a pooled unadjusted OR, the inverse variance method provided a pooled adjusted OR and the Standardized Mean Difference was used as summary statistic for continuous outcome measures. Studies were pooled using a random-effects meta-analysis, providing odds ratios for binary/categorical outcomes and means for continuous outcomes. Random-effects were used to compensate for heterogeneity, thereby addressing differences in study periods, regional/geographical characteristics and general trauma populations. Heterogeneity between the studies was assessed using both the chi-squared test and the I^2 statistic. I^2 values were used to interpret the amount of heterogeneity: 30-60% possible moderate, 50-90% possible substantial and 75-100% considerable.[17]

Results

The initial search identified 5,627 records (Figure 1). Two additional studies[8, 9] which were found with reference chasing, resulting in a total of 22 included studies[5-9, 18-34] in the systematic review (Table 1 and 2). After removing duplicate records 3,138 records were screened on title and abstract. Of the 109 articles that were identified as potentially eligible and selected for full-text assessment, 22 studies were included.[5-7, 18-34] Of these studies, 17 studies[5-7, 9, 20-28, 30-32, 34] were included in the meta-analysis on in-hospital mortality. A meta-analysis was not possible for non-fatal outcome in relation to different levels of trauma care due to incongruous outcome variables or inconsistent outcome measures.

Study characteristics

Sixteen (73%) studies[5, 6, 8, 9, 18, 19, 21-23, 27, 29-34] analyzed general trauma populations and 12 (55%) studies[5, 7, 9, 18, 20, 21, 23, 25, 26, 29, 30, 33] examined MT populations. The minimum age of included patients varied from 12 to 18 years between studies. Of the 22 included studies, 16 (73%) were retrospective cohort studies[7, 9, 19-27, 29-32, 34] and six (27%) studies [5, 6, 8, 18, 28, 33] were prospective cohort studies. The majority (68%) of the included studies were conducted in the USA[8, 9, 19-22, 24-27, 30-34], two (9%) studies were conducted in Germany[18, 28], two (9%) in Canada[7, 29], two (9%) in Malaysia[5, 6] and one (5%) in Australia.[23] With the exception of three (14%) studies[5, 6, 26], all studies were (trauma) registry based. Fifteen (68%) studies[18-30, 32, 34] compared level I trauma centers with non-level I trauma centers of which two (13%) studies[25, 32] focused solely on (American College of Surgeons (ACS) verified trauma centers. One study[31] focused on state designated centers and two studies[19, 27] compared different levels between ACS and state

designated trauma centers. Three studies[5-7] compared tertiary versus non-tertiary care hospitals and three studies[8, 9, 29] compared trauma centers with non-trauma centers.

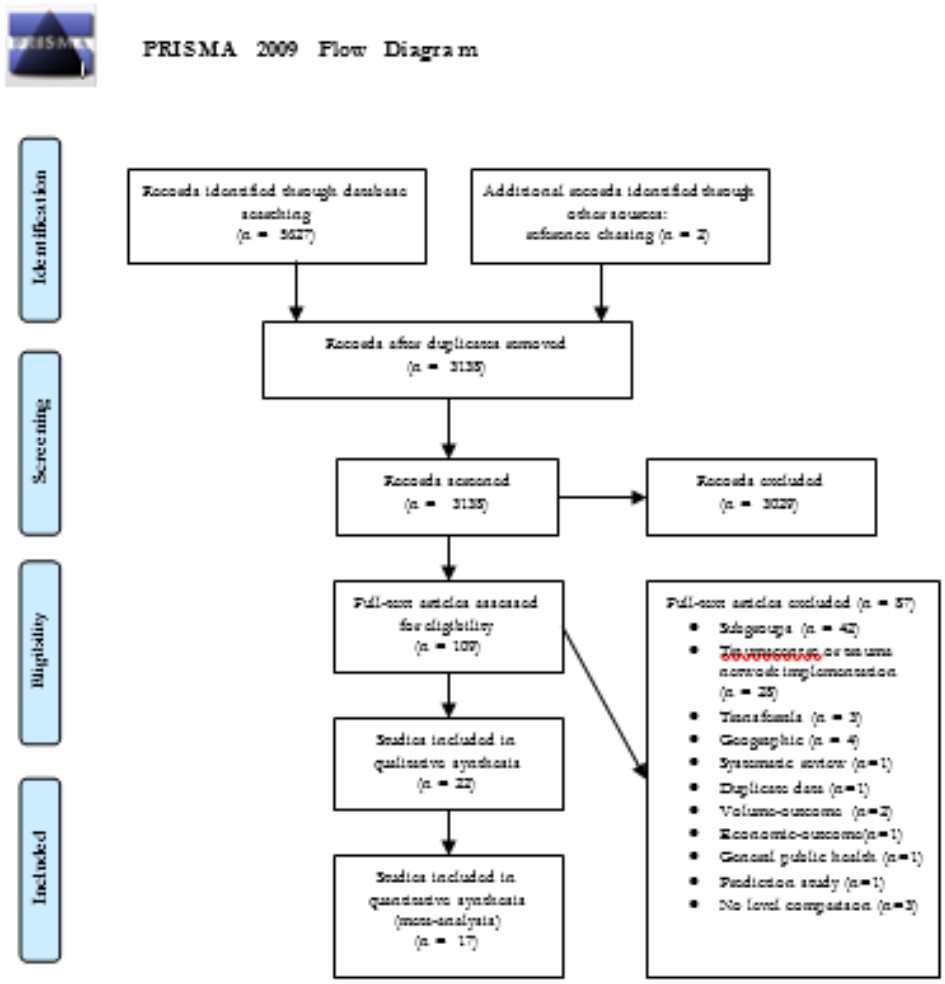

Figure 1. PRISMA 2009 flow diagram.

Study characteristics

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Mortality was reported as an outcome in 21 (95%) of the included studies.[5-9, 19-34] Seven studies[5, 6, 8, 20, 24, 25, 32] mention death on arrival specifically as an exclusion criterion and 30-day mortality rates were only reported in one study.[8] Other reported outcomes were quality of life[18], discharge status[20], functional independence measure[25] (FIM), (ICU) LOS[5, 6, 9, 20, 22, 23, 25, 28, 32], hospital charges[20], discharge destination[21], organ failure[28], Glasgow Coma Score (GCS)[28], trauma care resources[29], complications[30], severity of injury[31], patient volume[7], functional independence measure[33] (FIM), musculoskeletal functional assessment[5] (MFA), and Barthel Index[5, 6] (BI).

Quality assessment

All included studies had clearly defined inclusion and exclusion criteria and made a clear trauma center level classification (Figure 2). Most studies reported all confounders used in adjusted analyses (95%), reported ISS (86%) and were registry based (86%). All studies that used mortality as an patient outcome defined this as in-hospital mortality (95%). Unadjusted OR's were used to report mortality in 72% of the studies and adjusted OR's were reported in 82% of the included studies. (Regarding quality assessment an observed/expected ratio (O/E ratio)was scored as the presence of an OR, however were not used in the meta-analysis.) While 82% of the studies adjusted their analyses for injury severity and 77% adjusted for demographic characteristics, only 32% of the studies adjusted for comorbidity and 27% percent reported the AIS version that was used for coding injuries. Studies with low quality assessment scores, also scored lower using the Newcastle-Ottawa Scale[14] (NOS) for cohort studies (Figure 2).

Systematic review in-hospital mortality for General Trauma and Major Trauma

Of the 15 studies that reported in-hospital mortality for GT[5-9, 19, 21, 22, 27, 29-34] , nine (90%) studies[6-8, 19, 21, 22, 29, 30, 33] reported lower mortality for level I centers or a hierarchical survival benefit, four (27%) studies reported no differences between level I and level II centers and two (13%) studies[31, 32] reported a lower mortality rate for non-level I trauma centers. Of the 11 included studies reporting on MT[5, 20, 21, 23-26, 28-30, 33], nine (82%) studies[5, 21, 23-25, 28-30, 33] defined MT as an ISS >15, one study defined MT as having one of four predefined major injuries[20], and one study based MT on a CRAMS score of 1-6.[26] Nine (82%) studies[5, 21, 23-26, 28-30, 33] reporting on MT found a significant association between level of trauma care and mortality, reporting lower mortality rates for higher level trauma centers. Six (55%)studies[5, 20, 24, 26, 28, 30] compared level I centers with non-level I centers, two (18%) studies[29, 33] compared level I/II with level III centers, and three (27%) studies found no differences between level I and level II centers but did find a difference comparing level I and II centers with other level centers.[20, 21, 23]

Table 2. Characteristics and key findings of included articles.

Author, Year	Level comparison	Study Design	Country	Data Source	Period	Inclusion	Exclusion	Sample Size	Outcome	Overall Key findings
Angerpointer et al., 2019	level I vs. II	PCS	Germany	TNO (DGU)	2012-2014	Multiple injured patients, Complete EQ-5D-3L	Level III, Age ≤ 17, death	501	QoL, EQ-5D-3L, follow-up at 6, 12 and 24 months)	Increase of EQ-5D, level of reference population not reached two years after trauma. No differences level I and level II. (-)
Brown et al., 2013	level I vs. II (ACS verified vs. state designated)	RCS	USA	NTDB	2007-2008	Age ≥ 16	-	900,274	In-hospital mortality	level I have lower O/E and ACS lower O/E vs. state. ACS verification [illegible]
Clancy et al., 2001	level I vs. II	RCS	USA	NCTR-NTDB	1995-1996	Death, Major ICD-9-CM: thoracic aortic, liver, lung, pelvic	DOA, Admitted < 24h	1,283	In-hospital mortality, discharge status, (ICU) LOS, ICU admission, charges	Patients with the included major injuries may be optimally cared for in both level I and level II TC's. (-)
Clemmer et al., 1985	level I vs. II	RCS	USA	-	-	CRAMS score 1-6	CRAMS score 0 and 7-10	50	In-hospital mortality	Level I had a significantly reduced mortality rate compared to level II.
Cudnik et al., 2009	level I vs. II	RCS	USA	OHTR	2003-2006	Age ≥ 16, (primary) admitted > 48h, death, ICD-9 800-959.9	Isolated hip fractures	18,103	In-hospital mortality, discharge destination	Patients admitted to level I TC's had improved survival and better functional outcomes. These findings held for ISS > 15 patients. (+)

Author, Year	Level comparison	Study Design	Country	Data Source	Period	Inclusion	Exclusion	Sample Size	Outcome	Overall Key findings
Culica et al., 2007	level I vs. II vs. III/IV	RCS	USA	THCIC	1999-2000	Hospitalized patients with ICD-9 800-959.9	Isolated hip fractures, late effects trauma and CA	85,484	In-hospital mortality, LOS	Survival was lower at level II and mostly level I TC' s compared with other levels. Difference smaller after adjusting. (-)
Curtis et al., 2011	level I vs. II vs. III	RCS	Australia	NSW ITIM	2002-2007	ISS > 15, Age ≥ 16	Isolated spinal cord, severe burns	1,986	In-hospital mortality, LOS, ICU LOS	MT at level III had a higher MR vs. level I. No difference level I vs. II. ICU LOS shorter in level I vs. level II/III. Longer LOS level II vs. level I. (+)
Demetriades et al., 2005	level I vs. II	RCS	USA	NTDB	1996-2003	ISS > 15, Age ≥ 15	DOA	12,254	In-hospital mortality, ICU stay, severe disability at discharge	Mortality lower and better functional outcome level I vs. II and non-designated II/III/IV. No differences in ICU LOS. All subgroups followed same trend. (+)
Demetriades et al., 2006	level I vs. II vs. III vs. undesignated (ACS)	RCS	USA	NTDB	1994-2003	ISS > 15, Age ≥ 15	DOA	130,154	In-hospital mortality	ISS > 15 treated in level I ACS have better survival vs. level II/III ACS and undesignated facilities. (+)
Elkbuli et al., 2019	level I vs. II (ACS verified vs. state)	RCS	USA	NTDB	2013	GT	-	172,387	In-hospital mortality	ACS: similar O/E level I vs. II. State designated: similar O/E level I vs. II. (-)
Ernstberger et al., 2018	level I vs. II	PCS	Germany	TNO-DGU	2012-2014	ISS > 15, Primary admission	Transferred patients < 48h, incomplete RISC11-score	875	In-hospital mortality, LOS, OF, GOS	No differences mortality level I vs. II. Indices for injury severity and probability of death were higher in level I. Survival advantage level I vs. II. (+)

Author, Year	Level comparison	Study Design	Country	Data Source	Period	Inclusion	Exclusion	Sample Size	Outcome	Overall Key findings
Fleet et al., 2019	Urban level I and II vs. rural ED's	RCS	Canada	QTR	2009-2013	GT, rural to urban transferred patients	-	79,957	In-hospital mortality, trauma care resources	MR's were higher in rural ED's vs. urban level I/II. Similar results for ISS > 15. (+)
Glance et al., 2012	level I vs. II	RCS	USA	PTOS	2000-2009	Age ≥ 17, ICU or step down unit, LOS > 48h, death, incoming transferred patients	Burns, hip fractures, hypothermia, superficial/ unspecified injuries, transfers.	208,886	In-hospital mortality, complication	Patients in level I had a lower odds of mortality and increased odds of complications. Survival benefit level I was present for MT, and strongest for ISS ≥ 25. (+)
Helling et al., 2007	level I/II vs. III (state designated)	RCS	USA	MTR	2002-2003	GT	-	24,392	In-hospital mortality, severity of injuries	Acuity and injury severity higher at level I/II vs. III. Overall mortality lower at level III. (+)
Kaji et al., 2017	level I vs. II (ACS)	RCS	USA	LACT & EMIS	2012-2014	Age ≥ 15, ICD-9 800-959.9	DOA, isolated fractures hip/distal from elbow/ knee, late effect	63,614	In-hospital mortality	Level II TC's have lower MR's than level I TC's (for both TRISS and Haider). (+)
Liberman et al., 2005	Tertiary vs. secondary vs. primary hospitals	RCS	Canada	QTR	1997-2002	Age ≥ 16, Death, LOS ≥ 3, ICU admission, primary admission	Intoxication, drowning, electrocution, burns, secondary admission, prehospital	72,073	In-hospital mortality, patient volume	Tertiary TC's were associated with a reduction in risk-adjusted MR compared with both secondary and primary TC's. (+)

Author, Year	Level comparison	Study Design	Country	Data Source	Period	Inclusion	Exclusion	Sample Size	Outcome	Overall Key findings
MacKenzie et al., 2006	TC vs. NTC	PCS	USA	NS-COT	1999	Age 18-84 complete data, MAIS ≥ 3	> 24h after trauma, major burns, hip fracture & older than 65, not English or Spanish speaking	5,191	30-day, 90-day and 1-year mortality	Risk of death is significantly lower when care is provided in a TC than in a NTC and argue for continued efforts at regionalization. (+)
Nirula et al., 2006	level I/II vs. III/IV/V	PCS	USA	NTDB	1994-2001	Age ≥ 18	-	474,024	FIM	Level I/II is associated with improved functional outcomes regardless of injury severity and type of injury. (+)
Rogers et al., 2001	TC vs. CH	RCS	USA	VHDD	1995-1999	Trauma discharge diagnosis	Isolated femur fractures	16,354	In-hospital mortality	In a rural state without a formal trauma system, survival is similar at CH when corrected for injury severity and age. Also for MT. (-)
Rogers et al., 2011	level I vs. II	RCS	USA	PTOS	2004-2008	GT	Thermal injuries	148,323	In-hospital mortality	No different adjusted MR level I vs. II. Level I and II distinction smaller in mature trauma network. Need for non-hierarchical descriptors. (-)

Author, Year	Level comparison	Study Design	Country	Data Source	Period	Inclusion	Exclusion	Sample Size	Outcome	Overall Key findings
Sethi et al., 2002	CTRH vs. provincial TCH vs. DGH	PCS	Malaysia	-	1999	Age ≥ 13, Admitted > 72h, ICU admission, death	DOA, minor trauma	484	In-hospital mortality, disability at discharge	Direct admission to DGH and TCH associated with higher mortality vs. CTRH. Disability at discharge was associated with being severely injured. (+)
Sethi et al., 2007	Tertiary care vs. secondary care (DGH)	PCS	Malaysia	-	2000-2001	Age ≥ 13, admission >72 h, ICU admission, death	DOA, minor trauma	5,334	In-hospital mortality, MFA, BI	DGH associated with higher MR for ISS > 15. Beneficial effect of tertiary care was not significant for ISS < 16. Tertiary care associated with increased odds of disability and musculoskeletal impairment at discharge. (+)

EQ-5D-3L, EuroQol-5D-3L; QoL, Quality of Life; ACS, American College of Surgeons; *ICD-9, International Classification of Diseases, Ninth Revision; ICD-9-CM, International Classification of Diseases, Ninth Revision, Clinical Modification*, TC, Trauma Center; NTC, Non Trauma Center; RCS, retrospective cohort study; PCS, prospective cohort study; USA, United States of America; NTDB, National Trauma Data Bank; TNO, Trauma Network of Eastern Bavaria; DGU, Deutsche Gesellschaft für Unfallchirurgie; NCTR, North Carolina Trauma Registry; LOS, Length of Stay; ICU, Intensive Care Unit; CRAMS, Circulation Respiration Abdomen Motor and Speech; OHTR, State of Ohio Trauma Registry; THCIC, Texas Health Care Information Council; CA, Corpus Alienum; NSW ITIM, New South Wales Institute of Trauma and Injury Management data; GT, General Trauma Population; MT, Major Trauma Population; DOA, Death On Arrival; RISC II, Revised Injury Severity Classification version II; OF, Organ Failure; GOS, Glasgow Outcome Scale; QTR, Quebec Trauma Registry; MTS, Major Trauma Services; PTOS, Pennsylvania Trauma Outcome Study; MTR, Missouri Trauma Registry; SBP, Systolic Blood Pressure; LACT & EMIS, Los Angeles County Trauma and Emergency Medical Information System; FIM, Functional Independence Measure; MFA, Musculoskeletal Functional Assessment; BI, Barthel Index; DGH, District General Hospitals; CTRH, Central Tertiary Referral Hospital; TCH, Tertiary Care Hospital; NSCOT, National Study on the Costs and Outcomes of Trauma Care; MAIS, Maximum Abbreviated Injury Scale; CH, community hospital; VHDD, Vermont Hospital Discharge Database.

Table 1. Quality assessment and Newcastle-Ottawa Scale (NOS) of the included articles.

Author. Year	NOS total (9*)	NOS outcome (3*)	NOS comparability (2*)	NOS selection (4*)	Funding sources identified	Conflict of interest declared	Adjusted for transfer patients	Adjusted for comorbidity	Adjusted for demographics	Adjusted for injury severity	All confounders reported	OR adjusted	OR unadjusted/crude	OR with 95% CI	OR ICU admission	OR discharge destination	Median LOS	OR mortality	Clear distinction TC level	AIS version reported	ISS reported	Registry based	Nation- or region wide	In- and exclusion clear
Angerpointer et al., 2019	8*	2*	2*	4*	-	+	-	+	+	+	+	-	-	-	na.	na.	na	-	+	-	+	+	+	+
Brown et al., 2013	9*	3*	2*	4*	+	-	+	-	+	+	+	+	-	+	na.	na.	na.	-	+	-	+	+	+	+
Clancy et al., 2001	9*	3*	2*	4*	-	-	+	-	+	+	+	-	-	-	-	-	+	-	+	+	+	+	+	+
Clemmer et al., 1985	7*	3*	1*	3*	+	-	-	-	-	-	-	-	+	+	-	-	-	+	+	-	-	+	+	+
Cudnik et al., 2009	9*	3*	2*	4*	-	+	na.	+	+	+	+	+	-	+	na.	+	na.	+	+	-	+	+	+	+
Culica et al., 2007	9*	3*	1*	4*	-	+	+	+	+	-	+	+	-	+	na.	na.	na.	+	+	-	+	+	+	+
Curtis et al., 2011	8*	3*	2*	4*	+	+	na.	-	+	+	+	+	-	+	+	na.	+	+	+	-	+	+	+	+
Demetriades et al., 2005	9*	3*	2*	4*	-	+	-	-	+	+	+	+	+	+	+	na.	na.	+	+	-	+	+	+	+
Demetriades et al., 2006	9*	3*	2*	4*	-	+	-	-	+	+	+	+	+	+	na.	na.	na.	+	+	-	+	+	+	+
Elkbuli et al., 2019	9*	3*	2*	4*	+	+	-	-	+	+	+	+	+	-	na.	na.	na.	-	+	-	+	+	+	+
Ernstberger et al., 2018	9*	3*	2*	4*	+	-	na.	+	+	+	+	+	+	+	-	na.	-	+	+	+	+	+	+	+

Author. Year	Clear distinction TC level	AIS version reported	ISS reported	Registry based	Nation- or region wide	In- and exclusion clear	OR mortality	Median LOS	OR discharge destination	OR ICU admission	OR with 95% CI	OR unadjusted/crude	OR adjusted	All confounders reported	Adjusted for injury severity	Adjusted for demographics	Adjusted for comorbidity	Adjusted for transfer patients	Conflict of interest declared	Funding sources identified	NOS selection (4*)	NOS comparability (2*)	NOS outcome (3*)	NOS total (9*)
Fleet et al., 2019	+	-	+	+	+	+	+	na.	na.	na.	+	+	+	+	+	+	-	+	+	+	4*	2*	3*	9*
Glance et al., 2012	+	-	+	+	+	+	+	na.	na.	na.	+	+	+	+	+	+	+	-	+	+	4*	2*	3*	9*
Helling et al., 2007	+	-	+	+	+	+	-	na.	na.	na.	-	+	-	-	-	-	-	-	-		4*	-	3*	7*
Kaji et al., 2017	+	-	+	+	+	+	+	na.	na.	na.	+	+	+	+	+	+	+	+	+	+	4*	2*	3*	9*
Liberman et al., 2005	+	+	+	+	+	+	+	-	na.	-	+	-	+	+	+	-	-	-	-	+	4*	2*	3*	9*
MacKenzie et al., 2006	+	+	+	+	+	+	+	na.	na.	na.	-	+	+	+	-	+	-	+	+	+	4*	2*	3*	9*
Nirula et al., 2006	+	-	+	+	+	+	-	na.	na.	na.	+	-	+	+	+	+	-	-	-	-	4*	2*	3*	9*
Rogers et al., 2001	+	-	-	+		+	+	na.	na.	-	+	-	+	+	+	+	-	na.	-	-	3*	2*	3*	8*
Rogers et al., 2011	+	-	+	+		+	+	na.	na.	na.	-	-	+	+	+	+	-	-	-	-	4*	2*	3*	9*
Sethi et al., 2002	+	+	+	-		+	+	+	na.	na.	+	-	+	+	+	-	-	na.	-	+	2*	2*	3*	7*
Sethi et al., 2007	+	+	+	-		+	+	-	na.	na.	+	-	+	+	+	-	-	na.	-	+	2*	2*	3*	7*
Total +(%)*	100	27	100	86	82	100	73	43	33	29	73	45	82	91	82	77	32	38	36	55				

ISS, injury severity scale; AIS, abbreviated injury scale; TC, trauma center; OR, odds ratio; ICU, intensive care unit; CI, confidence interval; na., not applicable.

Meta-analysis in-hospital mortality for General Trauma

In the unadjusted meta-analysis, 11 (52%) studies[5-7, 9, 21, 22, 27, 30-32, 34] with a total of 1,017,802 patients were included to compare in-hospital mortality between level I and non-level I trauma centers for GT (Figure 2). This resulted in a pooled OR (95%CI) of 1.09 (0.97-1.22), $p = 0.13$. When comparing level I versus level II, the OR (95%CI) was 1.06 (1.01-1.11), $p = 0.01$. Both comparisons displayed strong heterogeneity for the included studies (I^2 95% and 66% respectively).

The adjusted meta-analysis comparing level I with non-level I trauma care included nine (43%) studies[5-7, 9, 21, 22, 30, 32, 34] (Figure 2, one study had two usable comparisons). The pooled effect estimate associated level I trauma care with lower in-hospital mortality compared with non-level I trauma care for GT (OR 0.97, 95%CI 0.61-1.52, $p = 0.88$, $I^2 = 97\%$). The six (29%) studies[5, 6, 21, 30, 32, 34] that performed the same comparison regarding level I versus level II centers resulted in a pooled OR (95% CI) of 0.98 (0.73-1.31), a *p-value* of 0.87 and an I^2 of 86%.

Meta-analysis in-hospital mortality for Major Trauma

Seven (64%) studies[20, 21, 23-26, 28] with a total of 145,049 severely injured patients were included in the analysis comparing unadjusted in-hospital mortality between level I and non-level I centers (Figure 3, one study had two usable comparisons). The pooled effect estimate found a lower in-hospital mortality rate in level I centers than in non-level I centers for MT (OR 0.87, 95% CI 0.77-0.97, $p = 0.02$, $I2 = 74\%$, Figure 3). NNTB was 31 for the level I versus non-level I analysis. When considering level I versus II comparisons exclusively, a similar association was present, however this association was non-significant (OR 0.88, 95% CI 0.76-1.02, $p = 0.09$, $I^2 = 76\%$). In the level I versus level II comparison NNTB increased to 98.

For an adjusted comparison of level I versus non-level I centers seven (33%) studies[5, 21, 23-25, 28, 30] were included (Figure 3, three studies had two usable comparisons). The pooled effect estimate found lower in-hospital mortality for level I centers compared with non-level I centers regarding MT (OR 0.77, 95% CI 0.69-0.87, $p < 0.000$, $I2 = 67\%$). When exclusively comparing level I and level II centers, seven (33%) studies[5, 21, 23, 24, 28, 30] were analyzed (one study having two usable comparisons), producing similar results (pooled OR 0.78, 95% CI 0.68-0.89, $p < 0.000$ and $I^2 = 67\%$). For both GT and MT there was no suggestion of publication bias (Figure 4). In both adjusted comparisons NNTB was incalculable due to missing values.

Systematic review non-fatal outcomes for General Trauma and Major Trauma

A total of four (19%) GT studies reported (ICU) LOS with either a mean or a median as part of basic descriptive statistics and not as a main result.[5, 6, 32, 34] When a median was reported there was no difference between level I and level II centers. When a mean was reported level I had a longer LOS compared to level II for GT.

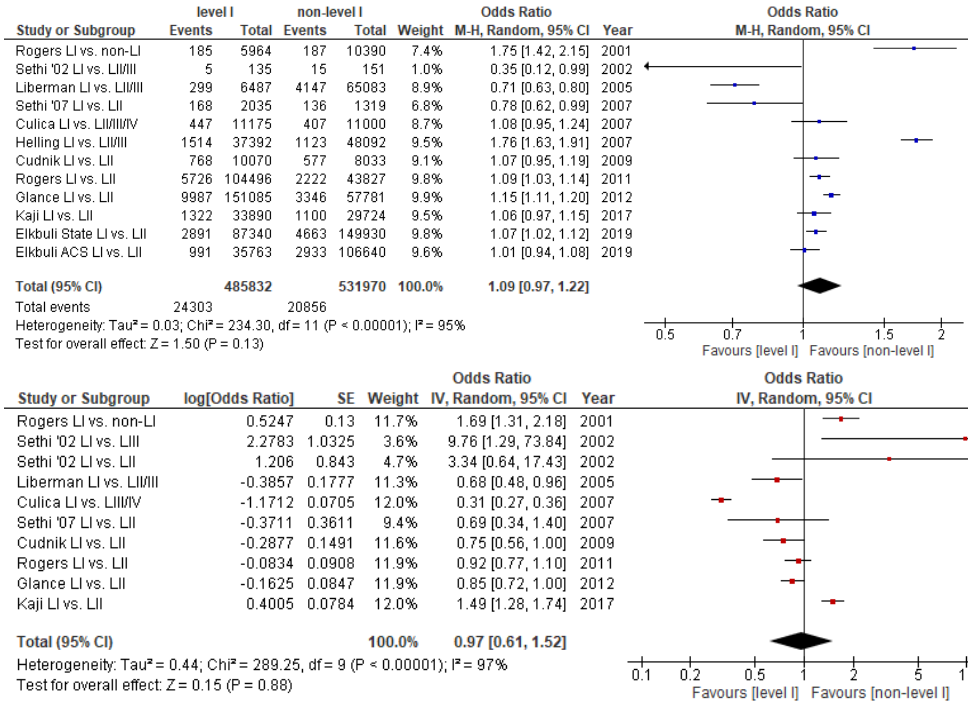

Figure 2. Meta-analysis in-hospital mortality: Unadjusted (above) and adjusted (below) in general trauma populations for level I versus non-level I trauma centers.

Four MT studies[20, 23, 24, 28] reported (ICU) LOS. Compared to non-level I centers, level I centers were reported to have either longer LOS[28] for MT, shorter LOS[23] or LOS was similar[20]. One (25%) study reported a higher ICU admission rate[28] and one (25%) study reported a lower ICU admission rate regarding MT.[23] The ICU LOS in level I centers was reported to be either longer[28], shorter[20, 23] or similar[25] compared to non-level I centers regarding MT.

Of the eight studies[5, 6, 18, 20, 21, 25, 28, 33] that reported functional outcomes, four (50%) studies[5, 6, 21, 33] reported on GT and seven (88%) studies[5, 18, 20, 21, 25, 28, 33] reported on MT. When a study examined both GT and MT, results were similar for both populations. Five (63%) studies[5, 6, 21, 25, 28] had favorable outcomes for level I centers compared to level II centers. One (13%) study[33] reported favorable outcomes for level I and II centers combined compared to other level centers and two (25%) studies[18, 20] reported no difference between level I and level II centers.

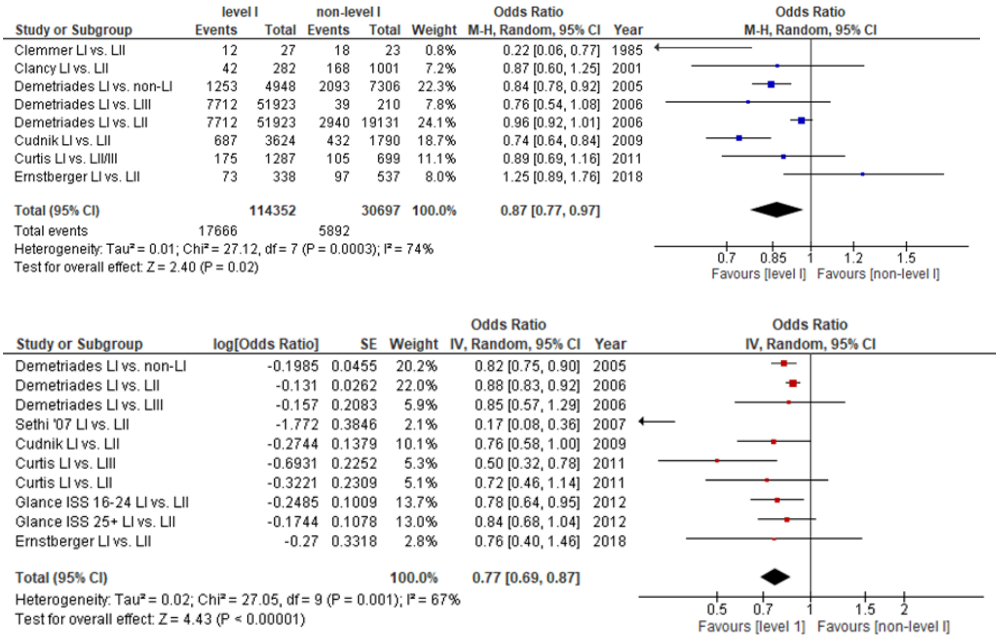

Figure 3. Meta-analysis in-hospital mortality: Unadjusted (above) and adjusted (below) in major trauma populations for level I vs. non-level I trauma centers.

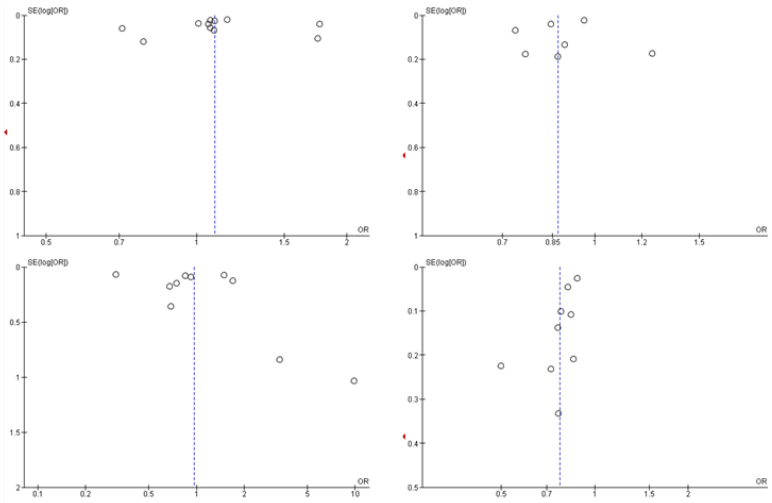

Figure 4. Funnel plots on publication bias: Unadjusted GT studies (upper left), adjusted GT studies (lower left), unadjusted MT studies (upper right), adjusted MT studies (lower right).

Discussion

This study aimed to assess the association between level of trauma care and fatal and non-fatal outcome measures in trauma patients. The systematic review included 22 studies, of which 17 studies were included in a meta-analysis. The results indicate that MT patients have a lower in-hospital mortality rates when treated in a level I center than MT patients treated in a non-level I trauma center (unadjusted OR 0.87, NNTB 31). When comparing level I with level II trauma centers the unadjusted OR was similar (0.78), and NNTB increased to 98. For general trauma populations this relationship was not present. The quality of the included studies was good, however adjustment for comorbidity and inter-hospital transfer was performed less frequently.

It seems logical that level I trauma centers perform better in treating MT patients. First, level I trauma centers treat more MT patients compared to non-level I trauma care which is associated with lower mortality rates.[10] Second, level I trauma centers more frequently have available resources like designated trauma services and in-house coverage of trauma surgeons for the management of MT patients which improve hospital and patient outcomes.[35, 36]

Implementing trauma systems results in a survival benefit and a functional benefit for trauma patients admitted to level I centers which even increased over time.[37, 38] There are studies that address quality of trauma care differences between urban and rural areas[29], the influence of geographical distances to a certain level of care[39] and the optimization of access to integrated trauma systems.[40, 41] It is important to consider geographical elements like distances to a level I trauma center when designing a trauma system since it could give an extra dimension to the association between level of trauma care and patient outcomes. When looking at survival, our results suggest that general trauma populations can be cared for at nearby trauma centers, while MT populations have a survival benefit from care in level I trauma centers despite a certain distance to that center.

A previous published systematic review on the impact of level of trauma care on outcome found a clear benefit of level I trauma centers compared to non-level I trauma care.[11] However, this study did not perform a meta-analysis and included fewer studies. Our meta-analysis provides new insights and more consistent results that level I trauma centers perform better in treating MT populations.

Almost all included studies defined MT as ISS > 15. Two of the included studies[20, 30] provided additional comparisons between different levels of trauma care and in-hospital mortality in patients with ISS > 24. One study[30] found a survival benefit in level I trauma centers compared to level II trauma centers. The second study[20] reported no case fatality differences between level I and level II trauma centers. An ISS > 24 meta-analysis was not possible. Studies focusing on specific populations were excluded from our systematic review. However, hierarchical survival benefits have for instance been reported for pediatric patients[42, 43], multiply injured elderly patients[44, 45], severe traumatic brain injury patients[46, 47] and hemodynamically unstable patients.[48, 49] Patients admitted to level I centers are associated with the occurrence of more complications[30] and a higher chance of organ failure.[28] These subgroup studies are relevant because these studies fill the gap of possible case-mix differences in major and general trauma populations between centers with a different level of trauma care.

Limitations

Our study has several limitations. First, only a few studies adjusted for comorbidity and transferred patients. There is a possibility that the results were confounded due to case-mix differences between different levels of trauma care. Six of the included studies excluded transferred patients. If transferred patients were not excluded and studies did not adjust for this group, the results should be interpreted with caution. When non-level I centers receive MT patients they will often transfer these patients to a level I center. This will result in an underestimation of the survival benefit of level I centers. Second, none of the included studies have corrected for injury severity within a specific body region. This could have been informative considering groups with specific injuries, like head injuries, might have been admitted to level I trauma centers because of regional agreements or availability of a neurosurgeon. Third, all studies were conducted in high income countries with the exception of two studies. There was a clear overrepresentation of studies conducted in the USA. If more studies originating from Europe, Latin America, Africa and Asia had been available for inclusion in this review, a broader representation of the maturation state of trauma networks and a more diverse representation of local and regional process elements of trauma care would have been presented in this review. Fourth, by restricting our search to publications in English, a possible language bias could have been introduced. Fifth, randomized trials were not available in the literature, probably due to ethical arguments. By including observational studies only, the results might have been confounded. Finally, we were only able to analyze mortality while non-fatal patient outcomes become more important. Few studies reported non-fatal outcomes and those that were reported were not structurally reported in a similar manner. A level of trauma care comparison regarding patient-reported outcomes was found in just one included study.[18] This study, focusing on level I and level II centers, reported no level classification benefit regarding quality of life.

Implications

Presumably, all studies that assessed the association between level of trauma care and in-hospital and patient-reported outcome measures were included. A survival benefit was found for MT populations when being treated in level I trauma centers. These results should be taken into account when implementing or evaluating trauma systems. Future research should focus on what specific subpopulations benefit from treatment in level I trauma centers and on non-fatal outcomes when assessing the association between level of trauma care and clinical and patient-reported outcome measures.

Conclusion

This systematic review and meta-analysis revealed that there is a survival benefit for major trauma patients treated in level I centers compared to major trauma patients treated in non-level I trauma centers. For the general trauma population, there was no association between level of trauma care and mortality. Future research should focus on subgroups and non-fatal outcomes to further broaden our understanding of the different levels of trauma care in association with in-hospital and patient-reported outcome measures.

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Appendix A

	hits	after removing duplicates
embase.com	1842	1825
Medline Ovid	1848	456
Web of science Core Collection	1569	643
Cochrane CENTRAL registry or trials	168	43
Google scholar	200	169
Total	5627	3136

embase.com 1842: ('emergency health service'/de OR 'emergency care'/de OR 'hospital emergency service'/de OR 'emergency ward'/de OR (((emergenc* OR trauma* OR acute) NEAR/3 (service OR hospital OR cent* OR medical-service* OR department* OR ward OR hospital))):ab,ti) AND ('tertiary health care'/de OR 'university hospital'/de OR 'helicopter'/de OR 'air medical transport'/de OR (level-1 OR higher-level OR level-one OR level-I OR ((tertiary OR universit* OR academic*) NEXT/1 (care OR healthcare OR hospital* OR trauma-cent* OR ED OR emergenc*-department* OR affiliat*)) OR helicopter* OR (air NEAR/3 (ambulance* OR transport*))):ab,ti) AND ('secondary health care'/de OR 'primary health care'/de OR (lower-level OR level-2 OR level-3 OR level-4 OR level-5 OR level-ii OR level-iii OR level-iv OR level-v OR level-two OR level-three OR level-four OR level-five OR nontertiary OR non-tertiary OR ((remote OR secondary OR primary OR peripheral*) NEXT/1 (care OR healthcare OR hospital* OR centre OR center* OR ED OR department*)) OR major-cent* OR major-trauma-cent*):ab,ti) AND ('mortality'/exp OR 'mortality risk'/exp OR 'survival'/exp OR 'length of stay'/de OR 'hospital discharge'/de OR 'intensive care unit'/exp OR 'treatment outcome'/exp OR 'fatality'/de OR (mortalit* OR surviv* OR ((length OR long* OR short*) NEAR/3 stay) OR discharge* OR intensive-care-unit* OR icu OR benefit* OR outcome* OR death* OR fatal*):ab,ti) NOT ([Conference Abstract]/lim AND [1800-2016]/py) AND [English]/lim NOT ([animals]/lim NOT [humans]/lim)

Medline Ovid 1848: (Emergency Service, Hospital/ OR Emergency Treatment/ OR Emergency Service, Hospital/ OR (((emergenc* OR trauma* OR acute) ADJ3 (service OR hospital OR cent* OR medical-service* OR department* OR ward OR hospital))).ab,ti.) AND (Tertiary Healthcare/ OR Tertiary Care Centers/ OR Hospitals, University/ OR Aircraft/ OR Air Ambulances/ OR (level-1 OR higher-level OR level-one OR level-I OR ((tertiary OR universit* OR academic*) ADJ (care OR healthcare OR hospital* OR trauma-cent* OR ED OR emergenc*-department* OR affiliat*)) OR helicopter* OR (air ADJ3 (ambulance* OR transport*))).ab,ti.) AND (Secondary Care / OR Primary Health Care / OR (lower-level OR level-2 OR level-3 OR level-4 OR level-5 OR level-ii OR level-iii OR level-iv OR level-v OR level-two OR level-three OR level-four OR level-five OR nontertiary OR non-tertiary OR ((remote OR secondary OR primary OR peripheral*) ADJ (care OR healthcare OR hospital* OR centre OR center* OR ED OR department*)) OR major-cent* OR major-trauma-cent*).ab,ti.) AND (Mortality/ OR Mortality .fs. OR Survival/ OR Length of Stay/ OR Intensive Care Units/ OR Treatment Outcome/ OR fatality/ OR (mortalit* OR surviv* OR ((length OR long* OR short*) ADJ3 stay) OR discharge* OR intensive-care-unit* OR icu OR benefit* OR outcome* OR death* OR fatal*).ab,ti.) NOT (news OR congres* OR abstract* OR book* OR chapter* OR dissertation abstract*).pt. AND english.la. NOT (exp animals/ NOT humans/)

Web of science Core Collection 1569: TS=(((((emergenc* OR trauma* OR acute) NEAR/2 (service OR hospital OR cent* OR medical-service* OR department* OR ward OR hospital)))) AND ((level-1 OR higher-level OR level-one OR level-I OR ((tertiary OR universit* OR academic*) NEAR/1 (care OR healthcare OR hospital* OR trauma-cent* OR ED OR emergenc*-department* OR affiliat*)) OR helicopter* OR (air NEAR/2 (ambulance* OR transport*)))) AND ((lower-level OR level-2 OR level-3 OR level-4 OR level-5 OR level-ii OR level-iii OR level-iv OR level-v OR level-two OR level-three OR level-four OR level-five OR nontertiary OR non-tertiary OR ((remote OR secondary OR primary OR peripheral*) NEAR/1 (care OR healthcare OR hospital* OR centre OR center* OR ED OR department*)) OR major-cent* OR major-trauma-cent*)) AND ((mortalit* OR surviv* OR ((length OR

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5

CHAPTER 6

Evaluating associations between level of trauma care and outcomes of patients with specific severe injuries: a systematic review and meta-analysis

Highlights

- *Level of trauma care classification is associated with improvements in outcomes for the severely injured.*
- *Populations of severely injured with specific injuries admitted to a level I trauma center have a survival benefit.*
- *The severely injured admitted to higher levels of care have a higher resource demand.*

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Abstract

Background Trauma networks have multiple designated levels of trauma care. This classification parallels concentration of major trauma care, creating innovations and improving outcome measures.

Objectives To assess associations of level of trauma care with patient outcomes for populations with specific severe injuries.

Methods A systematic literature search was conducted using six electronic databases up to April 19, 2022 (PROSPERO CRD42022327576). Studies comparing fatal, non-fatal clinical, or functional outcomes across different levels of trauma care for trauma populations with specific severe injuries or injured body region (Abbreviated Injury Scale ≥ 3) were included. Two independent reviewers included studies, extracted data, and assessed quality. Unadjusted and adjusted pooled effect sizes were calculated with random-effects meta-analysis comparing level I and level II trauma centers.

Results Thirty-five studies (1,100,888 patients) were included, of which 25 studies (n = 443,095) used for meta-analysis, suggesting a survival benefit for the severely injured admitted to a level I trauma center compared to a level II trauma center (adjusted OR 1.15 (95% CI 1.06-1.25)). Adjusted subgroup analysis on in-hospital mortality was done for patients with traumatic brain injuries (OR 1.23, 95% CI 1.01-1.50) and hemodynamically unstable patients (OR 1.09, 95% CI 0.98-1.22). Hospital and intensive care length of stay resulted in an unadjusted MD of -1.63 (95% CI -2.89--0.36) and -0.21 (95% CI -1.04-0.61), respectively, discharged home resulted in an unadjusted OR of 0.92 (95% CI 0.78-1.09).

Conclusion Severely injured patients admitted to a level I trauma center have a survival benefit. Non-fatal outcomes were indicative for a longer stay, more intensive care, and more frequently post-hospital recovery trajectories after being admitted to top levels of trauma care. Trauma networks with designated levels of trauma care are beneficial to the multidisciplinary character of trauma care.

Background

Trauma is one of the leading causes of death worldwide. Injuries account for eight percent of global mortality, taking the lives of nearly 4.5 million people around the world each year.[1] These deaths, represent a fraction of those injured each year and many trauma patients suffer from long-term morbidity. [2] In the pursuit of optimal care for trauma patients, regional trauma systems have been implemented worldwide, showing significant improvement in trauma outcomes.[3-7]

Regional trauma systems can be distinguished by inclusive and exclusive trauma networks. Within an exclusive trauma network, care is limited to several highly specialized hospitals, whereas all facilities within inclusive designated trauma networks participate in care for injured patients. Hospitals are commonly categorized by level based on criteria developed by professionals. These criteria sets are dependent on local public health care context. Higher level facilities have more continuously available resources for the most severely injured patients, lower level facilities are utilized for patients with minor injuries.[7, 8]

When assessing outcomes across levels of trauma care, major trauma (MT, injury severity score (ISS) > 15)) patients benefit from the highest level of trauma care.[9] However, defining major trauma based on an anatomical scoring system has restrictions. The ISS might underestimate the severity of injury for some trauma patients[10, 11] and major trauma populations are very heterogeneous. It would be of great interest zooming in on the beneficial effect of trauma center designation on patients with specific severe injuries.[12] This study aimed to provide an overview, including data synthesis, of clinical outcomes in subgroups of severely injured trauma populations across different levels of trauma care in trauma networks.

Methods

This systematic review was reported according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA[13]) checklist and was registered in the International Prospective Register of Systematic Reviews (PROSPERO[14]) under identification number CRD42022327576 (submission date April 24, 2022; publication date June 9, 2022).

Search strategy and selection criteria

On April 19, 2022 search engines Embase via embase.com, Medline ALL via Ovid, Web of science Core Collection, Cochrane Central registry of trials and Google scholar were used to identify publications examining trauma patient outcomes in relation to trauma center level comparison. Search terms were designed by an experienced biomedical information specialist (WMB), and provided in Appendix A. The search combined thesaurus terms and words and phrases in title and abstract in many variations for a) emergency service or trauma ward, b) tertiary center or academic hospital, c) lower level centers such as secondary or primary healthcare with d) outcomes such as mortality and length of stay. Titles and abstracts of retrieved references were reviewed using the method as published by Bramer et al[15] in EndNote[16] (version 20, The Endnote Team, Clarivate, Philadelphia, PA, USA).

Studies comparing different levels of trauma care for traumatic injuries in relation to fatal and non-fatal clinical outcome measures were considered eligible for inclusion. Studies were included if they examined specific severe injuries or severely injured body regions (Maximum Abbreviated Injury Scale (MAIS) ≥ 3 or ISS > 15), of all causes, and the studied population was aged ≥ 14 years. Studies focusing on general (major) trauma populations, transferred patients, burn patients, pediatric patients, or patients with an isolated hip fracture were excluded, as well as studies addressing trauma system implementation, geography, volume-outcome, economic evaluation, prediction, or general public health issues. Non-available full text articles, conference abstracts, forums, panel discussion, or experience talk were also excluded. Two reviewers (J.C.V.D. and C.A.S.) screened titles and abstracts for eligibility. Full text documents were retrieved and independently screened by two reviewers (J.C.V.D. and L.A.R.). Disagreements were resolved by consensus or by consulting a third reviewer (C.A.S.). Finally, all references of the full text inclusions were screened for additional potential inclusions.

Data extraction and quality assessment

Two reviewers (J.C.V.D. and L.A.R.) independently extracted characteristics on each included study: year of publication, type of trauma center level comparison, study design, country, study period, data source, sample size, in- and exclusion criteria, severity of injured population, population characteristics, study outcome measures, and key findings. Quality assessment was performed by two reviewers (J.C.V.D. and L.A.R.) for each included study. Studies were scored using the Newcastle-Ottawa Scale (NOS[17]), creating international standardized comparability. In addition, a quality assessment tool, based on existing literature, was created to assess quality, generalizability, and risk of bias of the included studies.[18] For data synthesis J.C.V.D. and L.A.R collected data independently. The primary outcome parameter was in-hospital mortality. Secondary outcome parameters included hospital length of stay (HLOS), ICU length of stay (ICU LOS) and discharge destination with or without, home health. Disagreements on characteristics of studies, quality assessment, or data extraction, were resolved through discussion, or by consulting a third reviewer (C.A.S).

Data analysis

Data was analyzed using the R Software Environment (version 4.1.1, The R Foundation for Statistical Computing, Vienna Austria).

To examine the association between trauma center level and clinical outcomes for traumatic injuries, a meta-analysis was performed. Subgroup analyses were performed for severely injured patients with injuries in a specific body region, patients with penetrating injuries, or hemodynamically unstable patients if ≥ 3 studies were found on specific injuries.

The main focus was a comparison of level I (highest level) and non-level I trauma care. If level distinction was not numerical, the highest level of care was used to compare with lower levels of trauma care. Tertiary, academic trauma care and major trauma centers were considered the equivalent of level I, if a study was conducted outside USA. When studies compared multiple levels, all individual comparisons were included in the meta-analysis. When studies merged levels in their comparison, results were only included in qualitative analysis.

For unadjusted meta-analysis crude numbers and adjusted odds ratios (OR) with 95% confidence intervals (95% CI) were extracted for binary/categorical outcome measures and means with standard deviation (SD) and absolute numbers for continuous outcome measures. For adjusted meta-analysis, adjusted OR with 95% CI were extracted. The Mantel-Haenszel method was used to provide a pooled unadjusted OR, the inverse variance method provided a pooled adjusted OR and the mean difference (MD) with 95% CI was used as summary statistic for unadjusted continuous outcome measures. Studies were pooled using a random-effects meta-analysis. Random effects were used to compensate for heterogeneity, thereby addressing differences in study periods, regional/geographical characteristics, and trauma populations. Heterogeneity between studies was assessed using both the I^2 and the X^2 statistics. I^2 values were used to interpret the amount of heterogeneity: 30-60% possible moderate, 50-90% possible substantial and 75-100% considerable.[19] Funnel plots were used to detect publication bias.[20]

As a comparative measure of effect for unadjusted OR, the number needed to treat for an additional beneficial outcome (NNTB) was calculated.

Results

Search

The study selection PRISMA flow diagram is depicted in Figure 1. The initial search identified 7,502 records. After removing duplicates, 4,151 records were screened on title and abstract, resulting in 122 potentially eligible studies. After full text screening 32 studies were included.[21-52] Three additional studies were identified using reference chasing[53-55] , resulting in 35 included studies for the systematic review ; ten studies on traumatic brain injuries (TBI) [22, 26, 29, 30, 33, 45, 49, 50, 53, 54], six studies on thoracic injuries [21, 25, 27, 28, 46, 55], six studies on abdominal injuries [34, 35, 38, 47, 48, 52], three studies on spinal cord injuries [23, 37, 41], five studies on lower extremity injuries [24, 39, 40, 42, 43], and five studies on hemodynamically unstable patients.[31, 36, 44, 51, 54]

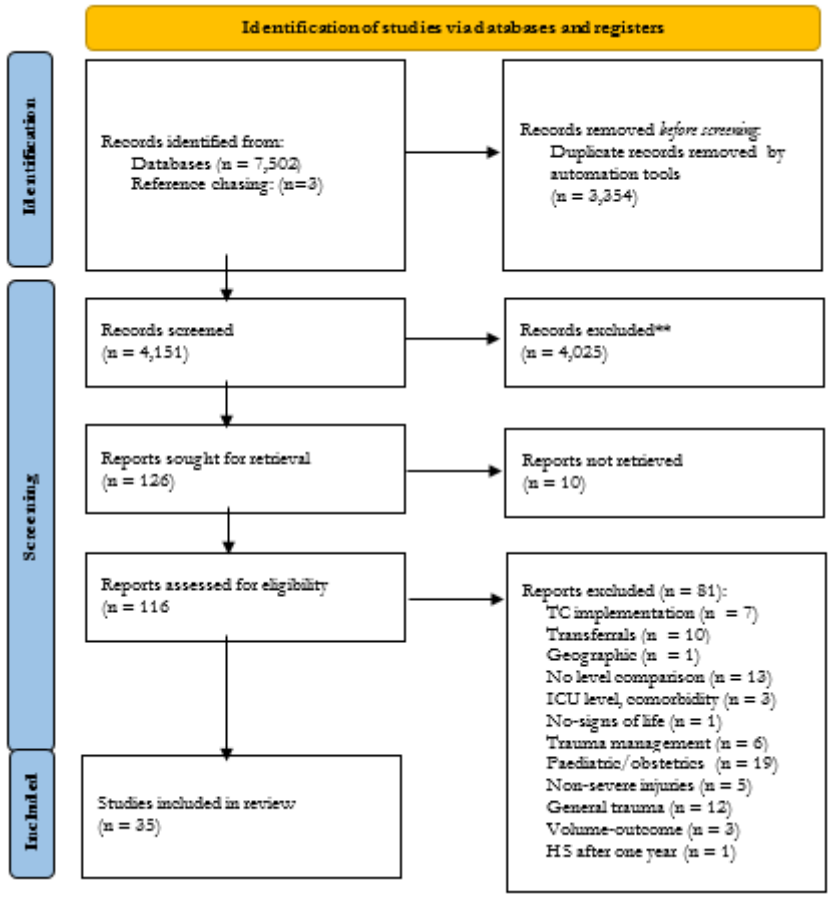


Figure 1. PRISMA 2020 flow diagram

Study Characteristics

The included studies comprised a total of 1,100,888 patients with a minimum age of 14. (Table 1) Most studies (n=32, 91%) studies were retrospective cohorts [21-34, 36, 37, 39, 41-53, 55], three (9%) studies were prospective cohorts.[35, 40, 54] The majority (n=32, 91%) was USA based[21-23, 25-30, 32-39, 41-55], one study was conducted in France [24], one in Israel [40], and one study in Canada [31]. A total of 26 (74%) studies[22-27, 29-32, 34-36, 38-40, 43-52] compared level I with level II trauma centers. Other studies compared level I with unranked[54, 55], level I with IV and unranked[42], level I/II with III/IV[21, 41], level I/II with unranked[53], level I with III[33], level I with II/III/IV[37], level I/II/III with unranked. [28]

Table 1. Characteristics and key findings of included articles.

Author, Year	Level Comparison	Study Design	Country	Data Source	Period	Inclusion	Exclusion	Sample Size	ISS (Mean, Median, Min)	Outcome	Overall Key Findings
Traumatic Brain Injury											
Alkhoury et al., 201122	Level I vs. II (ACS)	RCS	United States	NTDB	2001–2006	Isolated TBI, ED GCS score < 9	Incomplete records	31,736	(GCS score 3–4:74%)	Mortality, HLOS, ICU LOS, MVD, DD, major CR	Mortality crude: Level I = II. DD home: Level I > II. HLOS, ICU LOS, MVD, CR DVT: Level I > II.
Brown et al., 201050	Level I vs. Level II (ACS)	RCS	United States	NTDB	2002–2006	ED GCS score ≤ 12, survived to discharge	Incomplete FIM scores	25,170	GCS score ≤ 8: LI: 21 (13) LII: 21 (13) GCS score 9–12: LI: 15 (12) LII: 14 (11)	HLOS, FIM (FI, IE)	FI, IE, HLOS severe TBI: Level I > II. FI, IE, HLOS moderate TBI: Level I = II.
Chalouhi et al., 201926	Level I vs. Level II (PTSF)	RCS	United States	PTOS	2002–2017	Age ≥18 y, TBI GCS score < 9, craniotomy, craniectomy	-	3,980	LI: 29.5 (10.2 LII: 29.6 (9.5)	Mortality, HLOS, ICU LOS, FIM at discharge	Mortality: Level I < II. FIM, HLOS, ICU LOS: Level I > Level II.
Deng et al., 201929	Level I ACS vs. Level II ACS vs. other (level unknown and unranked)	RCS	United States	NTDB (NSP)	2003–2012	Age ≥18 y, TBI firearm injured	Missing data outcome variables	8,148	77% ISS > 15 10% ISS missing	Mortality, HLOS, ICU LOS, CR, DD	Mortality, HLOS, ICU LOS, CR: Level I = II. DD home: Level I > II.

Author, Year	Level Comparison	Study Design	Country	Data Source	Period	Inclusion	Exclusion	Sample Size	ISS (Mean, Median, Min)	Outcome	Overall Key Findings
DuBose et al., 200830	Level I vs. Level II (ACS)	RCS	United States	NTDB	5-year period	Isolated TBI MAIS ≥3, Other injury MAIS <3	DOA	16,035	LI: 20.6 (9.9) LII: 20.9 (9.7)	Mortality, HLOS, ICU LOS, MVD, CR, FIM	Mortality, CR: Level I < Level II. HLOS, ICU LOS: level I > II. MVD, FIM: level I = II.
Gupta et al., 202033	Level I vs. Level III (ACS)	RCS	United States	TR, Medical charts	2012–2014	Age ≥18 y, TBI GCS score ≥ 13, CT diagnosed minor injuries	Open skull fracture, intubation, HU, bleeding diathesis history, MAIS >2 other than head	191	LI: 16 (10–17) LIII: 10 (9–13)	Mortality, HLOS, ICU LOS, CR, need for TBI interventions	Mortality crude, CR, ICU LOS, need for TBI interventions: Level I = III. HLOS: level I > II.
Haas et al., 200854	Level I (ACS or state/regional) vs. non-designated TC	PCS	United States	NSCOT	7/2001–11/2002	Age 18–84 y, TBI MAIS ≥3, pupillary abnormality, CT midline shift, English/Spanish-speaking, US residents	No vital signs and death <30 m, presentation ≥24 h, age ≥65 y and isolated hip fracture, major burns, isolated gunshot head, incarcerated, homeless	766	TC: 30.9 (17.0) Non-TC: 23.6 (9.6)	Mortality, ICU admission	Mortality in patients receiving early operative intervention: level I < non-TC.

Author, Year	Level Comparison	Study Design	Country	Data Source	Period	Inclusion	Exclusion	Sample Size	ISS (Mean, Median, Min)	Outcome	Overall Key Findings
Kaufman et al., 201853	Level I/II vs. neurosurgery capable non-designated TC	RCS	United States	State ED Database, State Inpatient Database	2011–2012	TBI or neck MAIS ≥3, MAIS ≤2 other	Late effects or complications of injury	62,198	TC: 14 (10–17) Non-TC: 14 (10–16)	Mortality, DD	Mortality: TC = neurosurgery capable non-TC. DD home: TC > neurosurgery capable non-TC.
Plurad et al., 202145	Level I vs. Level II (ACS)	RCS	United States	TQP-PUF	2017	Age 16–90 y, TBI MAIS ≥3, MAIS <3 other	Transfers	39,764	LI: 16.6 (6.7) LII: 15.4 (7.1)	Mortality, HLOS, ICU LOS, DD, procedures performed, CR.	Mortality: Level I = level II. HLOS, ICU LOS, DD: level I > level II.
Yeates et al., 202049	Level I vs. II (ACS)	RCS	United States	TQIP	2010–2016	Age ≥18 y, TBI MAIS >3	Death <24 h, nonsurvivable TBI (MAIS = 6)	204,895	LI: 17 (12) LII: 17 (12)	Mortality, HLOS, ICU LOS, VTE rate, chemoprophylaxis initiation time	Mortality crude, HLOS, ICU LOS: level I = level II.

Author, Year	Level Comparison	Study Design	Country	Data Source	Period	Inclusion	Exclusion	Sample Size	ISS (Mean, Median, Min)	Outcome	Overall Key Findings
Spinal Injuries											
Baron et al., 202123	Level I vs. II (ACS)	RCS	United States	TQIP	2013–2015	Spinal trauma	Transfer, missing data on ACS level, MAIS spine = 6, death/discharge <24 h, MAIS >2 other than head	21,580	LI: MAIS ≥3 65%, LII: MAIS ≥3 64%	Mortality, HLOS, ICU LOS, CR	Mortality, HLOS: Level I = II. ICU LOS: Level I > II. CR: Level I < Level II.
Macias et al., 200941	Level I + II vs. non-TC	RCS	United States	State hospital discharge files MEDPAR	2001	Age ≥16 y, SCI with or without fracture	Late effects or complications due to medical/surgical care, foreign bodies, poisoning, external causes	4,121	TC: 19.1 (0.3) non-TC: 14.7 (0.2)	Mortality, paralysis rate	Mortality: Level I = II.
Williamson et al., 202137	Level I vs. II + III + IV (ACS)	RCS	United States	NTDB	2011–2014	Age ≥18 y, SCI with fracture	Concurrant TBI, self-reported multiple race, missing data on surgery/transfer/ACS level, ISS < 2, ED-SBP < 40, Invalid records	10,844	LI: 25 (16–33) LII + III + IV: 21 (14–29)	Mortality, HLOS, ICU LOS, MVD, DD	Mortality, MVD: Level 1 = Level II + III + IV. HLOS, ICU LOS, DD: Level I > level II + III + IV

Author, Year	Level Comparison	Study Design	Country	Data Source	Period	Inclusion	Exclusion	Sample Size	ISS (Mean, Median, Min)	Outcome	Overall Key Findings
Thoracic injuries											
Ahmed et al., 201921	Level I + II (ACS) vs. III + IV (ACS) + unranked institutions	RCS	United States	NTDB	2012–2014	Age ≥65 y, thoracic MAIS >0 after GLF	No signs of life	15,256	High level: 9 (5–13) low level: 9 (5–12)	Mortality, HLOS	Mortality, HLOS: TC level high = low.
Bukur et al., 201225	Level I vs. II vs. III + IV (ACS)	RCS	United States	NTDB	5-year period	Patients receiving thoracotomy	Missing time to procedure, Thoracotomy <1 h, Missing data on ACS level	2,367	LI: 31.3 (18.9) LII: 30.9 (19.2), LIII/IV: 32.0 (21.8)	Mortality, HLOS, ICU LOS, MVD	Mortality, HLOS, ICU LOS, MVD: level I = II = III + IV.
Checchi et al., 202027	Level I vs. II vs. other (ACS + non-ACS	RCS	United States	NTDB	2013–2016	Age ≥16 y, Penetrating injuries	Transfers	68,727	MAIS ≥3 16 (10–25)	Mortality	Mortality: level I = II.
Choi et al., 202128	Level I + II + III vs. IV + unranked (ACS)	RCS	United States	NEDS	2016	Age ≥18 y, rib fractures	Missing data on ACS level, transfers, death at ED	504,085	TC: 7.7 (0.3) non-TC: 3.8 (0.6)	ED mortality, ED DD, mortality, HLOS, SSRF, DD	Mortality: level I + II + III = IV + unranked. HLOS, DD: level I + II + III > IV + unranked
Oliver et al., 201955	Level I vs. non–Level I (state designated)	RCS	United States	NTDB	2014–2015	Patients receiving thoracotomy < 24 h	Missing time of thoracotomy, missing DD	3,183	LI: 25 (16–38) non-LI: 25 (16–36)	Mortality (in-hospital survival)	Mortality: level I < II.

Author, Year	Level Comparison	Study Design	Country	Data Source	Period	Inclusion	Exclusion	Sample Size	ISS (Mean, Median, Min)	Outcome	Overall Key Findings
Thoracic injuries											
Rockne et al., 202146	Level I vs. II (ACS)	RCS	United States	TQIP	2010–2015	Age ≥18 y, rib fractures with SSRF	—	14,046	LI: 22 (14–29), LII: 19 (14–27)	Mortality, HLOS, ICU LOS, MVD, respiratory CR, DD	Mortality, CR: level I = II. HLOS, DD: Level I > II. ICU LOS, MVD: level I < II.
Abdominal injuries											
Harbrecht et al., 200434	Level I vs. II (PTSF)	RCS	United States	PTOS	1998–2000	Age ≥16 y, Patients with splenic injuries	Death at ED, penetrating injuries	2,138	LI: 26.0 (0.4), LII: 26.2 (0.5)	Mortality, HLOS, ICU LOS, operative/nonoperative (success/failed) management	Mortality crude: Level I = II. HLOS, ICU LOS: Level I > II.
Helling et al., 199735	Level I vs. II (Missouri state designated)	PCS	United States	Hospital record sPatient charts	1987–1992	Patients with liver injuries	Death before liver CT or laparotomy, TBI MAIS ≥2, transfer <24 h	300	LI: 22 (14.2) LII: 20 (10.3)	Mortality, HLOS, ICU LOS, time to OR	Mortality crude, HLOS: Level I = II. ICU LOS: level I < II.
Hotaling et al., 201238	Level I vs. II vs. III + IV	RCS	United States	NTDB	2002–2007	Patients with renal injuries converted to AAST grades	Patients with AIS codes mapped >1 AAST grades	6,290	LI: 22.0 (20) LII: 20.1 (21) LIII-IV: 19.5 (23)	Mortality, HLOS, ICU LOS, DD, successful initial management, nephrectomy rates	Mortality crude: level I = II. HLOS, ICU LOS: level I > II. DD: level I < II. Conservative therapy: level I > II / III + IV. Definite initial therapy: level I > II / III + IV.

Author, Year	Level Comparison	Study Design	Country	Data Source	Period	Inclusion	Exclusion	Sample Size	ISS (Mean, Median, Min)	Outcome	Overall Key Findings
Abdominal injuries											
Lewis et al., 202152	Level I vs. II (ACS)	RCS	United States	TQIP	2013–2016	Age ≥16 y, blunt liver injuries (MAIS ≥3)	Penetrating injuries, transfer in, MAIS ≥3 other than liver, death <72 h, no LMWH administered for VTE prophylaxis	2,825	≥9 40% ISS > 15	Mortality, HLOS, ICU LOS, CR	Mortality, MVD: level I = II. HLOS, ICU LOS, CR: level I < II.
Sheehan et al., 202047	Level I vs. II (ACS)	RCS	United States	TQIP	2010–2016	Age ≥18 y, penetrating abdominal aortic injury	—	378	LI: 26.0 (9) LII: 25.0 (5)	Mortality, HLOS, ICU LOS, MVD, time to haemorrhage control,	Mortality, HLOS, ICU LOS, MVD, CR: Level I = II
Tignanelli et al., 201848	Level I vs. II (ACS)	RCS	United States	TQIP	2011–2016	Age ≥16 y, blunt liver injuries (MAIS ≥3)	No signs of live at ED, transfer	454	≥5 82% ISS > 15	Mortality, HLOS, ICU LOS, death <48 h, management strategy, CR, failure to rescue	Mortality: Level I < II. HLOS, CR: level I = II. ICU-LOS: level I > II.

Author, Year	Level Comparison	Study Design	Country	Data Source	Period	Inclusion	Exclusion	Sample Size	ISS (Mean, Median, Min)	Outcome	Overall Key Findings
Hemodynamically unstable											
Dufresne et al., 201731	Level I vs. II vs. III vs. IV (ACS)	RCS	Canada	Quebec TR	1998–2014	Age ≥16 y, SBP < 90, surgical care or death without <6 h, torso injury (MAIS ≥4)	TBI MAIS >3	922	>15	Mortality, surgical delay, CR, HLOS	Mortality: level I < II/III/IV. CR, HLOS: level I > II.
Haas et al., 200854	Level I (ACS or state) vs. nondesignated TC	PCS	United States	NSCOT	7/2001–11/2002	Age 18–84 y, penetrating injury (MAIS ≥3), SBP < 90, English/Spanish-speaking, US residents	No vital signs and death within 30 m, presentation ≥24 h, age ≥65 y and isolated hip fracture, major burns, isolated gunshot head, incarcerated, homeless	565	TC: 19.1 (22.0) non-TC: 17.9 (15.2)	Mortality, ICU admission	Mortality in patients receiving early operative intervention: level I < non-TC.
Hamidi et al., 201951	Level I vs. II (ACS)	RCS	United States	TQIP	2013–2014	Age ≥18 y, MTP, transfusion ≥10 units pRBC <24 h	Transfer in, DOA	2,776	LI: 29 (19–41), LII: 27 (18–38)	Mortality, HLOS, ICU/MV free LOS, blood transfusion, CR	Mortality, HLOS: Level I < II. CR: Level I > II

Author, Year	Level Comparison	Study Design	Country	Data Source	Period	Inclusion	Exclusion	Sample Size	ISS (Mean, Median, Min)	Outcome	Overall Key Findings
Hemodynamically unstable											
Herrera-Escobar et al., 201836	Level I vs. II (ACS)	RCS	United States	NTDB	2007–2012	Age 18–64 y, ISS > 15, SBP < 90	Transfer, DOA, Patients with burns, missing data on ED SBP / injury mechanism	13,846	LI: 27 (22–38) LII: 27 (22–38)	Mortality <24 h, mortality, ICU admission, MV requirement	Mortality 4–7 h postadmission: Level I < II.
Plurad et al., 202145	Level I vs. II (ACS)	RCS	United States	TQP-PUF	2017	Age ≥14 y, SBP < 90	Patients with severe/critical/MAIS = 6 of head/neck/extremities, missing data on ACS level, Transfer	7,264	LI: 19.3 (15), LII: 16.7 (14)	Mortality, HLOS, ICU LOS	Mortality, ICU LOS: Level I = II. HLOS: level I > II.
Penetrating torso injuries											
Grigorian et al., 201932	Level I vs. Level II (ACS)	RCS	United States	TQIP	2010–2016	Patients with gunshot injuries	Patients with Isolated acetabular fractures	17,965	LI: 14 (9–24) LII: 14 (9–22)	Mortality, HLOS, ICU LOS, MVD, blood products transfusion, thoracotomy, time to surgical intervention, CR	Mortality: Level I < II. HLOS, MVD: level I = II. ICU LOS, CR: Level I > II.

Author, Year	Level Comparison	Study Design	Country	Data Source	Period	Inclusion	Exclusion	Sample Size	ISS (Mean, Median, Min)	Outcome	Overall Key Findings
Lower-extremity injuries											
Bouzat et al., 201324	Level I vs. Level II	RCS	France	Trenau	2009	Patients with pelvic injuries (MAIS ≥3)	Patients with Isolated acetabular fractures	65	LI: 30 (13–75), LII: 22 (9–59)	Mortality, TRISS	Mortality crude: level I < II. Mortality O/E: Level I = II.
Jakob et al., 202139	Level I vs. Level II (ACS)	RCS	United States	TQIP	2013–2016	Age ≥18 y, pelvic fracture (MAIS ≥3), Primary admission	Penetrating injuries death <72 h, MAIS ≥3 other than pelvic, Angiography >24 h, Unknown or VTE prophylaxis other than UH/LMWH	3,906	≥9 26% ISS >15	Mortality, HLOS, ICU LOS, CR	Mortality, HLOS: Level I = II. ICU-LOS, CR: Level I < II
Khoury et al., 201640	Level I vs. II	PCS	Israel	NTR, EMS, ED, hospital records, survey	—	Age ≥18 y, femoral shaft fracture (AO/OTA 32 group)	Age ≥65 y patients with pathological fractures, Discharged without signing IC	238	≥9 52% ISS > 15	Mortality, HLOS >11 days, ICU admission, CR, DD	Mortality crude, CR: Level I > II. HLOS >11 d, DD: Level I = II.

Author, Year	Level Comparison	Study Design	Country	Data Source	Period	Inclusion	Exclusion	Sample Size	ISS (Mean, Median, Min)	Outcome	Overall Key Findings
Lower-extremity injuries											
Morshed et al., 201542	Level I vs. IV + other	RCS	United States	NSCOT	2001–2002	Age 18–84 y, Pelvic/Acetabular injury, Other MAIS ≥3, English speaking, US residents	No vital signs and death within 30 m, presentation ≥24 h age ≥65 y and isolated hip fracture, major burns, homeless,	2,644	LI: 11.3 (14.7), Non-TC: 22.5 (22.3), LI: 22.3 (44.8) Non-TC: 21.0 (25.0) (weighted)	Mortality, death <90 days, SF-36 and MFA after 1 year	Mortality: Level I = non-trauma centers. SF-36, MFA 1 y: Level I > non-TC.
Oliphant et al., 201843	Level I vs. II (ACS)	RCS	United States	MTQIP	2011–2017	Age ≥16, ISS ≥ 5, (partially unstable) pelvic ring fracture	Penetrating injuries, No signs of life ED transfer, missing critical data	1,220	≥5 71% ISS > 15	Mortality, death <48 h, HLOS, ICU LOS, initial management, orthopaedic strategy, CR, failure to rescue	Mortality: Level I < II. HLOS, ICU LOS, CR: Level I = II.

In-hospital mortality is addressed as mortality, unless stated otherwise. ACS, American College of Surgeons; Retrospective Cohort Study; USA, United States of America; NTDB, National Trauma Data Bank; TBI, Traumatic Brain Injury; ED, Emergency Department; GCS, Glasgow Coma Scale; LOS, Length of Stay; HLOS, Hospital LOS, ICU LOS, Intensive Care Unit LOS; MVD, Mechanical Ventilation duration; DD, Discharge Destination; CR, Complication Rate; DVT, Deep Venous Thrombosis; FIM, Functional Independence Measure; GLF, Ground Level Fall; FI, Functional Independence; IE, Independent Expression; PTOS, Pennsylvania Trauma Outcome Study; NSP, National Sample Program; DOA, Dead On Arrival; TR, Trauma Registry; CT, Computerized Tomography; HU, Hemodynamically Unstable; MAIS, Maximum Abbreviated Injury Scale; TC, Trauma Center; NSCOT, National Study on Costs and Outcomes of Trauma; TQP-PUF, Trauma Quality Program Participant Use File; TQIP, Trauma Quality Improvement Program; VTE, Venous Thromboembolic Event; MEDPAR, Medicare Provider Analysis and Review; SCI, Spinal Cord Injury; NEDS, National Emergency Department Sample; SSRF, Surgical Stabilization of Rib Fractures; PTSF, Pennsylvania Trauma System Foundation; AAST, The American Association for the Surgery of Trauma; LMWH, Low Molecular Weight Heparin; UH, Unfractionated Heparin; SBP, Systolic Blood Pressure; MTP, Massive Transfusion Protocol; pRBC, Packed Red Blood Cell; TRISS, Trauma Revised Injury Severity Score; O/E, Observed Expected; MTQIP, Michigan Trauma Quality Improvement Program; PCS, Prospective Cohort Study; NTR, National Trauma Registry; EMS, Emergency Medical Services; AO/OTA, Arbeitsgemeinschaft für Osteosynthesefragen/Orthopedic Trauma Association; IC, Informed Consent; SF-36, Short Form-36; MFA, Musculoskeletal Function Assessment.

Table 2. Quality assessment and Newcastle-Ottawa Scale (NOS) of included studies

Study, year, subgroup	Head	Alkhoury, 2011	Brown, 2010	Chalouhi, 2019	Deng, 2019	DuBose, 2008	Gupta, 2020	Haas, 2018	Kaufman, 2018	Plurad, 20213	Yeates, 2020
NOS total (9*)		6*	9*	9*	9*	9*	7*	8*	9*	9*	9*
NOS outcome (3*)		3*	3*	3*	3*	3*	3*	3*	3*	3*	3*
NOS comparability (2*)		0*	2*	2*	2*	2*	0*	2*	2*	2*	2*
NOS selection (4*)		3*	4*	4*	4*	4*	4*	3*	4*	4*	4*
Funding identified		-	-	-	-	+	+	+	+	+	-
Conflict of interest declared		-	-	+	+	-	+	+	+	+	-
Adjusted for transfer		Na	-	-	-	-	na	+	-	na	na
Adjusted for comorbidity		Na	+	-	+	-	na	+	+	+	na
Adjusted for demographics		Na	+	+	+	+	na	+	+	+	na
Adjusted for injury severity		Na	+	+	+	+	na	+	+	+	na
All confounders reported		Na	+	+	+	+	na	+	+	+	na
OR's with 95% CI		Na	+	+	+	+	na	+	+	+	na
Discharge home per level (adj.)		-	-	-	+	-	-	-	+	-	-
Discharge home per level (crude)		+	-	-	+	-	-	-	-	+	-
ICU LOS per level (adj.)		-	-	+	+	-	-	-	-	-	-
ICU LOS per level (crude)		+	-	+	-	+	+	-	-	+	+
HLOS per level (adj.)		-	-	+	+	-	-	-	-	-	-
HLOS per level (crude)		+	+	+	-	+	+	-	-	+	+
Mortality per level (adj.)		-	-	+	+	+	-	+	+	+	-
Mortality per level (crude)		+	-	+	+	+	+	+	+	+	+
Baseline per level		+	+	+	-	+	+	+	+	+	+
ISS per level		-	+	+	-	+	+	+	+	+	+
Overall ISS		-	-	-	+	+	-	-	-	+	-
Age ≥ 16		-	-	+	+	-	+	+	-	+	+
2 TC levels separated		+	+	+	+	+	+	-	-	+	+
Definition TC level		+	+	+	+	+	+	+	+	+	+
AIS/ICD revision reported		+	+	-	+	-	-	+	+	-	-
Registry based		+	+	+	+	+	+	+	+	+	+
Nation- or region wide		+	+	+	+	+	-	+	+	+	+
Clear in- and exlusion criteria		+	+	+	+	+	+	+	+	+	+

Study, year, subgroup	Spinal injuries	Baron, 2021	Macias, 2009	Williamson, 2021	Thoracic injuries	Ahmed, 2019	Bukur, 2012	Checchi, 2020	Choi, 2021	Oliver, 2019	Rockney, 2021	Oliphant, 2018
NOS total (9*)		9*	9*	9*		9*	9*	7*	9*	8*	9*	9*
NOS outcome (3*)		3*	3*	3*		3*	3*	3*	3*	3*	3*	3*
NOS comparability (2*)		2*	2*	2*		2*	2*	2*	2*	2*	2*	2*
NOS selection (4*)		4*	4*	4*		4*	4*	4*	4*	3*	4*	4*
Funding identified		-	+	-		+	-	+	-	-	+	+
Conflict of interest declared		+	-	+		+	-	+	+	-	-	+
Adjusted for transfer		na	-	na		-	-	na	na	-	-	+
Adjusted for comorbidity		-	+	na		+	+	-	-	+	+	-
Adjusted for demographics		+	+	na		+	+	+	-	+	-	+
Adjusted for injury severity		+	+	na		+	+	+	+	+	+	+
All confounders reported		+	+	na		+	+	+	-	+	+	+
OR's with 95% CI		+	+	na		+	+	+	+	+	+	-
Discharge home per level (adj.)		-	-	-		-	-	-	-	-	-	-
Discharge home per level (crude)		-	-	+		-	-	-	+	-	+	-
ICU LOS per level (adj.)		+	-	-		-	-	-	-	-	-	+
ICU LOS per level (crude)		+	-	+		-	+	-	-	-	+	-
HLOS per level (adj.)		+	-	-		-	-	-	-	-	-	+
HLOS per level (crude)		+	-	+		+	+	-	+	-	+	-
Mortality per level (adj.)		+	+	-		+	+	+	+	+	+	+
Mortality per level (crude)		+	+	+		+	+	+	+	+	+	-
Baseline per level		+	+	+		+	+	-	+	+	+	+
ISS per level		-	+	+		+	+	-	+	+	+	-
Overall ISS		-	-	-		+	-	+	-	-	-	-
Age ≥ 16		-	+	+		+	-	+	+	-	+	+
2 TC levels separated		+	-	-		-	+	+	-	-	+	+
Definition TC level		+	+	+		+	+	+	+	-	+	+
AIS/ICD revision reported		-	+	+		+	+	+	+	+	+	+
Registry based		+	+	+		+	+	+	+	+	+	+
Nation- or region wide		+	+	+		+	+	+	+	+	+	+
Clear in- and exlusion criteria		+	+	+		+	+	+	+	+	+	+

6

Study, year, subgroup	Clear in- and exlusion criteria	Nation- or region wide	Registry based	AIS/ICD revision reported	Definition TC level	2 TC levels separated	Age ≥ 16	Overall ISS	ISS per level	Baseline per level	Mortality per level (crude)	Mortality per level (adj.)	HLOS per level (crude)	HLOS per level (adj.)	ICU LOS per level (crude)	ICU LOS per level (adj.)	Discharge home per level (crude)	Discharge home per level (adj.)	OR's with 95% CI	All confounders reported	Adjusted for injury severity	Adjusted for demographics	Adjusted for comorbidity	Adjusted for transfer	Conflict of interest declared	Funding identified	NOS selection (4*)	NOS comparability (2*)	NOS outcome (3*)	NOS total (9*)
Abdominal injuries																														
Harbrecht, 2004	+	+	+	+	+	+	+	+	+	+	+	-	+	-	+	-	-	-	Na	Na	Na	Na	Na	Na	+	-	4*	2*	3*	7*
Helling, 1997	+	-	-	-	+	+	-	-	+	+	+	-	+	-	+	-	-	-	na	na	na	na	na	na	-	-	4*	0*	3*	7*
Hotaling, 2012	+	+	+	+	+	+	-	-	+	+	+	-	+	-	+	-	-	+	na	na	na	na	na	na	-	-	3*	2*	3*	8*
Lewis, 2021	+	+	+	-	+	+	+	-	+	+	+	+	+	-	+	-	-	-	+	+	+	+	-	-	+	+	4*	2*	3*	9*
Sheehan, 2020	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	-	-	-	+	+	+	+	-	-	+	+	4*	2*	3*	9*
Tignanelli, 2018	+	+	+	+	+	+	+	-	-	+	-	+	-	+	-	+	-	-	-	+	+	+	-	-	+	+	4*	2*	3*	9*
Hemodynamically unstable																														
Dufresne, 2017	+	+	+	-	+	+	+	-	-	+	+	+	+	+	-	-	-	-	+	+	+	+	+	na	+	+	4*	2*	3*	9*
Haas, 2018	+	+	+	+	+	-	+	-	+	+	+	+	-	-	-	-	-	-	+	+	+	+	+	+	+	+	3*	2*	3*	8*
Hamidi, 2019	+	+	+	-	+	+	+	+	+	+	+	+	+	-	-	-	-	-	+	+	+	+	-	na	+	+	4*	2*	3*	9*
Herrera-Escobar, 2017	+	+	+	-	+	+	+	-	+	+	+	+	-	-	-	-	-	-	na	na	na	na	na	na	+	+	4*	2*	3*	9*

Study, year, subgroup	Clear in- and exlusion criteria	Nation- or region wide	Registry based	AIS/ICD revision reported	Definition TC level	2 TC levels separated	Age ≥ 16	Overall ISS	ISS per level	Baseline per level	Mortality per level (crude)	Mortality per level (adj.)	HLOS per level (crude)	HLOS per level (adj.)	ICU LOS per level (crude)	ICU LOS per level (adj.)	Discharge home per level (crude)	Discharge home per level (adj.)	OR's with 95% CI	All confounders reported	Adjusted for injury severity	Adjusted for demographics	Adjusted for comorbidity	Adjusted for transfer	Conflict of interest declared	Funding identified	NOS selection (4*)	NOS comparability (2*)	NOS outcome (3*)	NOS total (9*)
Hemodynamically unstable																														
Plurad, 2021	+	+	+	-	+	+	-	+	+	+	+	+	+	-	+	-	-	-	+	+	+	+	+	na	+	+	4*	2*	3*	9*
Torso penetrating injuries																														
Grigorian, 2019	+	+	+	+	+	+	-	-	+	+	+	+	+	-	+	-	-	-	+	+	+	+	+	na	+	+	4*	2*	3*	9*
Pelvic injuries & femoral shaft fractures																														
Bouzat, 2013	+	-	+	-	+	+	-	-	+	+	+	+	-	-	-	-	-	-	na	na	na	na	na	na	+	-	4*	1*	3*	8*
Jakob, 2021	+	+	+	+	+	+	+	-	-	+	+	+	+	-	+	-	-	-	+	+	+	+	+	na	+	+	4*	2*	3*	9*
Khoury, 2016	+	+	+	-	+	+	+	-	-	+	+	-	-	-	-	-	-	-	na	na	na	na	na	na	+	+	2*	0*	3*	5*
Morshed, 2015	+	+	+	+	+	-	+	+	-	+	+	+	+	-	-	-	-	-	+	+	+	+	+	-	+	+	3*	2*	3*	8*
Oliphant, 2018	+	+	+	+	+	+	+	-	-	+	-	+	-	+	-	+	-	-	-	+	+	+	-	+	+	+	4*	2*	3*	9*
Total + (%)	100	92	97	61	97	75	67	22	72	94	92	72	64	17	50	14	19	6	94	97	100	94	72	61	72	61				

AIS, Abbreviated Injury Scale ICD, International Classification of Diseases; TC, Trauma Center; ISS, Injury Severity Score; adj., adjusted; HLOS, Hospital Length of Stay; ICU LOS, Intensive Care Unit Length of Stay; OR, Odds Ratio; CI, Confidence Interval; NOS, Newcastle-Ottawa Scale; na, not applicable.

Quality assessment

Included studies had clear in- and exclusion criteria (n=35, 100%), distinct trauma center level definitions (n=34, 97%), were registry based (n=34, 97%), were national or regional (n=32, 91%), and reported ISS per level (n=25, 71%) (Table 2). A minimum age of 16 or 18 was used as inclusion criterion in 66% (n=23) of the studies and 61% (n=21) reported the AIS- or International Classification of Diseases (ICD) revision used for coding injuries. Crude in-hospital mortality per level was reported in 91% (n=32) of the included studies and 63% (n=23) reported adjusted in-hospital mortality. A fair amount of these studies, reported confounders used in adjusted analysis (n=23, 66%); 69% (n=24) of studies adjusted analysis for injury severity, 69% (n=24) for demographics, 43% (n=15) for comorbidity, and 6% (n=2) for transfers (54% (n=19) of studies excluded transfers). Quality assessment and Newcastle-Ottawa Scale (NOS)[17] scores were comparable, studies scoring low on the NOS, scored low on quality assessment as well (69%(n=24) had a perfect score).

In-hospital mortality - Systematic review

Of all 34 studies reporting in-hospital mortality [21-49, 51-55], 11 studies (32%)[24, 26, 30-32, 36, 43, 48, 51, 54, 55] found level I trauma centers are associated with lower in-hospital mortality versus non-level I trauma centers (Table 1). Of these 11 studies, nine studies (82%)[24, 26, 30-32, 36, 43, 48, 51] compared level I with level II trauma centers. A total of 22 studies (65%)[21-23, 25, 27-29, 33-35, 37-39, 41, 42, 44, 46, 47, 49, 52, 53] reported no difference in in-hospital mortality across different levels of trauma care. (Table 1). Of these 22 studies, 17 studies (77%)[22, 23, 25, 27, 29, 34, 35, 38, 39, 41, 44-47, 49, 52, 55] compared level I with level II trauma centers. One study found level I trauma centers to be associated with higher in-hospital mortality rates compared to level II.[40]

Meta-analysis – unadjusted

Of 34 studies reporting in-hospital mortality, 22 studies (65%)[22-27, 29-31, 34-36, 38-40, 44-47, 49, 51, 52] were included in the unadjusted meta-analysis on in-hospital mortality, comparing level I and level II trauma centers, comprising a total of 405,684 trauma patients (Figure 2). The overall pooled unadjusted OR (95% CI) was 1.10 (1.02-1.20), I^2 = 84% (Figure 2). Subgroup analysis was possible for TBI (OR (95% CI) 1.10 (0.91-1.33))[22, 26, 29, 30, 45, 49], thoracic injuries (OR (95% CI) 1.10 (0.57-2.13))[25, 27, 46], abdominal injuries (OR (95% CI) of 1.04 (0.89-1.22))[34, 35, 38, 47, 52], and hemodynamically unstable patients (OR (95% CI) of 1.14 (0.82-1.59)) [31, 36, 44, 51]. Overall and for subgroups, heterogeneity was strong (I^2 81-94%). There was no suggestion of publication bias (Figure 4).

Meta-analysis – adjusted

Adjusted meta-analysis on in-hospital mortality comparing level I and level II trauma centers, included 15 (44%) studies[23, 25, 26, 29-31, 36, 39, 43-47, 51, 52] (n=135,861) with a pooled adjusted OR (95% CI) of 1.15 (1.06-1.25), I^2=50% (Figure 2). Subgroup analysis was possible for TBI (OR (95% CI) 1.23 (1.01-1.50))[26, 29, 30, 45] and hemodynamically unstable patients (OR (95% CI) 1.09 (0.98-1.22))[31, 36, 44, 51]. Overall and for subgroups, heterogeneity was strong (I^2 50-85%). There appeared to be no publication bias (Figure 4).

Hospital length of Stay - Systematic Review

Of all studies, 26 studies (74%)[21-23, 25-35, 37-39, 43-52] reported on HLOS comparing higher with lower level trauma centers, of which 19 studies (73%)[22, 23, 25, 26, 30-32, 34, 35, 38, 39, 44-47, 49-52] compared level I with level II trauma centers (Table 1). A total of 13 studies (50%)[22, 26, 28, 30, 31, 33, 34, 37, 38, 44-46, 50] found lower level trauma centers associated with shorter HLOS than at higher levels, 11 studies (42%)[21, 23, 25, 29, 32, 35, 39, 43, 47-49] reported no significant difference, and 2 studies (11%)[51, 52] found a significant difference in HLOS in favor of level I trauma centers.

Meta-analysis

Twelve studies (46%)[26, 30, 31, 34, 35, 38, 44, 45, 47, 50, 52], comparing level I and level II trauma centers, reported a mean (SD) HLOS, comprising a total of 99,531 trauma patients, resulting in an overall pooled unadjusted mean difference (MD) (95% CI) -1.63 (-2.89 - -0.36), I^2 = 97%, X^2= 4.93, p <0.18) (Figure 3). Subgroup analysis was possible for TBI patients (MD (95% CI) -1.84 (-3.20—0.48))[26, 30, 45, 50], and patients with abdominal injuries (MD (95% CI) of -0.83 (-3.05-1.38)).[34, 35, 38, 47, 52] Overall and for subgroups, heterogeneity was strong (I^2 60-97%). There was an indication of possible publication bias (Figure 4). As a side note, three of the included studies[25, 29, 35] based HLOS solely on survivors.

Intensive Care Unit length of Stay - Systematic review

Of all studies, 21 studies (60%)[22, 23, 25, 26, 29, 30, 32-35, 37-39, 43-49, 52] reported ICU LOS comparing higher and lower level trauma centers (Table 1). A total of ten studies (48%) [22, 23, 26, 30, 32, 34, 37, 38, 45, 48] found lower level trauma centers associated with shorter ICU LOS compared to higher levels, seven studies (33%)[25, 29, 33, 43, 44, 47, 49] reported no significant differences in ICU LOS between higher and lower level trauma centers, and four studies (19%)[35, 39, 46, 52] found a significant lower ICU LOS in level I trauma centers.

Meta-analysis

Ten studies (43%)[25, 26, 30, 34, 35, 38, 39, 44, 45, 52], comparing level I and level II trauma centers, reported a mean (SD) ICU LOS, comprising a total of 84,337 trauma patients, resulting in an overall pooled unadjusted MD (95% CI) of -0.21 (-1.04-0.61), I^2 = 94%, X^2= 16.37, p <0.01) (Figure 3). Subgroup analysis was possible for TBI (MD (95% CI) of -1.07 (-2.78-0.63))[26, 30, 45] and patients with abdominal injuries (MD (95% CI) of 0.25 (-2.21-2.72))[34, 35, 38, 52]. Overall and for subgroups, heterogeneity was strong (I^2 91-94%). There was an indication of possible publication bias (Figure 4). As a side note, three of the included studies[25, 29, 35] based ICU LOS solely on survivors.

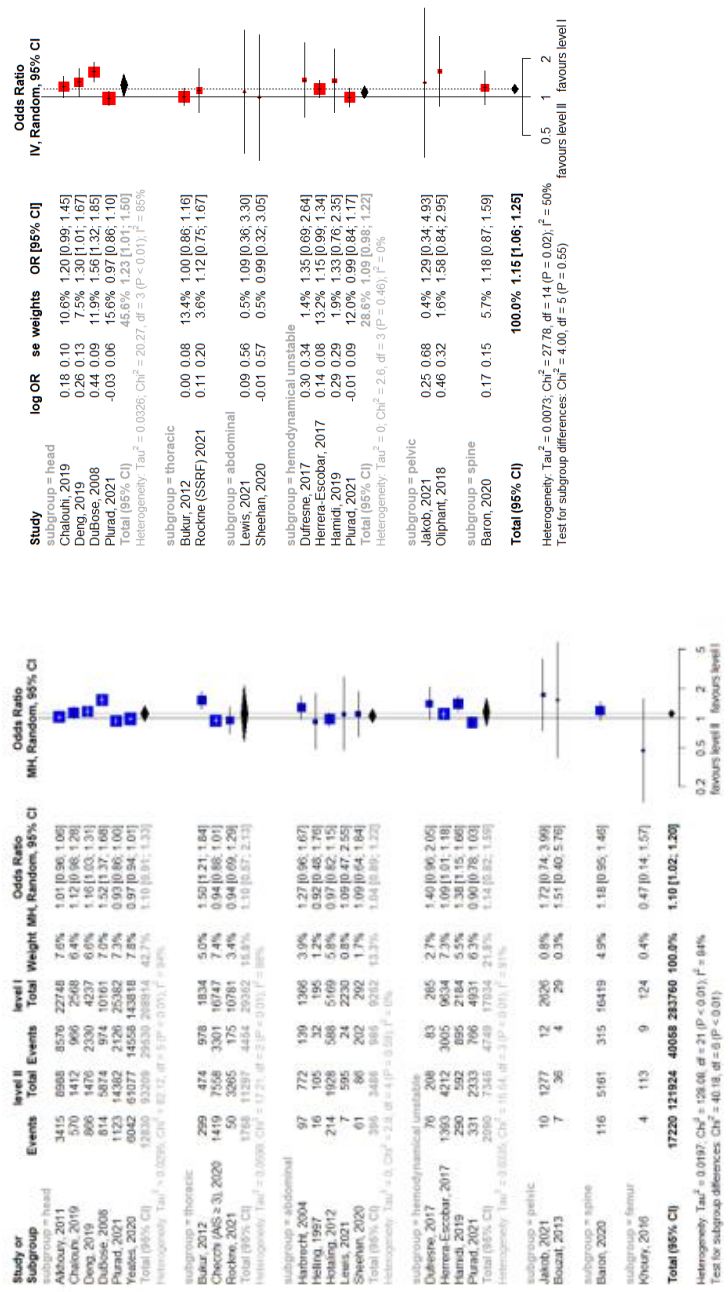
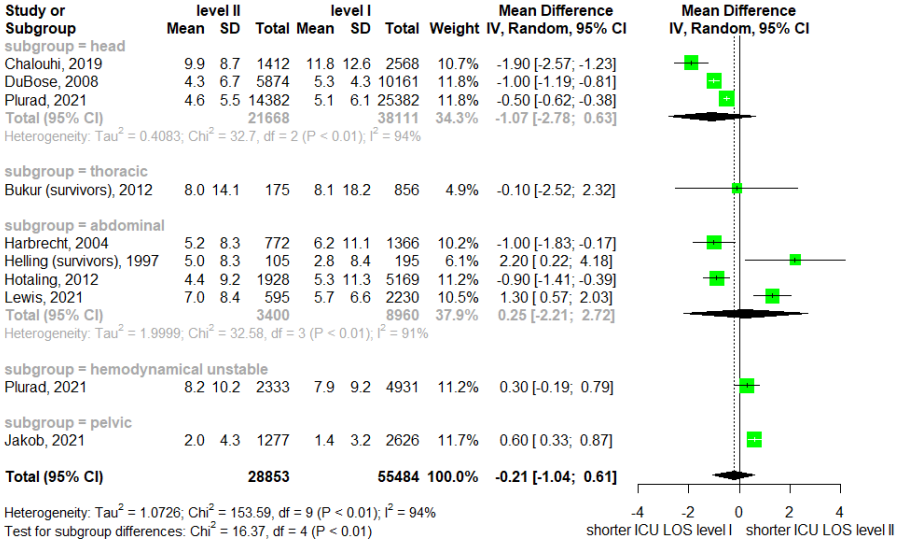


Figure 2. Meta-analysis for unadjusted (left) and adjusted (right) in-hospital mortality in severely injured trauma populations for level I versus level II trauma centers.



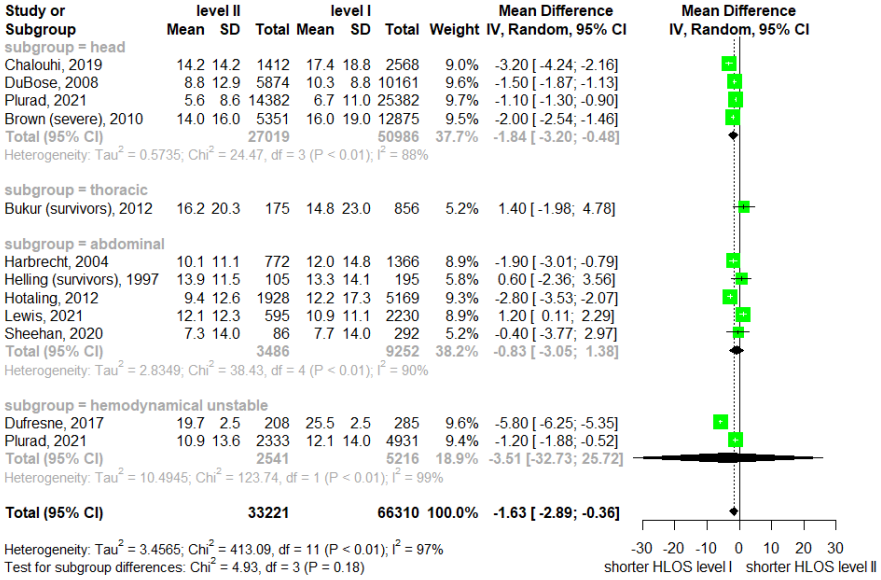


Figure 3. Meta-analysis unadjusted hospital (upper) and intensive care unit (lower) length of stay in severely injured trauma populations for level I versus level II trauma centers.

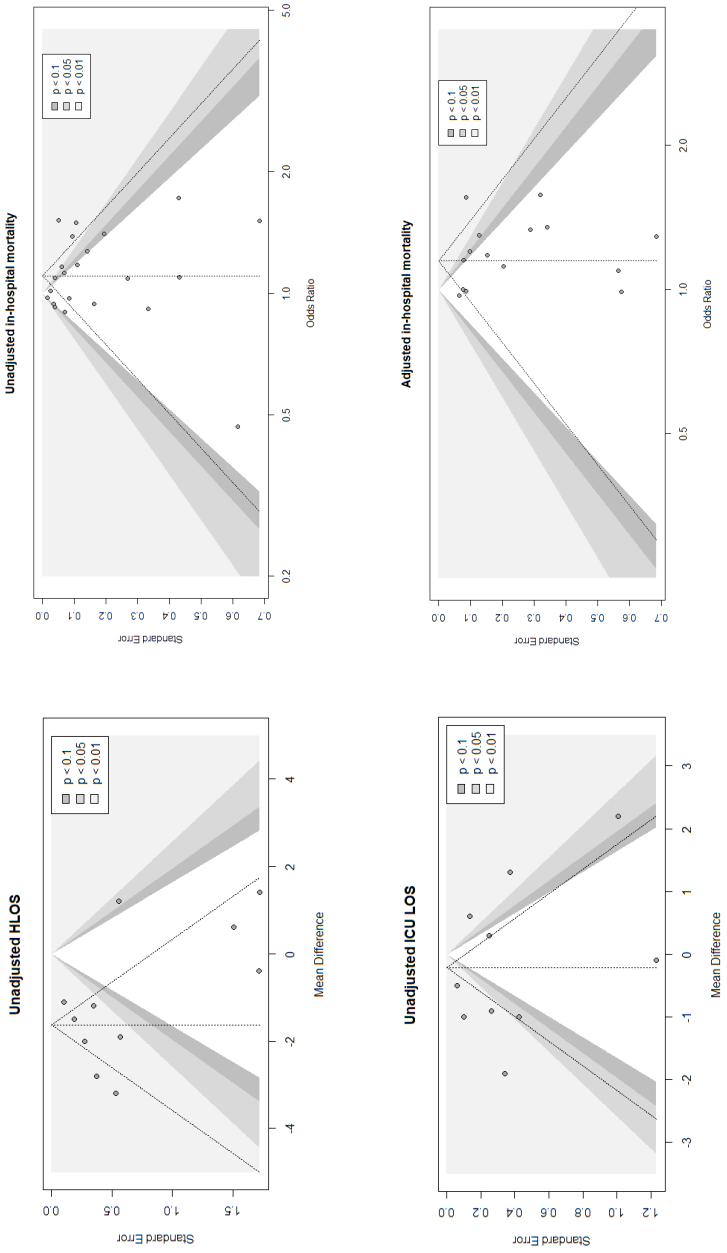
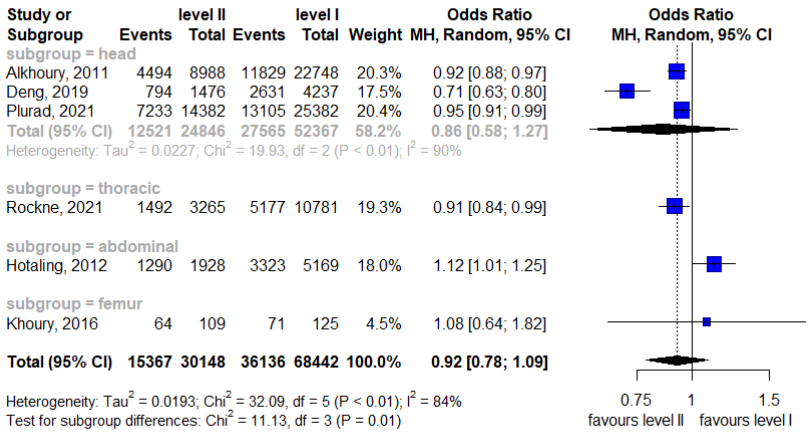


Figure 4. Funnel plots on publication bias: Upper left unadjusted in-hospital mortality, upper right adjusted in-hospital mortality, lower left unadjusted hospital length of stay, lower right unadjusted intensive care unit length of stay.



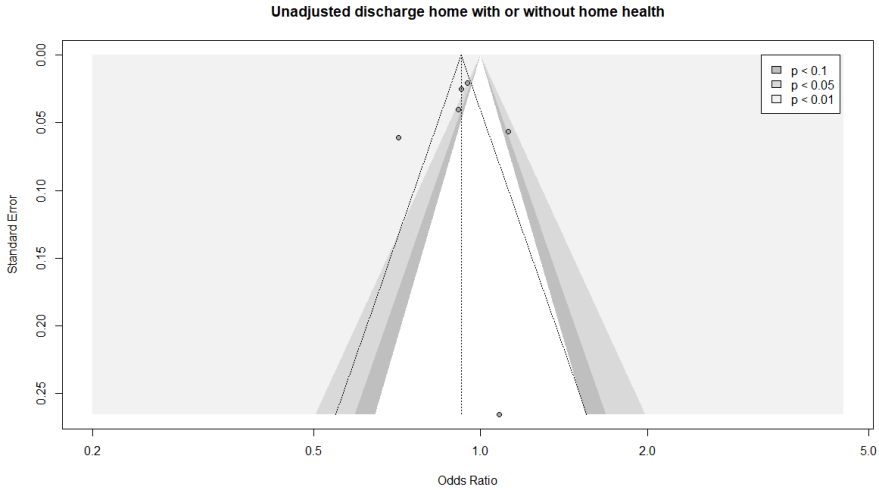


Figure 5. Meta-analysis unadjusted discharge home with or without home health (upper) and funnel plot on publication bias (lower) in severely injured trauma populations for level I versus level II trauma centers.

Mechanical Ventilation duration - Systematic Review

Mechanical ventilation duration was reported by eight studies[22, 25, 30, 32, 37, 46, 47, 52], comparing higher with lower level trauma centers, of which seven studies[22, 25, 30, 32, 46, 47, 52] compared level I with level II trauma centers (Table 1); five studies[25, 30, 32, 47, 52] found no significant differences, two studies[22, 37] reported longer, and one study[46] found shorter mechanical ventilation duration in level I trauma centers.

Complications - Systematic Review

Complications of any kind were reported by 16 studies (46%)[22, 23, 29-33, 37, 39, 40, 43, 46-48, 51, 52], comparing higher with lower level trauma centers (Table 1); seven studies[22, 29, 31, 33, 40, 47, 48] found no significant differences between level I and non-level I trauma centers, and five studies [39, 43, 46, 51, 52] reported no differences, except for a higher rate in level I trauma centers of acute respiratory distress syndrome (ARDS), a ventilator assisted pneumonia[52], and pulmonary embolism.[46] Lower complication rates of any kind in level I trauma centers were found in two studies[23, 30] , and one study[32] found higher complication rates of any kind but similar rates of ARDS and DVT in level I trauma centers.

Discharge destination home (with or without home health) - Systematic Review

Of all included studies, nine studies[22, 28, 29, 37, 38, 40, 45, 46, 53] (26%) reported discharge destination home comparing higher and lower level trauma centers (Table 1); six studies[22, 28, 29, 45, 46, 53] (67%) found higher level trauma centers to be associated with a larger percentage of patients discharged home, two studies[37, 40] (22%) reported no significant difference, and one study[38] (11%) associated lower level trauma centers with a larger percentage of patients discharged to home.

Meta-analysis

Of the nine studies reporting discharge destination home, six studies (67%) were included in the unadjusted meta-analysis, comparing level I and level II trauma centers, comprising a total of 98,950 patients (Figure 5). The overall pooled unadjusted OR (95% CI) was 0.92 (0.78-1.09), I^2 = 84% (Figure 2). Subgroup analysis was possible for TBI (OR (95% CI) 0.86 (0.58-1.27)). Heterogeneity was strong; overall I^2 was 84% and for TBI I^2 was 90%. There was no suggestion of publication bias (Figure 5).

Functional Outcome Measures Systematic Review

Three TBI studies[26, 30, 50] compared the functional independence measure (FIM) between level I and level II trauma centers (Table 1); two studies[26, 50] found level I trauma centers to be associated with better functioning, whereas one study[30] found no differences. Health-related quality of life, measured after one year by short form-36 (SF-36[56]), and the Musculoskeletal Function Assessment (MFA)[57], was associated with better functioning after being admitted to a level I trauma center than to a non-level I trauma center (level IV + other).[42]

Discussion

In an attempt to analyze major trauma care in networks, this study assessed the association of patients with specific severe injuries admitted to a specific level of trauma care and (non-)fatal outcome measures. This systematic review included 35 studies with a total population of 1,100,888 trauma patients. The results of 25 studies (n = 443,095) that compared level I with level II trauma centers suggest a survival benefit for the severely injured admitted to a level I trauma center (unadjusted OR 1.1, NNTB 84; adjusted OR 1.15, NNTB 57). A few subgroup analyses for adjusted in-hospital mortality could be done: Patients with TBI have a survival benefit when admitted to a level I trauma center (OR 1.23 95% CI 1.01-1.50), and there was an indicative survival benefit for hemodynamically unstable patients and patients with penetrating injuries when admitted to a level I trauma center.(OR 1.09 95% CI 0.95-1.22 OR 1.04 95% CI 0.78-1.38 respectively (Supplemental Figure 1 and 2). Overall, there was an unadjusted non-significant tendency for shorter HLOS and longer ICU in level I trauma centers, mechanical ventilation duration was similar between level I and level II trauma centers, and a larger part of patients admitted to level II trauma centers were discharged home, which could be addressed to differences on population level.

Even though non-major but severely injured patients (ISS 9-14) were included in this study, results were similar to previous reviews for general major trauma populations.[9, 58] All studies and subgroups combined in the present study could be considered a general severely injured trauma population as well. Various (excluded) studies around the same theme are worth mentioning: no survival benefit for combined burn and major trauma patients in either level I or II trauma centers[59], survival benefit in level I trauma centers for patients with severe specific injuries[12, 60], level I and II trauma centers with low mortality rates prevent and treat complications better in the severely injured[54, 61], and patients admitted to level I trauma centers with severe lower extremity injuries have a higher chance of limb salvage.[62] Several studies analyzed specific age groups in association to level of trauma care, the largest groups being pediatrics and geriatrics. Most pediatric studies compare severely injured children admitted to pediatric, adult and mixed trauma centers, indicating benefits of a regionalized pediatric (major) trauma center.[63-66] Studies on severely injured (very) elderly indicate beneficial care in higher level trauma centers, despite many geriatric trauma patients being admitted to lower level trauma centers as a stable older trauma patient with lower energy injury mechanisms.[67-69] Comparing top levels of trauma care indicate no differences between centers.[68-71]

In the present study a level of care association with outcomes has been studied from a subgroup perspective mostly based on injured body region. When looking at case mix differences between levels of trauma, what is considered as severely injured is under debate. A minimum of MAIS 3 was considered severe, but when looking at a subgroup with specific injured body regions one can imagine a lot of detail is lost. Severe is a catch-all-term, while MAIS 3-5 or ISS >15 and ISS >24 are quite differential, not to speak of a differentiation of specific injured organs or a combination of injuries in different body regions. It might very well be that studies finding no differences between levels of trauma care are biased because of a certain overtriage (admit-all-term) in the context of concentration of the severely injured. If overtriage makes sure that a small group of critical injured patients associated with high

mortality rates are admitted as fast as possible to level I trauma centers, a beneficial true effect for small groups might statistically remain unnoticed in standard analysis on a population level. In addition, compliance to field triage protocols by emergency medical services might not be optimal. By reducing under- and overtriage, the quality of health care has still much to be gained. However, on-scene triage is good enough to result in an beneficial effect in the trauma networks included in the current study.

Limitations

An overall strong heterogeneity seems logical considering the multidisciplinary character of trauma care when combining all subgroups. Statistically, homogeneity might be more favorable, especially when looking at subgroups. Therefore, results should be carefully interpreted. Studies per subgroup were limited in all outcomes, especially in adjusted analysis. Looking at (adjusted) outcome measures, in-hospital mortality was best represented. Hospital, intensive care unit, and mechanical ventilation duration displayed inconsistencies of summary measure, were missing, and if not, adjusted values were scarce. When adjustments were done, physiological biomarkers were seldom available or used. Complications rates were often reported, however overall and specific complications were not interchangeable between studies. Discharge destination and functional outcome measures were least represented for individual levels of trauma care, making it difficult to create a robust non-fatal overview.

The three included studies not originating from the USA, where conducted in France, Israel, and Canada. These studies all compared numeric designated levels of trauma care, and where considered to be the same as the numeric levels of trauma care in the USA. It is difficult to address what influential elements of trauma management like level criteria, hospital volume, local (field) protocols, and activation of helicopter emergency medical services have on the included studies. Local health care context can be of great importance in the light of time to admission (geo-spatial elements), transfers, and maturation of trauma networks.

Generalizability of the current results to other care systems or middle-low income countries is questionable, the studies for that account are too homogeneous. No randomized trials could be identified (probably due to ethical issues) creating resulting in methodological limitations. Finally, the search was restricted to English written publications, creating a language bias. An additional search on all languages resulted in 53 extra studies, potentially resulting in one missing study proportionally to an English restricted search only, making publication bias negligible.

Strength

Severely injured patients were represented on a broad injury spectrum. All studies comparing any level of trauma care were included, and as many non-fatal outcomes as possible were studied. All but one study were based on data from the 21st century, creating an thorough overview of contemporary trauma networks with a clinical focus. This framework does right to the multidisciplinary approach and chain of trauma care.

Conclusion

Level of trauma care is associated with in-hospital mortality when specific severely injured trauma populations are combined; Level I trauma center resources add most to a survival benefit compared with non-level I trauma centers, also in severely injured non-major trauma populations. Unadjusted non-fatal clinical outcomes were indicative for a longer stay, more intensive care, and a greater need for post-hospital recovery trajectories after being admitted to top levels of trauma care, which could be addressed to differences on a population level. Functional outcome measures were underreported. Trauma networks with designated levels of trauma care are beneficial to the multidisciplinary character of trauma care.

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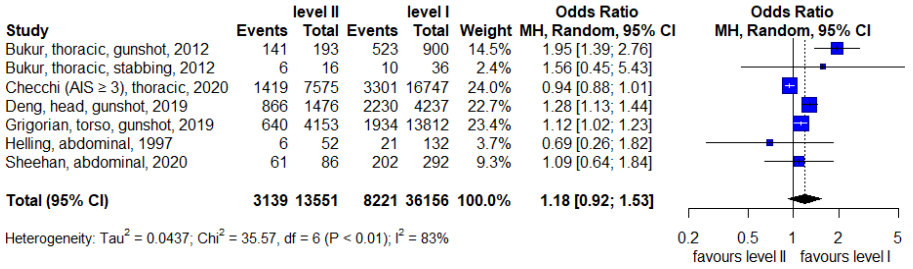
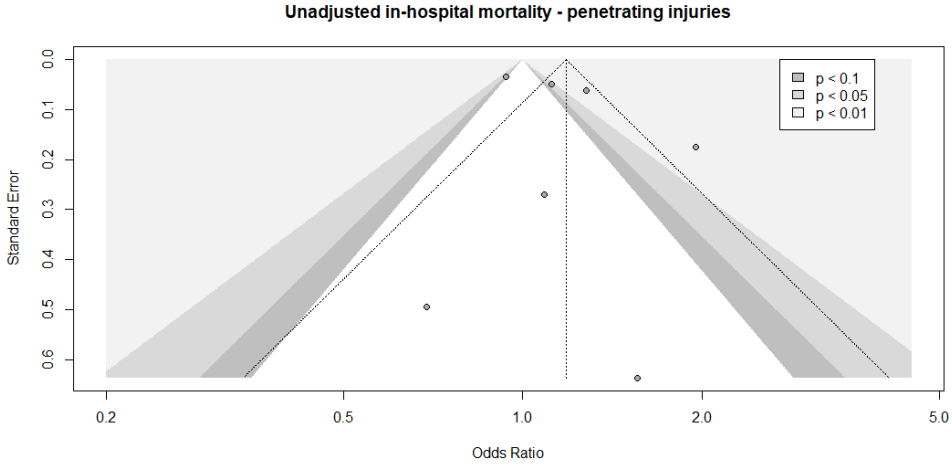
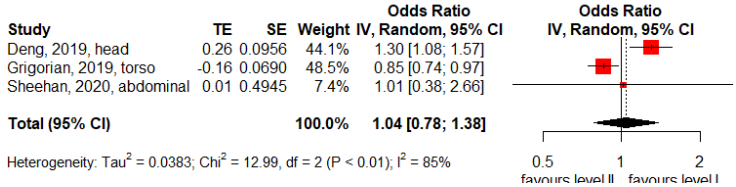




Supplemental Figure 1. Meta-analysis for unadjusted in-hospital mortality in trauma populations with severe penetrating injuries for level I versus level II trauma centres, combined with funnel plot on publication bias.



Supplemental Figure 2. Meta-analysis for adjusted in-hospital mortality in trauma populations with severe penetrating injuries for level I versus level II trauma centres, combined with funnel plot on publication bias.

CHAPTER 7

Identifying the severely injured benefitting from a specific level of trauma care in an inclusive network: a multicentre retrospective study

Highlights

- *Level of trauma care was not indicative for in-hospital mortality among severely injured patients, although patients admitted to the level I TC were more severely injured.*
- *Subgroups of patients by injured body region or ISS, with a survival benefit or more favourable clinical outcome measures were not identified.*
- *Analysis on clinical outcome measures across different levels of trauma care in an inclusive trauma network is too simplistic if subgroups are based on injuries in specific body region or ISS only.*

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Abstract

Introduction Defining major trauma (MT) with an Injury Severity Score (ISS) > 15 has limitations. This threshold is used for concentrating MT care in networks with multiple levels of trauma care.

Objective This study aims to identify subgroups of severely injured patients benefiting on in-hospital mortality and non-fatal clinical outcome measures in an optimal level of trauma care.

Methods A multicentre retrospective cohort study on data of the Dutch National Trauma Registry, region South West, from January 1, 2015 until December 31, 2019 was conducted. Patients ≥ 16 years admitted within 48h after trauma transported with (H)EMS to a level I trauma centre (TC) or a level II/III facility with a Maximum Abbreviated Injury Scale (MAIS) ≥ 3 were included. Patients with burns or patients of ≥ 65 years with an isolated hip fracture were excluded. Logistic regression models were used for comparing level I with non-level I. Subgroup analysis were done for MT patients (ISS > 15) and non-MT patients (ISS 9-14).

Results A total of 7,493 records were included. In-hospital mortality of patients admitted to a non-level I TC did not differ significantly from patients admitted to the level I TC (adjusted Odds Ratio (OR): 0.94; 95% confidence interval (CI) 0.68-1.30). This was also applicable for MT patients (OR: 1.06; 95% CI 0.73-1.53) and non-MT patients (OR: 1.30; 95% CI (0.56-3.03). Hospital and ICU LOS were significantly shorter for patients admitted to a non-level I TC's, and patients admitted to a non-level I TC were more likely to be discharged home. Findings were confirmed for MT and non-MT patients, per injured body region.

Conclusion All levels of trauma care performed equally on in-hospital mortality among severely injured patients (MAIS ≥ 3), although patients admitted to the level I TC were more severely injured. Subgroups of patients by body region or ISS, with a survival benefit or more favorable clinical outcome measures were not identified. Subgroups analysis on clinical outcome measures across different levels of trauma care in an inclusive trauma network is too simplistic if subgroups are based on injuries in specific body region or ISS only.

Introduction

Since the implementation of trauma networks, care for the most severely injured patients is much more organised and in-hospital mortality has been reduced.[1] Severely injured patients treated in level I trauma centres (TC) have a survival benefit as compared to non-level I TC's.[2-6] The Dutch trauma system consists of regionalised inclusive trauma networks, in which hospitals have designated levels of trauma care following specific criteria established by the Dutch Trauma Society. Level III facilities are intended for stable patients with isolated or minor injuries. Level II facilities are able to provide acute care for severely injured patients, if these patients are hemodynamically stable and do not require neurosurgical care. Level I TC's provide a fully equipped TC with twenty-four-seven availability of neurosurgery, and an Intensive Care Unit (ICU) with a minimum capacity of twelve beds, with one ICU bed available for acute trauma at all times. Level I TC's are intended for the most severely injured, also referred to as major trauma (MT) patients, and have to meet volume requirements of more than 240 MT patients per year. National regulations require that 90% of all MT patients must be primary admitted to level I TC's.[2, 7-9]

As in the Netherlands, MT is generally defined as an Injury Severity Score (ISS) > 15.[10, 11] Classifying MT based on ISS alone has limitations.[12] Defining MT with an anatomical sum score does not compensate for many possible combined injuries, and multiple lesions in the same body region. The new ISS (NISS) does compensate for the latter, however is not implemented as an quality indicator. Severely injured, major trauma, severe monotrauma (barytrauma), and polytraumatised patients can all have different injury patterns, with the same ISS. Other factors that determine severe injuries, such as physiological parameters, are also not part of the ISS.

The ISS has an evaluative character and is not readily available during on-scene acute care management.[2] Despite national guidelines of treating 90% of all MT patients in level I TC's, approximately one third of all MT patients are admitted to Dutch non-level I TC's.[9, 13] This addresses discrepancies of what is considered to be a MT by paramedics and physicians on-scene with following clinical acute care setting, compared with an anatomical sum score in retrospect. In addition, a recent Dutch study showed around 50% of trauma patients secondary transferred from a level II facility to a level I TC had an ISS < 15.[14] The current definition of MT, possibly does not include all patients benefiting a specific level of trauma care. Either, severely injured patients without an ISS > 15 can benefit from level I TC care, or severely injured patients with an ISS > 15 do not necessary depend on level I TC care for a favorable outcome.

This calls for an evaluation of clinical outcome measures of the severely injured across different levels of trauma care from an inclusive trauma region perspective. This study aims to identify severely injured (Maximum Abbreviated Injury Scale (MAIS) ≥ 3) patients, with an ISS > 15 or not, benefiting on in-hospital mortality and non-fatal clinical outcome measures in an optimal level of trauma care.

Methods

Study design

A multicentre retrospective cohort study was reported in accordance with the STROBE statement.[15] Data from the Dutch National Trauma Registry (DNTR),[16] collected in trauma region Southwest Netherlands, was used. All hospitals in trauma region Southwest Netherlands participate in the DNTR and entail one level I TC, five level II and five Level III trauma facilities. Dutch TC level criteria requirements are similar to those of the American College of Surgeons Committee on Trauma (ACS-COT).[17] All patients admitted to an emergency department (ED), within 48 hours after trauma, following hospitalisation or death in the ED, excluding dead on arrival, are included in the DNTR, and injuries are coded using AIS 2005 update 2008.[18]

All trauma patients, aged ≥ 16, with a maximum abbreviated injury scale (MAIS) ≥ 3, admitted to a level I TC, or level II, or III trauma facility, between January 1, 2015, and December 31, 2019, were included for this study. Initial transport to the ED was provided by (helicopter) emergency medical services ((H)EMS). If patients were transferred between hospitals within 48 hours after trauma, the primary registry was excluded, to avoid patient doubling. Patients with burn injuries, or ≥ 65 years with an ISS < 15 and a proximal femoral or femoral shaft fracture incurred in a private setting, were excluded to avoid selection bias (Supplemental Table S).

Data collection included patient demographics (age, sex, comorbidities by the American Society of Anaesthesiologists physical status classification (ASA)), ED physiological parameters (best motor response (BMR), respiratory rate (RR), systolic blood pressure (SBP)), injury characteristics (ISS, MAIS per body region, type of injury (blunt or penetrating), cause of injury), and level of trauma care. A transfer variable was created, to adjust for potential selection bias. The primary outcome measure was in-hospital mortality, and secondary outcome measures were hospital length of stay (LOS), ICU length of stay (ICU LOS), and discharge home (yes/no).

The local Medical Research Ethics Committee exempted this study for the level I trauma centre (MEC-2022-0280). Following review of the protocol, they concluded that the study is not subject to the Medical Research Involving Human Subjects Act. Other hospital have not reviewed the protocol. Patient consent was not asked.

Statistical analysis

Statistical analyses were done using the R Project for Statistical Computing (version 4.0.3).[19]

First, a descriptive analysis was performed for level I versus non-level I regarding patient, injury and outcome characteristics. Patients were further divided into MT (ISS > 15) and non-MT (ISS 9-14) for subgroup analysis.

Shapiro-Wilk's test was used to test the normality of data. Parametric variables were tested with a Student's t test for two groups and Analysis of Variance for multiple groups. Non-parametric variables were tested with the Mann-Whitney U test for two groups and the

Kruskall-Wallis test for multiple groups, followed by a pairwise comparison with the Mann-Whitney U test as applicable. Descriptive figures were presented with means and standard deviations for parametric continuous data, median and first-third quartile for non-parametric continuous data, and numbers and percentages for categorical data. Missing values were reported when appropriate.

Second, covariates RR, SBP, BMR, and ASA were imputed with multilevel multiple imputation dependent on mechanism of missingness with the mice package.[20]

Unadjusted and adjusted analyses were performed using a fixed effects logistic regression model for in-hospital mortality and discharge home (yes/no), and a fixed effects linear regression model for hospital LOS and ICU LOS. Levels of trauma care were divided into level I and non-level I, with the level I TC being the reference category. Level of trauma care, transfer, type of injury, ISS, BMR, RR, SBP, ASA, age, and sex were set as independent variables for all analyses. RR and BMR were log transformed, ISS was modelled with a spline function with 3 knots, and an interaction term age*sex was added in accordance with the TARN and TRISS model.[21] For each outcome measures subgroup analyses were performed for MT (ISS > 15) and non-MT (ISS 9-14) patients per injured body region.

Results

Study characteristics

A total of 7,493 patient records were included, of which 2,762 patients were admitted to the level I TC, 3,092 patients to a level II, and 1,638 patients to a level III facility (Figure 1). Patients admitted to the level I TC were younger, more often male, and had less comorbidities than patients admitted to a non-level I TC (Table 1). A larger part of the level I patients were secondarily admitted after transfer from other hospitals (n=433, 15.7%), as opposed to patients admitted to a non-level I facility (n=147, 3.1%).

Patients admitted to the level I TC, were more severely injured than patients admitted to a non-level I facility (ISS respectively 17 (13-26),11.4 (4.7))), and were more likely to suffer from penetrating injuries (n=226, 8.2%; n=49, 1.0%), respectively). Overall, 2,336 MT patients were included; 1,732 (74.1%) were admitted to the level I TC and 604 (25.8%) to a non-level I facility (Table 1). The proportion non-MT patients (n=5,157) differed across levels of trauma care as well; 1,030 (20.0%) were admitted to the level I TC and 4,127 (80.0%) to a non-level I facility.

Overall, the most frequent injured body regions (MAIS ≥ 3) were lower extremities (n=2,949, 39.4%), head (n=2,349, 31.3%), thorax (n=1,787, 23.8%), and spine (n=798, 10.6%) (Table 1). Similar, in non-level I facilities the most frequent affected body region was lower extremities n=2365, 50%), head (n=1071, 22.6%), thorax (n=910, 19.2%)), and spine (n=296, 6.3%). The most frequent injured body region of patients admitted to the level I TC were, head (n=1,278, 46.3%), thorax (n=877, 31.8%), lower extremities (n=584, 21.1%), and spine (n=502, 18.18%).

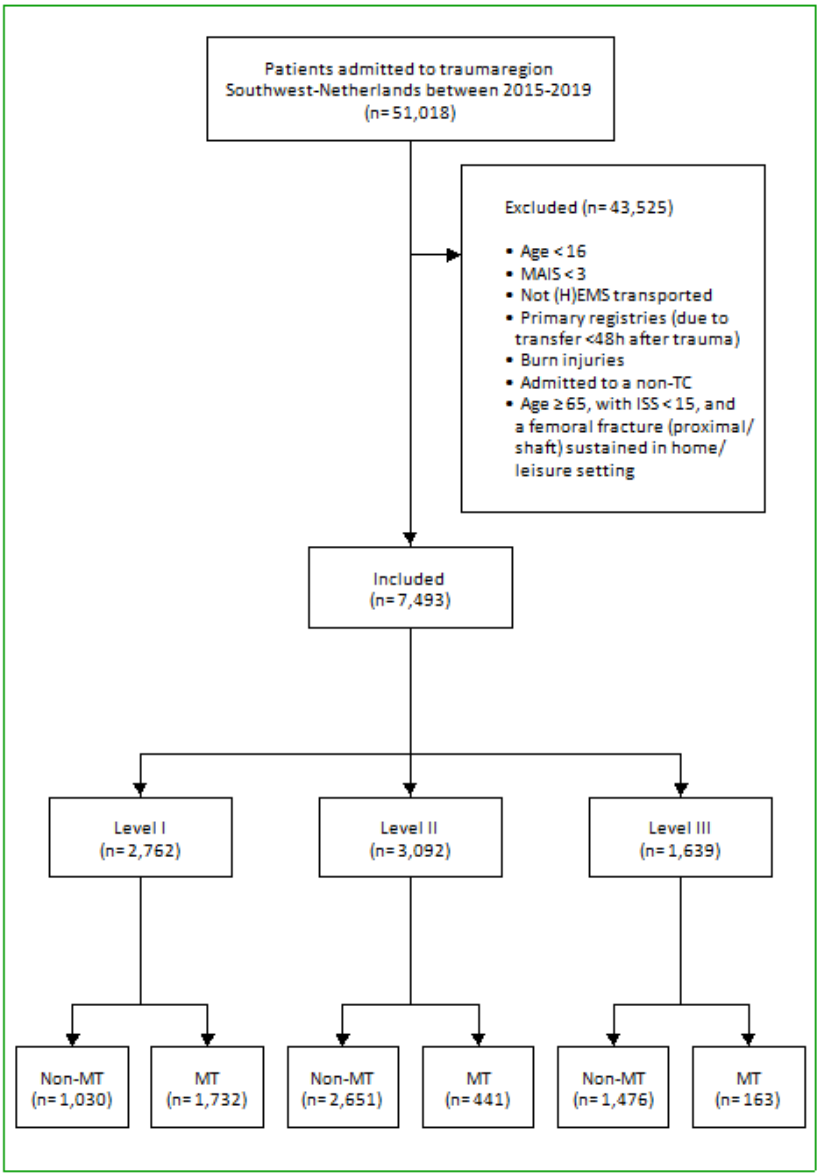

Figure. 1. Flowchart of patient record selection.

Table 1. Baseline characteristics per level of trauma care overall, and per ISS category.

		Overall			ISS > 15			ISS 9-14		
		Level I (n= 2762)	non-Level I (n= 4731)	p-value	Level I (n=1732)	non-Level I (n=604)	p-value	Level I (n=1030)	non-Level I (n=4127)	p-value
Sex male		1967 (71.2)	2511 (53.1)	<0.001	1241 (71.7)	342 (56.6)	<0.001	726 (70.5)	2169 (52.6)	<0.001
Age		50 (21)	64.7 (18.9)	<0.001	51.3 (20.4)	67.9 (20.7)	<0.001	49 (21)	64 (9)	<0.001
Comorbidity	**Healthy**	1275 (47.8)	1396 (29.6)	<0.001	780 (47.4)	145 (24.2)	<0.001	495 (48.6)	1251 (30.4)	<0.001
	Mild	1112 (41.7)	2493 (52.9)		694 (42.2)	324 (54.0)		418 (41.0)	2169 (52.8)	
	Severe	224 (8.4)	746 (15.8)		145 (8.8)	113 (18.8)		79 (7.8)	633 (15.4)	
	Unstable	54 (2.0)	77 (1.6)		27 (1.6)	18 (3.0)		27 (2.7)	59 (1.4)	
SBP < 90		152 (5.8)	58 (1.3)	<0.001	135 (8.4)	19 (3.3)	<0.001	17 (1.7)	39 (1.0)	0.072
RR		18.9 (6.1)	16.9 (4.7)	<0.001	18 (16, 22)	18 (15, 21)	0.006	18 (15, 20)	16 (14, 18)	<0.001
BMR		4.6 (2.1)	5.9 (0.6)	<0.001	6 (1,6)	6 (6,6)	<0.001	6 (6,6)	6 (6,6)	<0.001
Transfer in		433 (15.7)	147 (3.1)	<0.001	279 (16.1)	12 (2.0)	<0.001	154 (15.0)	135 (3.3)	<0.001
ISS		20.8 (11.8)	11.4 (4.7)	<0.001	25 (18, 30)	19 (17, 25)	<0.001	10 (9, 13)	9 (9, 10)	<0.001
Injury	**Penetrating**	226 (8.2)	49 (1.0)	<0.001	109 (6.3)	6 (1.0)	<0.001	117 (11.4)	43 (1.0)	<0.001
	Blunt	2536 (91.8)	4682 (99.0)		1623 (93.7)	598 (99.0)		913 (88.6)	4084 (99.0)	
MAIS ≥ 3	**Head**	1278 (46.3)	1071 (22.6)	<0.001	982 (56.7)	317 (52.5)	0.073	296 (29)	754 (18.3)	<0.001
	Face	71 (2.6)	24 (0.5)	<0.001	62 (3.6)	10 (1.7)	0.019	9 (0.9)	14 (0.3)	0.021
	Neck	65 (2.4)	10 (0.2)	<0.001	43 (2.5)	4 (0.7)	0.006	22 (2.1)	6 (0.2)	<0.001
	Thorax	877 (31.8)	910 (19.2)	<0.001	715 (41.3)	211 (34.9)	0.006	162 (15.7)	699 (16.9)	0.352
	Abdomen	213 (7.7)	93 (2.0)	<0.001	182 (10.5)	53 (8.8)	<0.001	31 (3.0)	40 (1.0)	<0.001
	Spine	502 (18.2)	296 (6.3)	<0.001	332 (19.2)	53 (8.8)	<0.001	170 (16.5)	243 (5.9)	<0.001
	Arm	104 (1.3)	101 (2.1)	<0.001	38 (2.2)	4 (0.7)	0.015	66 (6.4)	65 (1.6)	<0.001
	Leg	584 (21.1)	2365 (50.0)	<0.001	311 (18.0)	105 (17.4)	0.752	273 (26.5)	2260 (54.8)	<0.001
	External	103 (3.7)	101 (2.1)	<0.001	82 (4.7)	38 (6.3)	0.135	21 (2.0)	63 (1.5)	0.245

Continuous variables are displayed as mean (SD; % missing) or median (P25-P75; % missing), categorical variables are displayed as n (%; % missing). SBP, Systolic Blood Pressure; RR, Respiratory Rate; BMR, Best Motor Response; ISS, Injury Severity Score; MAIS, Maximum Abbreviated Injury Scale. Overall, comorbidity, SBP, RR, and BMR had missing value (1.5%, 7%, 37.5%, 16.5%, respectively), the other variables had no missing values.

Table 2. Clinical outcome measures per level of trauma care overall, and per ISS category.

	Overall		
	Level I (n=2,762)	**non-Level I (n=4,731)**	**p-value**
Mortality	413 (15.0)	181 (3.8)	<0.001
HLOS	8 (4, 15)	6 (4, 9)	<0.001
ICU	1186 (42.9)	828 (17.5)	<0.001
ICU LOS	4 (2, 11)	2 (2, 3)	<0.001
Discharged home	1338 (48.4)	2915 (61.6)	<0.001
	ISS > 15		
	Level I (n=1,732)	**non-Level I (n=604)**	**p-value**
Mortality	401 (23.2)	105 (17.4)	0.003
HLOS	10 (4, 19)	7 (4, 12)	<0.001
ICU	1029 (59.4)	249 (41.2)	<0.001
ICU LOS	5 (2, 11)	3 (2, 5)	<0.001
Discharged home	582 (33.6)	262 (43.4)	<0.001
	ISS 9-14		
	Level I (n=1,030)	**non-Level I (n=4.127)**	**p-value**
Mortality	12 (1.2)	76 (1.8)	0.133
HLOS	6 (3, 10)	5 (4, 9)	0.027
ICU	157 (15.2)	579 (14.0)	0.319
ICU LOS	3 (2, 4)	2 (1, 3)	0.006
Discharged home	756 (73.4)	2653 (64.3)	<0.001

Data are shown as median (P25-P75) or as n (%).
LOS, Length Of Stay; ICU, Intensive Care Unit.

Outcomes

In-hospital mortality

In-hospital mortality differed across levels of trauma care; level I n=413, 15.0%; non-level I facility n=181, 3.8% ($p < 0.001$, Table 2). Univariate analysis showed a lower mortality for non-level I TC's than the level I TC (OR 0.23 (95% CI 0.19-0.27), $p < 0.0001$, Table 3). After adjusting for confounders, no difference in in-hospital mortality was found (OR 0.94 (95% CI 0.68-1.30), p=0.709, Table 3, Figure 2). In the multivariate analysis MT patients showed no difference in in-hospital mortality (OR 1.06 (95% CI 0.73-1.53), p=0.7663, Table 3, Figure 2). Among non-MT patients, there was no significant difference for adjusted in-hospital mortality (OR: 1.30 (95% CI 0.56-3.03), p=0.546, Table 3, Figure 2). With regard to body regions, the biggest difference in overall crude in-hospital mortality was found in patients with severe head

injuries (level I n=287, 22.5%; level II n=53, 7.6%; level III n=29, 7.8%; Supplemental Table S2). Univariate analysis showed a lower in-hospital mortality in patients admitted to non-level I TC's for all body regions, which was significant for patients injured to the head, thorax, spine, and lower extremities (Table 3). In multivariable analyses all body regions showed no significant in-hospital mortality difference between non-level I and level I TC's (Table 3, Figure 2).

Hospital LOS

MT patients had a significant shorter hospital LOS in level II and III facilities (6.0 (4.0-9.0)) than in the level I TC (9.5 (4.0, 19.0), p<0.001, Table 2). Comparing the level I TC with non-level TC's resulted in an unadjusted SMD (95% CI) of -5.22 (-6.58-3.86, p<0.001), and an adjusted SMD (95% CI) of -3.42 (-5.00-1.84, p<0.001, Table 3). For non-MT patients, multivariable analyses showed a significant shorter hospital LOS in non-level I TC's (SMD (95% CI) -1.93 (-2.431.44), p<0.001, Table 3). When comparing hospital LOS per injured body region across different levels of trauma care, patients admitted to non-level I TC's were shorter hospitalized in all analyses (Table 2, Table 3, Supplemental Table S2).

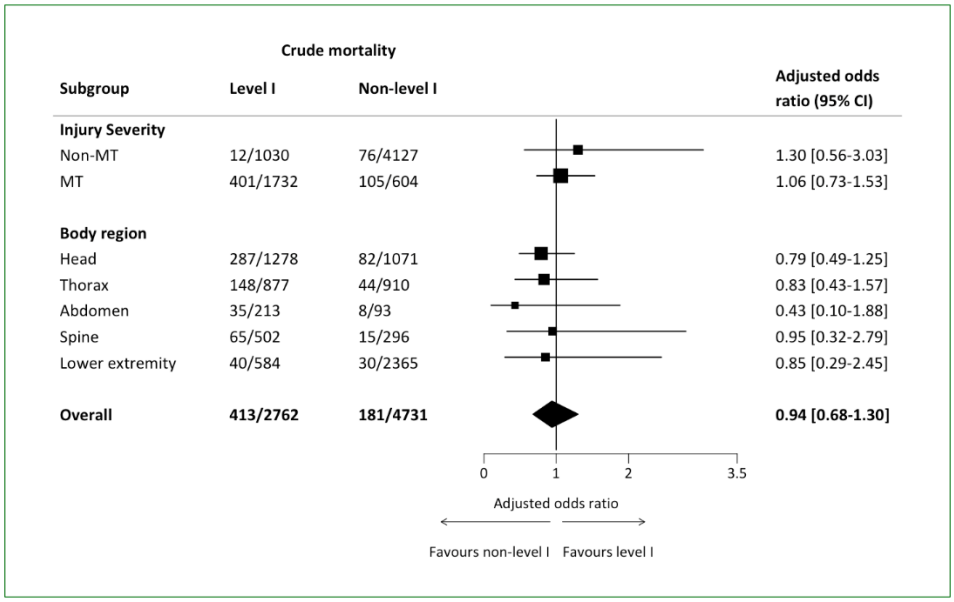

Figure. 2. Forest plot adjusted odds ratios of in-hospital mortality from patients admitted to non-level I trauma facilities versus the level I trauma centre.

ICU LOS

The level I TC had more ICU-admitted patients (n=1186, 42.9%) than non-Level I facilities (n=828, 17.5%) facilities (Table 2). Patients admitted to the ICU in non-level I TC's had a shorter ICU LOS, remaining significant in multivariable analysis (SMD (95% CI) -2.04 (-2.98—1.10), p<0.001, Table 3). The ICU admission rate of MT patients in the level I TC was higher (n=1029, 59.4%) than in non-level I facilities (n=1029, 59.4%, p<0.001, Table 2).

Table 2. Odds ratios and standardised mean differences of in-hospital mortality, hospital LOS, ICU LOS, and discharged home of patients admitted to non-level I TC's versus level 1 TC.

	In-hospital mortality				Hospital LOS			
	OR (95% CI)		OR (95% CI)		SMD (95% CI)		SMD (95% CI)	
	Unadjusted	p-value	Adjusted	p-value	Unadjusted	p-value	Adjusted	p-value
Overall	0.23 (0.19-0.27)	<0.001	0.94 (0.68-1.30)	0.709	-5.03 (-5.49--4.56)	<0.001	-2.87 (-3.48--2.26)	<0.001
ISS 9-14	1.59 (0.86-2.94)	0.137	1.30 (0.56-3.03)	0.546	-1.45 (-1.89--1.01)	<0.001	-1.93 (-2.43--1.44)	<0.001
ISS > 15	0.70 (0.55-0.89)	0.003	1.06 (0.73-1.53)	0.766	-5.22 (-6.58--3.86)	<0.001	-3.42 (-5.00--1.84)	<0.001
Head	0.29 (0.22-0.37)	<0.001	0.79 (0.49-1.25)	0.311	-6.23 (-7.26--5.19)	<0.001	-2.09 (-3.43--0.76)	0.002
Thorax	0.25 (0.18-0.36)	<0.001	0.83 (0.43-1.57)	0.558	-5.89 (-7.04--4.73)	<0.001	-1.60 (-3.13--0.07)	0.041
Abdomen	0.48 (0.21-1.08)	0.075	0.43 (0.10-1.88)	0.264	-6.31 (-9.83--2.80)	<0.001	-3.66 (-7.80--0.47)	0.083
Spine	0.36 (0.20-0.64)	<0.001	0.95 (0.32-2.79)	0.925	-7.25 (-9.16--5.33)	<0.001	-4.45 (-6.80--2.11)	<0.001
Upper extremity	0.24 (0.03-2.04)	0.191	26.21 (0.00-inf)	0.491	-7.84 (-11.58--4.11)	<0.001	-7.08 (-11.36--2.81)	0.001
Lower extremity	0.17 (0.11-0.28)	<0.001	0.85 (0.29-2.45)	0.758	-9.44 (-10.23--8.65)	<0.001	-6.30 (-7.32--5.28)	<0.001
	ICU LOS				**Discharge home**			
Overall	1.71 (1.56-1.88)	<0.001	1.38 (1.18-1.61)	<0.001	-4.76 (-5.45--4.06)	<0.001	-2.04 (-2.98--1.10)	<0.001
ISS 9-14	0.65 (0.56-0.76)	<0.001	1.07 (0.88-1.31)	0.494	-1.35 (-2.07--0.64)	<0.001	-0.69 (-1.54-0.16)	0.112
ISS > 15	1.51 (1.25-1.83)	<0.001	1.97 (1.50-2.58)	<0.001	-4.41 (-5.68--3.14)	<0.001	-2.75 (-4.18--1.32)	<0.001
Head	2.92 (2.47-3.46)	<0.001	1.73 (1.31-2.27)	<0.001	-5.61 (-7.27--3.95)	<0.001	-3.57 (-5.43--1.70)	<0.001
Thorax	2.47 (2.04-2.99)	<0.001	1.50 (1.08-2.08)	0.015	-5.45 (-6.49--4.42)	<0.001	-2.20 (-3.67--0.74)	0.003
Abdomen	2.27 (1.34-3.87)	0.003	3.11 (1.41-6.85)	0.005	-4.40 (-7.21--1.58)	0.003	-1.58 (-5.15-1.99)	0.387
Spine	1.61 (1.21-2.16)	0.001	1.12 (0.71-1.77)	0.622	-6.14 (-10.55--1.72)	0.007	-3.49 (-8.50-1.51)	0.173
Upper extremity	0.95 (0.49-1.83)	0.877	0.29 (0.10-0.84)	0.022	-6.80 (-13.53--0.07)	0.058	-2.05 (-9.45-5.34)	0.593
Lower extremity	1.14 (0.95-1.37)	0.158	0.99 (0.72-1.36)	0.946	-6.79 (-8.51--5.08)	<0.001	-2.09 (-4.80-0.63)	0.133

Level I is the reference in all analyses. Adjusted analyses were run with age, sex, comorbidity, best motor response, systolic blood pressure, and respiratory rate. CI, Confidence Interval; OR, Odds Ratio; SMR, Standardized Mean Differences.

MT patients showed a significant shorter ICU LOS in level II and III facilities in adjusted analysis (SMD (95% CI) -2.75 (-4.18—1.32), p<0.001, Table 3). Multivariable analysis for non-MT patients resulted in a non-significantly different ICU LOS across level of trauma care (SMD (95% CI) -0.69 (-1.54-0.16), p=0.112, Table 3). When comparing ICU LOS per injured body region across the different levels of trauma care, patients admitted to non-level I TC's were indicative for a shorter ICU LOS in all analysis and was significantly shorter for patients with head (adjusted SMD (95% CI) -3.57 (-5.43--1.70), p<0.001) or thoracic (SMD (95% CI) -2.20 (-3.67--0.74), p=0.003) injuries, in adjusted analysis (Table 2, Table 3).

Discharge home

Overall, patients admitted to a level II or a level III facility were significantly more often discharged home (n=2915, 61.6%) than in level I (n=1338, 48.8%, p<0.001, Table 2). This was similar for MT patients (non-level I n=262, 43.4%; level I n=583, 33.6%, p<0.001, Table 3), remaining significant throughout multivariable analysis (OR (95% CI) 1.97 (1.50-2.58), p<0.001, Table 3). Non-MT patients admitted to the level I TC were more often discharged home (n=756, 73.4%) than patients admitted to non-level I facilities (n=2653, 64.3%, p<0.001, Table 2). In multivariate analysis this difference disappeared (OR (95% CI) 1.07 (0.88-1.31), p=0.494, Table 3). Patients with head, thorax, or abdominal injuries had a higher chance to be discharged home when admitted to a non-level I TC in multivariate analysis (respectively OR (95% CI) 1.73 (1.31-2.27), p<0.001; OR (95% CI) 1.50 (1.08-2.08), p=0.015; OR (95% CI) 3.11 (1.41-6.85), p=0.005). For patients with injured upper extremities multivariate analysis showed they were more likely to return home when admitted to the level I TC (OR (95% CI) 0.29 (0.10-0.84), p=0.022). The proportion of patients discharged home with spinal or lower extremity injuries did not differ across levels of trauma care in multivariate analysis.

Discussion

This study aimed to identify severely injured patients benefiting on in-hospital mortality and non-fatal clinical outcome measures in an optimal level of trauma care. Level I TC's perform equally as non-level I TC's, when looking at in-hospital mortality among severely injured patients (MAIS ≥ 3), even though patients admitted to level I TC's were more severely injured. Patients admitted to a non-level I TC had a shorter hospital and ICU stay, and were more likely to be discharged home. These results were consistent across level of trauma care for MT patients (ISS > 15) and non-MT patients (ISS 9-14), as well as for analyses per injured body region. Compared to other body regions, there was a high difference in the number of head trauma, and associated in-hospital mortality, of this population in the level I TC compared to non-level I trauma facilities. It seems reasonable this was due to the regional function of the level I TC as a neuro-surgical centre around the clock.

Previously reported survival benefits for MT patients admitted to a level I TC,[2-4, 22, 23] did not match our current findings. Studies reporting similar performance of level I and level II facilities are not uncommon. Such results have been described in general MT populations and geriatric trauma patients, as well as in more specific populations, such as trauma patients with severe thoracic injuries, elderly with thoracic injuries, severe traumatic brain injuries, severe traumatic abdominal injuries, severe traumatic pelvic injuries and traumatic spine injuries. [24-36]

In addition, a recent study comparing clinical outcomes between level I and II TC's of patients with combined burn injuries and other physical trauma, a group known to have high rates of morbidity and mortality, found no in-hospital mortality difference.[37]

Studies reporting similar performance of level I and non-level I TC's are USA originated and included American College of Surgeons Committee on Trauma (ACS-COT) verified TC's. The Dutch TC level criteria requirements are quite similar to those of ACS-COT, making Dutch and American studies comparable.[8, 17] A plausible explanation for the current results and above mentioned studies reporting similar performance of level I and non-level I TC's, is that the difference between level I and level II trauma care has reduced since the trauma networks were implemented 30 years ago.[35] Medical advances, intensive collaboration between hospitals and better prehospital triage in trauma regions have accelerated quality of care in the Netherlands and led to a mature trauma system, in terms of in-hospital mortality rates and efficiency in the trauma chain construct such as type of surgeon and the availability of HEMS.[38, 39]Another point of consideration is the definition of MT based on an anatomical sum score, this is a general criterion. As mentioned, the ISS has limitations. Also, it does not include physiological parameters, or trauma mechanism, and it does not take multiple injuries in the same body region into account (NISS could serve as an alternative, but is still anatomy based). For example, TBI patients with or without rapid neurological deterioration can have the same ISS, but require different treatment. The first patient might require acute neurosurgery and extensive care, thus admittance to a level I TC, whereas the latter could be safely managed with (initial) conservative treatment in a level II facility. This was illustrated by a recent study including traumatic brain injury (TBI) patients with an acute subdural hematoma comparing surgical evacuation with initial conservative treatment. That study reported that acute surgical evacuation was not associated with better functional outcome.[40]

Adding physiological parameters as introduced with the Berlin polytrauma definition, can be of additive value for classification of patients with multiple severe injuries and a high mortality risk.[41-43] This definition does not include patients with severe isolated injuries (SII, MAIS ≥4), which makes up for 50% of the MT population in the Netherlands and is considered a high risk entity as well.[44] Both MT patients following the BPD and MT patients with severe isolated injuries are part of the MT population defined with ISS>15. Both MT groups have different injury patterns and can result in a different physiological response. In that sense, the greater part of a ISS > 15 threshold for major trauma patients seems well defined (a combination of SII and BPD). It would be of great value for policy makers to create an overview of which specific combination of severe injuries and what specific isolated severe injuries create a high risk patient profile.

Demetriades *et a*l. examined patients with specific, isolated severe injuries and found a survival benefit for patients admitted to an ACS level I TC as compared to level II TC's.[6] Based on this study, one could argue that a large proportion of overtriage is needed for a small group of patients with specific severe injuries to have a benefit of trauma care by being admitted to a level I TC.

By identifying patient profiles in need of a specific level of trauma care, contemporary trauma care could be more efficient and cost-effective, while improving clinical outcomes and quality of life. Additional research should focus on identifying which severely injured patients require

a specific level of trauma care, in order to optimise the current trauma care network chain. Combining predictive parameters for ISS > 15 or alternative classification parameters in the prehospital and clinical setting, will improve our knowledge of which trauma patients are admitted to the appropriate trauma facility for optimal care. Complementary, this way the quality indicator, how it is presented now, will be able to evolve following contemporary trauma care.

Strengths

A strength is the use of a large dataset from a trauma region in which all hospitals participate in trauma registration. The dataset contained most relevant clinical parameters for predicting in-hospital mortality [45] and there were hardly any missing data, which allowed multivariable analysis. By adjusting for transfers and excluding elderly patients with isolated hip fractures, selection bias was minimised. Second, looking at MT populations and non-MT populations, per injured body region, has given a broad overview of clinical outcome measures across levels of trauma care based on anatomically coded injuries.

Limitations

First, the retrospective design is limited with several biases. Second, patients admitted to the level I TC were younger, had less comorbidities, poorer ED physiological parameters, higher injury severity scores, and were more likely to be secondary admitted than patients admitted to a non-level I TC. Although we adjusted for these confounders, unmeasured confounding such as time from injury to treatment, presence of the systemic inflammatory response syndrome[46], undiagnosed comorbidities, or the presence of obesity[47], cannot be excluded. Third, another important limitation is statistical power. Even though the overall sample size consists of 7,493 patient records, sample sizes of some subgroups were small, especially subgroups in non-level I trauma centres. Fourth, field triage criteria that can adequately predict MT (ISS > 15) do not yet exist.[2] Instead, paramedics and physicians use on scene vital parameters, guidelines, and maybe even more importantly instinct and experience to determine which patients require level I trauma care, for which we could not adjust.

Conclusion

This study found that a level I TC performed equally as non-level I TC's comparing in-hospital mortality among severely injured patients, while patients admitted to level I TC's were more severely injured. Hospital and ICU length of stay were significantly shorter for patients admitted to non-level I TC's and patients admitted to non-level I TC's were more likely to be discharged home, subgroup analysis confirmed these findings for MT and non-MT patients and as well for the subgroups per injured body region. Subgroups analysis on clinical outcome measures across different levels of trauma care in an inclusive trauma network is too simplistic if subgroups are based on injuries in specific body region or ISS only.

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Supplemental Table S1. AIS codes used to exclude patients with isolated hip fractures caused in the home/leisure setting above the age of 65 with an ISS < 15.

AIS 2005 update 2008	Injury Description
853000.3	Femur fracture not further specified
853001.3	Femur fracture not further specified – open
853111.3	Proximal femur fracture not further specified
853112.3	Proximal femur fracture not further specified – open
853151.3	Proximal femur fracture trochanteric; intertrochanteric
853152.3	Proximal femur fracture trochanteric; intertrochanteric - open
853161.3	Proximal femur fracture femoral neck
853162.3	Proximal femur fracture femoral neck - open
853171.3	Proximal femur fracture femoral head; Pipkin
853172.3	Proximal femur fracture femoral head – open
853221.3	Femur Shaft fracture not further specified
853222.3	Femur Shaft fracture not further specified – open
853251.3	Femur Shaft fracture simple; spiral; oblique; transverse; *Winquist I*
853252.3	Femur Shaft fracture simple; spiral; oblique; transverse; *Winquist I* - open
853261.3	Femur Shaft fracture wedge; "butterfly"; *Winquist II or III*
853262.3	Femur Shaft fracture wedge; "butterfly"; *Winquist II or III* – open
853271.3	Femur Shaft fracture complex; comminuted; segmental; *Winquist IV*
853272.3	Femur Shaft fracture complex; comminuted; segmental; *Winquist IV* – open

Supplemental Table S2. Outcome variables per body region, divided by level of trauma care and ISS.

	Level I	Level II	Level III	p-value		Level I	Level II	Level III	p-value
Head (n)	**1,278**	**697**	**374**		**Abdomen (n)**	**213**	**75**	**18**	
Mortality	287 (22.5)	53 (7.6)	29 (7.8)	<0.001	**Mortality**	35 (16.4)	8 (10.7)	0 (0.0)	0.098
hospital LOS	7.0 (3.0, 16.0)	4.0 (2.0, 9.0)	4.0 (3.0, 8.0)	<0.001	**hospital LOS**	10.0 (5.0, 21.0)	8.0 (5.0, 11.0)	7.5 (6.3, 10.8)	0.022
ICU admission	725 (56.7)	77 (11.1)	50 (13.4)	<0.001	**ICU admission**	110 (51.6)	53 (70.7)	16 (88.9)	<0.001
ICU LOS	5.0 (2.0, 12.0)	2.0 (2.0, 4.0)	2.0 (2.0, 3.0)	<0.001	**ICU LOS**	4.0 (2.0, 8.0)	3.0 (2.0, 4.0)	2.0 (2.0, 3.0)	0.107
Discharge home	465 (36.4)	426 (61.1)	244 (65.2)	<0.001	**Discharge home**	116 (54.5)	52 (69.3)	16 (88.9)	0.003
Spine (n)	**502**	**203**	**93**		**Upper Extremity (n)**	**104**	**52**	**17**	
Mortality	65 (13.0)	12 (5.9)	3 (3.2)	0.001	**Mortality**	6 (5.8)	1 (1.9)	0 (0.0)	0.347
hospital LOS	9.0 (4.0, 18.0)	6.0 (3.0, 9.0)	4.0 (3.0, 7.0)	<0.001	**hospital LOS**	8.0 (4.0, 15.3)	3.0 (2.0, 6.0)	3.0 (2.0, 4.0)	<0.001
ICU admission	197 (39.2)	20 (9.9)	10 (10.8)	<0.001	**ICU admission**	19 (18.3)	5 (9.6)	6 (35.3)	0.049
ICU LOS	6.0 (2.0, 13.0)	3.0 (2.0, 5.0)	3.0 (2.0, 5.0)	0.009	**ICU LOS**	8.0 (2.0, 11.5)	3.0 (2.0, 6.0)	2.0 (1.3, 2.0)	0.115
Discharge home	192 (38.3)	96 (47.3)	52 (55.9)	0.002	**Discharge home**	72 (69.2)	34 (65.4)	13 (76.5)	0.685
Thorax (n)	**877**	**573**	**337**		**Lower Extremity (n)**	**584**	**1,550**	**815**	
Mortality	148 (16.9)	28 (4.9)	16 (4.8)	<0.001	**Mortality**	40 (6.9)	21 (1.4)	9 (1.1)	<0.001
hospital LOS	10.0 (5.0, 19.0)	8.0 (5.0, 13.0)	6.0 (4.0, 10.0)	<0.001	**hospital LOS**	11.0 (6.0, 22.3)	6.0 (4.0, 9.0)	5.0 (4.0, 8.0)	<0.001
ICU admission	464 (52.9)	268 (46.8)	165 (49.0)	0.065	**ICU admission**	202 (34.6)	84 (5.4)	112 (13.7)	<0.001
ICU LOS	5.0 (2.0, 12.0)	3.0 (2.0, 4.0)	2.0 (2.0, 3.0)	<0.001	**ICU LOS**	5.0 (2.0, 12.0)	2.0 (2.0, 3.3)	1.0 (1.0, 2.0)	<0.001
Discharge home	408 (46.5)	372 (64.9)	249 (73.9)	<0.001	**Discharge home**	319 (54.6)	864 (55.8)	503 (61.8)	0.007

Data are shown as median (P_{25}, P_{75}) or n (%). LOS, Length Of Stay; ICU, Intensive Care Unit.

Supplemental Table S2. Outcome variables per body region, divided by level of trauma care and ISS.

	Level I			Level II			Level III			
	ISS 9-14	ISS > 15	p-value	ISS 9-14	ISS > 15	p-value	ISS 9-14	ISS > 15	p-value	
Head (n)	**296**	**982**		**477**	**220**		**277**	**97**		
Mortality	5 (1.7)	282 (28.7)	<0.001	14 (2.9)	39 (17.7)	<0.001	5 (1.8)	24 (24.7)	<0.001	
hospital LOS	4.0 (3.0, 8.0)	8.0 (3.0, 19.0)	<0.001	3.0 (2.0, 7.0)	6.0 (3.0, 11.0)	<0.001	4.0 (2.0, 7.0)	6.0 (3.0, 10.0)	<0.001	
ICU admission	68 (23.0)	657 (66.9)	<0.001	33 (6.9)	44 (20.0)	<0.001	25 (9.0)	25 (25.8)	<0.001	
ICU LOS	3.0 (2.0, 4.3)	6.0 (2.0, 14.0)	<0.001	2.0 (1.0, 3.0)	3.0 (2.0, 4.0)	0.04	3.0 (2.0, 3.0)	2.0 (1.0, 4.0)	0.217	
Discharge	202 (68.2)	263 (26.8)	<0.001	338 (70.9)	88 (40.0)	<0.001	209 (75.5)	35 (36.1)	<0.001	
Spine (n)	**170**	**332**		**160**	**43**		**83**	**10**		
Mortality	3 (1.8)	62 (18.7)	<0.001	4 (2.5)	8 (18.6)	<0.001	3 (3.6)	0 (0.0)	0.541	
hospital LOS	5.0 (3.0, 10.0)	12.0 (6.0, 22.3)	<0.001	5.0 (3.0, 8.0)	7.0 (3.0, 15.0)	0.054	4.0 (3.0, 6.5)	7.5 (3.3, 15.0)	0.176	
ICU admission	15 (8.8)	182 (54.8)	<0.001	8 (5.0)	12 (27.9)	<0.001	6 (7.2)	4 (40.0)	0.002	
ICU LOS	2.0 (1.5, 4.5)	7.0 (3.0, 14.8)	0.002	3.0 (1.8, 4.3)	3.5 (2.0, 5.3)	0.483	2.5 (2.0, 3.0)	5.5 (4.3, 6.0)	0.12	
Discharge	119 (70.0)	73 (22.0)	<0.001	86 (53.6)	10 (23.3)	<0.001	47 (56.6)	5 (50.0)	0.69	
Thorax (n)	**162**	**715**		**416**	**157**		**283**	**54**		
Mortality	1 (0.6)	147 (20.6)	<0.001	12 (2.9)	16 (10.2)	<0.001	12 (4.2)	4 (7.4)	0.316	
hospital LOS	6.0 (4.0, 10.0)	11.0 (5.5, 22.0)	<0.001	7.0 (4.0, 11.0)	10.0 (7.0, 14.0)	<0.001	6.0 (4.0, 9.0)	9.0 (5.0, 12.8)	0.006	
ICU admission	24 (14.8)	440 (61.5)	<0.001	159 (38.2)	109 (69.4)	<0.001	125 (44.2)	40 (74.1)	<0.001	
ICU LOS	2.0 (1.0, 2.3)	6.0 (2.0, 12.0)	<0.001	2.0 (2.0, 3.5)	3.0 (2.0, 5.0)	<0.001	2.0 (2.0, 3.0)	3.0 (2.0, 4.3)	0.28	
Discharge	131 (80.9)	277 (38.7)	<0.001	287 (69.0)	85 (54.1)	<0.001	216 (76.3)	33 (61.1)	0.02	

Data are shown as median (P_{25}, P_{75}) or n (%). LOS, Length Of Stay; ICU, Intensive Care Unit.

Supplemental Table S2. Outcome variables per body region, divided by level of trauma care and ISS.

	Level I			Level II			Level III			
	ISS 9-14	ISS > 15	p-value	ISS 9-14	ISS > 15	p-value	ISS 9-14	ISS > 15	p-value	
Abdomen (n)	31	182		33	42		7	11		
Mortality	0 (0.0)	35 (19.2)	0.008	1 (3.0)	7 (16.7)	0.058	0 (0.0)	0 (0.0)	NA	
hospital LOS	6.0 (5.0, 9.0)	11.5 (5.3, 23.0)	0.003	6.0 (5.0, 9.0)	8.5 (6.3, 13.0)	0.015	7.0 (5.5, 9.0)	8.0 (7.0, 11.0)	0.294	
ICU	5 (16.1)	105 (57.7)	<0.001	18 (54.6)	35 (83.3)	0.007	6 (85.7)	10 (90.9)	0.732	
ICU LOS	2.0 (1.0, 4.0)	4.0 (2.0, 8.0)	0.134	2.0 (2.0, 3.0)	3.0 (2.0, 4.0)	0.031	2.5 (2.0, 3.0)	2.0 (2.0, 2.8)	0.472	
Discharge	26 (83.9)	90 (49.5)	<0.001	25 (75.8)	27 (64.3)	0.285	6 (85.7)	10 (90.9)	0.732	
Arm (n)	**66**	**38**		**49**	**3**		**16**	**1**		
Mortality	0 (0.0)	6 (15.8)	<0.001	1 (2.0)	0 (0.0)	0.803	0 (0.0)	0 (0.0)	NA	
hospital LOS	7.0 (4.0, 13.8)	12.0 (6.3, 27.8)	0.016	3.0 (2.0, 6.0)	6.0 (5.5, 7.0)	0.118	3.0 (2.0, 4.0)	32.0 (32.0,	0.097	
ICU	5 (7.6)	14 (36.8)	<0.001	3 (6.1)	2 (66.7)	<0.001	5 (31.3)	1 (100)	0.163	
ICU LOS	2.0 (2.0, 10.0)	8.5 (2.3, 12.5)	0.456	2.0 (1.5, 4.5)	4.5 (3.8, 5.3)	0.564	2.0 (1.0, 2.0)	3.0 (3.0, 3.0)	0.114	
Discharge	53 (80.3)	19 (50.0)	0.0013	34 (69.4)	0 (0.0)	0.014	13 (81.3)	0 (0.0)	0.063	
Leg (n)	**273**	**311**		**1,470**	**80**		**790**	**25**		
Mortality	1 (0.4)	39 (12.5)	<0.001	13 (0.9)	8 (10.0)	<0.001	6 (0.8)	3 (12.0)	<0.001	
hospital LOS	9.0 (5.0, 14.0)	16.0 (8.0, 28.5)	<0.001	6.0 (4.0, 9.0)	8.0 (5.8, 15.0)	<0.001	5.0 (4.0, 8.0)	9.0 (7.0, 11.0)	<0.001	
ICU	26 (9.5)	176 (56.6)	<0.001	60 (4.1)	24 (30.0)	<0.001	103 (13.0)	9 (36.0)	0.001	
ICU LOS	2.0 (1.0, 3.0)	6.0 (2.0, 13.0)	<0.001	2.0 (2.0, 3.0)	2.5 (2.0, 6.0)	0.023	1.0 (1.0, 2.0)	4.0 (1.0, 4.0)	0.003	
Discharge	205 (75.1)	114 (36.7)	<0.001	844 (57.5)	20 (25.0)	<0.001	500 (63.4)	3 (12.0)	<0.001	

Data are shown as median (P_{25}, P_{75}) or n (%). LOS, Length Of Stay; ICU, Intensive Care Unit.

Supplemental Table S3. Baseline characteristics per level of trauma care overall, and per ISS category.

		Level I Overall (n=2,762)	Level II Overall (n=3,092)	Level III Overall (n=1,639)	p-value overall
Sex male		1967 (71.2)	1665 (53.9)	846 (51.6)	<0.001
Age		50 (21)	64 (20)	66 (18)	<0.001
Comorbidity	**Healthy**	1275 (47.8; 3.5)	874 (28.4; 0.5)	522 (31.9; 0.2)	<0.001
	Mild	1112 (41.7)	1643 (53.4)	850 (52.0)	
	Severe	224 (8.4)	507 (16.5)	239 (14.6)	
	Unstable	54 (2.0)	53 (1.7)	24 (1.5)	
SBP < 90		152 (5.8; 5.7)	45 (1.6; 8.0)	13 (0.9; 7.3)	<0.001
RR		18 (15, 21; 46.3)	16 (14, 20; 34.5)	16 (14, 18; 28.3)	<0.001
BMR		6 (2, 6; 5.0)	6 (6, 6; 22.5)	6 (6, 6; 24.2)	<0.001
Transfer in		433 (15.7)	107 (3.5)	40 (2.4)	<0.001
ISS		17 (13, 26)	10 (9, 13)	9 (9, 11)	<0.001
Injury	**Penetrating**	226 (8.2)	39 (1.3)	10 (0.6)	<0.001
	Blunt	2536 (91.8)	3053 (98.7)	1629 (99.4)	
MAIS ≥ 3	**Head**	1278 (46.2)	697 (22.5)	374 (22.8)	<0.001
	Face	71 (2.6)	17 (0.6)	7 (0.4)	<0.001
	Neck	65 (2.4)	9 (0.3)	1 (0.1)	<0.001
	Thorax	877 (31.8)	573 (18.5)	337 (20.6)	<0.001
	Abdomen	213 (7.7)	75 (2.4)	18 (1.1)	<0.001
	Spine	502 (18.2)	203 (6.6)	93 (5.7)	<0.001
	Arm	104 (3.8)	52 (1.7)	17 (1.0)	<0.001
	Leg	584 (21.1)	1550 (50.1)	815 (49.7)	<0.001
	External	103 (3.7)	79 (2.6)	22 (1.3)	<0.001

Continuous variables are displayed as mean (SD; % missing) or median (((P25-P75; % missing), categorical variables are displayed as n (%; % missing). SBP, Systolic Blood Pressure; RR, Respiratory Rate; BMR, Best Motor Response; ISS, Injury Severity Score; MAIS, Maximum Abbreviated Injury Scale. Overall, comorbidity, SBP, RR, and BMR had missing value (1.5%, 7%, 37.5%, 16.5%, respectively), the other variables had no missing values.

Supplemental Table S3. Baseline characteristics per level of trauma care overall, and per ISS category.

		Level I			Level II			Level III		
		ISS 9-14 (n=1,030)	ISS > 15 (n=1,732)	p-value	ISS 9-14 (n=2,651)	ISS > 15 (n=441)	p-value	ISS 9-14 (n=1,476)	ISS > 15 (n=163)	p-value
Sex male		726 (70.5)	1241 (71.7)	0.513	1412 (53.3)	253 (57.4)	0.109	757 (51.3)	89 (54.6)	0.422
Age		49 (21)	51 (20)	0.006	64 (19)	67 (21)	0.004	65 (18)	71 (19)	<0.001
Comorbidity	**Healthy**	495 (48.6)	780 (47.4)	0.223	762 (28.9)	112 (25.6)	0.39	489 (33.2)	33 (20.4)	<0.001
	Mild	418 (41.0)	694 (42.2)		1405 (53.2)	238 (54.3)		764 (51.9)	86 (53.1)	
	Severe	79 (7.8)	145 (8.8)		429 (16.3)	78 (17.8)		204 (13.9)	35 (21.6)	
	Unstable	27 (2.7)	27 (1.6)		43 (1.6)	10 (2.3)		16 (1.1)	8 (4.9)	
SBP < 90		17 (1.7)	135 (8.4)	<0.001	29 (1.2)	16 (3.8)	0.001	10 (0.7)	3 (1.9)	0.13
RR		18 (15, 20)	18 (16, 22)	0.004	16 (14, 19)	18 (15, 22)	<0.001	15 (14, 18)	17 (14, 20)	<0.001
BMR		6 (6, 6)	6 (1, 6)	<0.001	6 (6, 6)	6 (6, 6)	<0.001	6 (6, 6)	6 (6, 6)	<0.001
Transfer in		154 (15.0)	279 (16.1)	0.419	95 (3.6)	12 (2.72)	0.359	40 (2.7)	0 (0.0)	0.0333
ISS		10 (9, 13)	25 (18, 30)	<0.001	9 (9, 10)	19 (17, 25)	<0.001	9 (9, 10)	18 (17, 22)	<0.001
Injury	**Penetrating**	117 (11.4)	109 (6.3)	<0.001	33 (1.2)	6 (1.4)	0.84	10 (0.7)	0 (0.0)	0.292
	Blunt	913 (88.6)	1623 (93.7)		2618 (98.8)	435 (98.6)		1466 (99.3)	163 (100)	
MAIS ≥ 3	**Head**	296 (28.7)	982 (56.7)	<0.001	477 (18.0)	220 (49.9)	<0.001	277 (18.8)	97 (59.5)	<0.001
	Face	9 (0.9)	62 (3.6)	<0.001	10 (0.4)	7 (1.6)	0.002	4 (0.3)	3 (1.8)	0.004
	Neck	22 (2.1)	43 (2.5)	0.561	5 (0.2)	4 (0.9)	0.01	1 (0.1)	0 (0.0)	0.74
	Thorax	162 (15.7)	715 (41.3)	<0.001	416 (15.7)	157 (35.6)	<0.001	283 (19.2)	54 (33.1)	<0.001
	Abdomen	31 (3.0)	182 (10.5)	<0.001	33 (1.2)	42 (9.5)	<0.001	7 (0.5)	11 (6.8)	<0.001
	Spine	170 (16.5)	332 (19.2)	0.079	160 (6.0)	43 (9.8)	0.004	83 (5.6)	10 (6.1)	0.789
	Arm	66 (6.4)	38 (2.2)	<0.001	49 (1.9)	3 (0.7)	0.077	16 (1.1)	1 (0.6)	0.574
	Leg	273 (26.5)	311 (18.0)	<0.001	1470 (55.5)	80 (18.1)	<0.001	790 (53.5)	25 (15.3)	<0.001
	External	21 (2.0)	82 (4.7)	<0.001	46 (1.7)	33 (7.5)	<0.001	17 (1.2)	5 (3.1)	0.044

Continuous variables are displayed as mean (SD; % missing) or median (((P25-P75; % missing), categorical variables are displayed as n (%; % missing). SBP, Systolic Blood Pressure; RR, Respiratory Rate; BMR, Best Motor Response; ISS, Injury Severity Score; MAIS, Maximum Abbreviated Injury Scale. Overall, comorbidity, SBP, RR, and BMR had missing value (1.5%, 7%, 37.5%, 16.5%, respectively), the other variables had no missing values.

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CHAPTER 8

Primary admission and secondary transfer of trauma patients to Dutch level I and level II trauma centres: predictors and outcomes

Highlights

- *This study provided several possible predictors regarding transfer of trauma patients, most prominent age and neurotrauma.*
- *Half of the patients transferred to the level I trauma centre are severely injured, but non-major trauma patients.*
- *Focus should be on specific subgroups that are currently under triaged and primarily admitted to non-level I trauma care.*

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Abstract

Purpose The importance and impact of determining which trauma patients need to be transferred between hospitals, especially considering prehospital triage systems, is evident. The objective of this study was to investigate the association between mortality and primary admission and secondary transfer of patients to level I and II trauma centres, and to identify predictors of primary and secondary admission to a designated level I trauma centre.

Methods Data from the Dutch Trauma Registry South West (DTR SW) was obtained. Patients ≥ 18 years who were admitted to a level I or level II trauma centre were included. Patients with isolated burn injuries were excluded. In-hospital mortality was compared between patients that were primarily admitted to a level I trauma centre, patients that were transferred to a level I trauma centre, and patients that were primarily admitted to level II trauma centres. Logistic regression models were used to adjust for potential confounders. A subgroup analysis was done including major trauma (MT) patients (ISS > 15). Predictors determining whether patients were primarily admitted to level I or level II trauma centres or transferred to a level I trauma centre were identified using logistic regression models.

Results A total of 17,035 patients were included. Patients admitted primarily to a level I centre, did not differ significantly in mortality from patients admitted primarily to level II trauma centres (Odds Ratio (OR): 0.73; 95% confidence interval (CI) 0.51–1.06) and patients transferred to level I centres (OR: 0.99; 95%CI 0.57–1.71). Subgroup analyses confirmed these findings for MT patients. Adjusted logistic regression analyses showed that age (OR: 0.96; 95%CI 0.94–0.97), GCS (OR: 0.81; 95%CI 0.77–0.86), AIS head (OR: 2.30; 95%CI 2.07–2.55), AIS neck (OR: 1.74; 95%CI 1.27–2.45) and AIS spine (OR: 3.22; 95%CI 2.87–3.61) are associated with increased odds of transfers to a level I trauma centre.

Conclusions This retrospective study showed no differences in in-hospital mortality between general trauma patients admitted primarily and secondarily to level I trauma centres. The most prominent predictors regarding transfer of trauma patients were age and neurotrauma. These findings could have practical implications regarding the triage protocols currently used.

Introduction

Injuries are an important cause of morbidity and mortality, both in the developed world and the developing world [1]. Although the global burden of injuries has declined over the past years morbidity and mortality caused by injuries are still substantial [1]. In order to treat trauma patients, many countries have adopted a regionalised trauma network. Trauma care within the Netherlands is set up to contain designated trauma centres (TCs) spanning eleven trauma regions. Each region has a designated level I TC for the treatment of major trauma (MT) patients (Injury Severity Score (ISS)>15) and level II and III centres for the stable patients. With such an exclusive trauma system survival rates of trauma patients have increased the past 15 years [2-5]. Within this system a trauma classification scheme (level I to III) has been established, with optimal 24/7 resources in level I TCs.

In the Netherlands, level I TCs are frequently academic teaching hospitals which have to meet minimum volume standards regarding the number of MT patients. Level II TCs offer less specialised trauma care and are not equipped for acute neuro-surgical procedures for head trauma and less prepared for severely injured patients[6, 7]. This description highlights the differences between level I and level II TCs, however, currently there is no consensus concerning whether there is a difference in outcomes between level I and level II TCs within an established and mature trauma system[8-11]. Prehospital triage guidelines are important to ensure trauma patients are admitted as quick as possible to their respective TCs. Although this concept seems simple, the decision to which hospital, and thus the right level of care, a patient needs to be transported is made by emergency medical service (EMS) providers. Compliance rates of triage protocols and experience of EMS providers are decisive to make the right judgement and dependent of a large number of variables, such as assessment of injury severity and local health care context.

Whether injured trauma patients have worse outcomes when secondarily admitted via transfer to a level I TC instead of being primarily admitted is unclear[12, 13]. Some studies suggest a difference, reporting patients with traumatic brain injury and severe injuries[14, 15] have a survival benefit when primarily admitted to a level I TC. In contrast, other studies found no difference in outcomes between level I and level II TCs (8), examined transfers without comparison to primary admission [16] or analysed level I and level II TCs combined[15, 16].

The aim of this study is to compare in-hospital mortality between trauma patients primarily admitted to a level I TC, trauma patients primarily admitted to a level II TC and patients secondarily transferred to a level I TC. The secondary aim was to identify predictors for primary admission to a level I or level II TC, and for secondary admission from level II to level I TCs via transfer.

Methods

Study design

Data for this study was obtained from trauma region Southwest of the Dutch National Trauma Registry (DNTR), which is a database that is maintained by eleven administrative TCs nationwide. The DNTR handle general inclusion criteria; all patients admitted to the

emergency department (ED) within 48 hours after trauma, followed by either hospitalisation, transfer to other hospitals or death are included, excluding patients that are dead on arrival. Information on patient demographics, prehospital care and injuries are coded using the Abbreviated Injury Scale (AIS), and outcomes are registered[17]. In total, the region Southwest Netherlands consists of one Level I TC and five Level II TCs.

A retrospective cohort study was performed including all trauma patients ≥ 18 years who were admitted to the level I or level II TCs between January 1 2015 and December 31 2018. Transfer is defined as primarily presented at a level II TC and transferred to a level I TC within 48 hours. Patients with isolated burn injuries were excluded because these patients are treated at one of the three nationally coordinated burn centres, of which one is located within the trauma region Southwest. Patients treated in level III TCs or originating from level III TCs were excluded due to the large difference in case mix of patients presented and/or admitted to level III TCs compared to patients admitted to level I and II TCs. The primary outcome measure was in-hospital mortality.

Type of Hospital Admission: primary and secondary

Patients were divided into three groups: trauma patients presented and admitted at the level I TC (PA level I), trauma patients primarily presented at a level II TC followed by a secondary transfer to the level I TC (ST level I), and trauma patients presented and admitted at a level II TC (PA level II).

Statistical analysis

First, a descriptive analysis was executed for the three patient groups regarding patient characteristics, injury characteristics and outcome characteristics. For continuous and ordinal variables, medians with 25th and 75th percentiles were reported. For nominal variables, frequencies with percentages were reported. The transfer group was further divided into ISS > 15 and ISS < 15 for a subgroup analysis. Second, missing values were imputed with multilevel multiple imputation dependent on mechanism of missingness [18-20]. Outcome measures were not imputed since these variables had no missing values. Third, a random effects logistic regression model was made to evaluate the association between type of hospital admission and in-hospital mortality. This provided an unadjusted estimate. After that, we added the following confounders to the model: age, gender, mechanism of injury, ISS, and prehospital vital parameters (systolic blood pressure (SBP), Glasgow Coma Scale (GCS), respiratory rate (RR)). Additionally, an ISS > 15 (MT) subgroup analysis was done. Continuous variables were tested for non-linearity using restricted cubic splines. When non-linearity was assumed, variables were split into two continuous linear variables with the optimal cut-off achieved from the restricted cubic spline [21].

To identify predictors determining whether trauma patients are primarily admitted to a level I or level II TC and to identify what predictors determine secondary admission to the level I TC univariate analyses were performed using two logistic regression models, one for the outcome primary admission to level I versus secondary transfer to level I and one for the outcome primary admission to level II versus secondary transfer from level II to level I. The following variables were analysed for an association with hospital admission: age (continuous), sex,

mechanism of injury, AIS scores for head, chest, abdomen and extremities (continuous), and prehospital vital parameters (SBP, GCS, RR, continuous). After that, two multivariable logistic regression models were created, one with outcome primary admission to level I versus secondary transfer to level I and one for the outcome primary admission to level II versus secondary transfer from level II tot level I, in which the following variables were analysed for an association with hospital admission: age (continuous), sex, mechanism of injury, AIS scores for head, chest, abdomen and extremities (continuous), and prehospital vital parameters (SBP, GCS, RR, continuous). Continuous predictors were tested for non-linearity using restricted cubic splines and non-linear variables were cut into categories based on the restricted cubic spline.

Data was analysed using the R Software Environment (version 3.5.1, the R Foundation for Statistical Computing, Vienna Austria). This study was done in accordance with the STROBE Statement.

Results

Study characteristics

A total of 17,035 records of trauma patients were included, of which 3658 patients were primarily admitted to a level I TC, 301 patients were transferred from a level II to a level I TC, and 13,076 patients were primarily admitted to a level II TC (Figure 1). All patients were transferred within 48 hours and 276 (92%) were transferred within 6 hours to a Level I TC.

Patients primarily admitted to level II TCs tended to be older than patients transferred or primarily admitted to a level I TC (Table 1). Males (n=2589, 70.8%) were more often primarily admitted to a level I TC or transferred to a level I TC than females (n=1069, 29.2%). Patients with an GCS of ≤8 seem to mostly be either primarily admitted to a level I TC or transferred to a level I TC. Patients with an ISS >15 (1768) tend to be primarily admitted to a level I TC or transferred to a level I TC; a total of 1206 (68.2%) patients with an ISS >15 are primarily admitted to a level I TC and a total of 1358 (76.8%) patients when transfers are added. Patients primarily admitted to a level I TC or transferred to a level I TC had a higher unadjusted mortality rate. Patients transferred to level I TCs with an ISS < 15 had less signs of shock (SBP <90) and were less severely injured.

Impact on outcome

The overall mortality was 3.9% (Table 1). The highest unadjusted mortality occurred in primary admissions to level I TCs (8.4%), followed by the secondary transfer group (7.6%) and primary admissions to level II TCs (2.6%). Univariate analysis shows a lower mortality for primary admissions to level II TCs compared to primary admissions to level I TCs (OR, 0.29; 95% CI, 0.23–0.37; p <0.001, Table 2). Multivariable analysis adjusting for gender, age, GCS, RR, SBP, ISS, and mechanism of injury showed that the adjusted mortality in the transfer group and primary admission to level II TCs group did not differ significantly from the primary admission to level I TCs group.

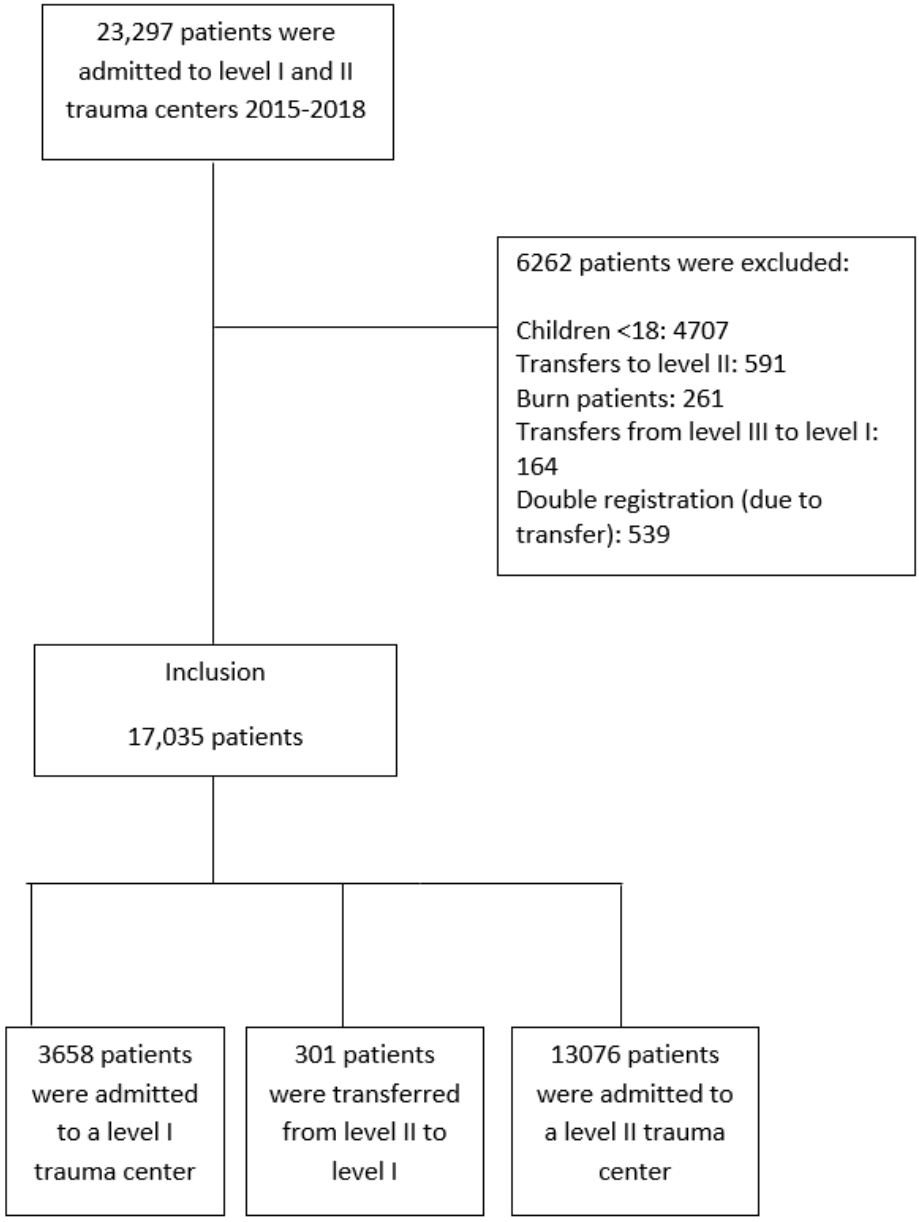

Figure 1. Flowchart.

Table 1. Baseline characteristics for patients primarily admitted to level I TCs (n=3658), transferred to level I TCs (n=301) and primarily admitted to level II TCs (n=13,076).

		Level I (n=3658)	Transfer to level I (n=301)	Level II (n=13,076)	p-value
Patient characteristics					
Male		2589 (70.8%)	193 (64.1%)	5656 (43.3%)	<0.001
Age - year		49 (31 - 66)	58 (40 - 70)	75 (57 - 85)	<0.001
Mechanism of injury					
Traffic	**Motorised vehicle**	329 (9.0%)	20 (6.6)	468 (3.6)	<0.001
	Motorcycle	132 (3.6%)	5 (1.7)	141 (1.1)	
	Moped/scooter	238 (6.5%)	19 (6.3)	408 (3.1)	
	Bike	462 (12.6)	36 (12.0)	1425 (10.9)	
	Pedestrian	164 (4.5)	9 (3.0)	162 (1.2)	
	Other	31 (0.8)	2 (0.7)	72 (0.6)	
Shooting incident		89 (2.4)	2 (0.7)	20 (0.2)	
Stabbing		182 (5.0)	5 (1.7)	114 (0.9)	
Blunt object		200 (5.5)	15 (5.0)	260 (2.0)	
fall on same level		1063 (29.1)	132 (43.9)	9151 (70.0)	
fall from higher level		341 (9.3)	26 (8.6)	327 (2.5)	
Explosion		18 (0.5)	0 (0.0)	12 (0.1)	
Drowning		37 (1.0)	0 (0.0)	13 (0.1)	
Asphyxiation		28 (0.8)	1 (0.3)	34 (0.3)	
Other		344 (9.4)	29 (9.6)	469 (3.6)	
Systolic blood pressure		135 (116 - 154)	140 (121 - 155)	141 (121 - 161)	<0.001
SBP <90		188 (5.9)	3 (1.2)	154 (1.3)	<0.001
GCS		15 (13 - 15)	15 (14 - 15)	15 (15 - 15)	<0.001
GCS ≤8		554 (15.7)	36 (13.5)	81 (0.8)	<0.001
RR		15 (12 - 20)	15 (12 - 18)	15 (12 - 18)	0.001
Injury characteristics					
ISS		9 (5 - 18)	16 (9 - 22)	9 (4 - 9)	<0.001
ISS >15		1206 (33.0)	152 (50.5)	410 (3.1)	<0.001
AIS head ≥3		934 (25.5)	125 (41.5)	624 (4.8)	<0.001
AIS thorax ≥3		660 (18.0)	36 (12.0)	537 (4.1)	<0.001
AIS abdomen ≥3		143 (3.9)	9 (3.0)	74 (0.6)	<0.001
AIS upper extremities ≥3		77 (2.1)	4 (1.3)	53 (0.4)	<0.001
AIS lower extremities ≥3		587 (16.0)	22 (7.3)	5404 (41.3)	<0.001
Outcome characteristics					
In-hospital mortality		309 (8.4)	23 (7.6)	342 (2.6)	<0.001
LOS ICU		0 (0 - 0)	0 (0 - 2)	0 (0 - 0)	<0.001
LOS		4.0 (2.0 - 10.0)	5.5 (3.0 - 11.0)	5.0 (2.0 - 9.0)	<0.001

Categorical variables represented with n (%); continuous variables represented with median (p25 – p75); p25 – p75, 25th percentile – 75th percentile; GCS, Glasgow coma score; ISS, injury severity score; AIS, abbreviated injury scale; ICU, intensive care unit; LOS, length of stay.

When solely focusing on MT patients, univariate analysis showed a lower mortality for both transfer patients as well as primary admissions to level II TCs. Multivariable analysis for MT patients showed that the adjusted mortality in the transfer group (adjusted OR, 0.72; 95% CI, 0.40 – 1.31; $p = 0.28$) and primary admission to level II TCs group (adjusted OR, 0.70; 0.45 – 1.11; p = 0.13) did not differ significantly from the primary admission to the level I TC group (Table 2).

Table 2. Odds ratios in-hospital mortality of transferred patients (n=301) and patients primarily admitted to level II TCs (n=13,076) compared to patients primarily admitted to level I TCs (n=3658).

	Unadjusted OR (95% CI)	p-value	Adjusted OR (95% CI) *	p-value
Transfer	0.90 (0.58–1.39)	0.63	0.99 (0.57–1.71)	0.97
Level 2	0.29 (0.23–0.37)	<0.001	0.73 (0.51-1.06)	0.10
ISS >15				
Transfer	0.50 (0.30–0.81)	0.01	0.72 (0.40–1.31)	0.28
Level 2	0.49 (0.35–0.67)	<0.001	0.70 (0.45–1.11)	0.13

*Adjusted for age, gender, mechanism of injury, ISS, prehospital systolic blood pressure, prehospital GCS and prehospital respiratory rate. OR, odds ratio; 95% CI, 95% confidence interval; GCS, Glasgow coma scale.

Predictors of transfer

Univariate analyses comparing patients transferred to the level I TC to patients primarily admitted to level I TCs showed that transfer patients are more likely to be older and are less likely to be male (Table 3). When conducting multivariable analyses comparing patients transferred to level I TCs to patients primarily admitted to level I TCs, transfer patients were found more likely to have head injuries (adjusted OR, 1.37; 95% CI, 1.25 – 1.50) and spine injuries (adjusted OR, 1.61; 95% CI, 1.47 – 1.76). Additionally, transfer patients are more likely to have face injuries and (superficial) skin injuries (Table 3).

When comparing patients transferred to the level I TCs to patients admitted primarily to level II TCs univariate analyses showed that, transfer patients are more likely to be male and are less likely to have lower extremities injuries. Multivariable analyses adjusting for other possible predictors showed that patients transferred to level I TCs are less likely to be older (≥70), are more likely to have a GCS < 8 (adjusted OR, 0.81; 95% CI, 0.76 – 0.85) and are found more likely to have head injuries (adjusted OR, 2.36; 95% CI, 2.04 – 2.50) compared to patients admitted primarily to level II TCs (Table 4).

Table 3. Predictors for being transferred: odds ratios of transfer patients (n=301) compared to patients primarily admitted to level I TCs (n=3658).

	Univariate OR (95% CI)	Multivariable* OR (95% CI)
Gender (male)	0.74 (0.58-0.94)	0.80 (0.61-1.05)
Age	1.01 (1.01-1.02)	1.01 (0.999-1.014)
GCS	1.02 (0.99-1.06)	1.05 (1.00-1.10)
Respiratory rate <18	1.07 (0.99-1.15)	1.06 (0.99-1.15)
Respiratory rate ≥18	0.87 (0.78-0.97)	0.91 (0.82-1.01)
Systolic blood pressure <140	1.01 (1.00-1.02)	1.01 (1.00-1.03)
Systolic blood pressure ≥140	0.99 (0.981-0.999)	0.99 (0.976-0.997)
AIS head	1.19 (1.11-1.26)	1.37 (1.25-1.50)
AIS face	0.74 (0.62-0.88)	0.63 (0.52-0.76)
AIS neck	1.00 (0.77-1.30)	1.08 (0.81-1.44)
AIS spine	1.43 (1.33-1.55)	1.61 (1.47-1.76)
AIS thorax	0.81 (0.72-0.90)	0.76 (0.67-0.87)
AIS abdomen	0.87 (0.73-1.04)	1.11 (0.91-1.34)
AIS upper extremities	0.84 (0.72-0.97)	0.97 (0.83-1.13)
AIS lower extremities	0.76 (0.67-0.85)	0.85 (0.75-0.96)
AIS external	0.57 (0.40-0.82)	0.60 (0.40-0.91)
Mechanism of injury		
Traffic: pedestrian	0.40 (0.15-1.10)	0.44 (0.15-1.31)
Traffic: bike	0.91 (0.63-1.30)	0.65 (0.39-1.06)
Traffic: motorised vehicle	0.71 (0.40-1.26)	0.62 (0.36-1.06)
Traffic: scooter/moped	0.95 (0.59-1.53)	1.00 (0.56-1.81)
High energy fall	0.86 (0.58-1.28)	0.62 (0.37-1.04)
Low energy fall	1.68 (1.32-2.14)	0.87 (0.58-1.31)
Other	0.81 (0.59-1.13)	1.61 (0.91-2.85)

*Adjusted for all other predictors in this analysis. OR, odds ratio; 95% CI, 95% confidence interval; GCS, Glasgow coma scale; AIS, abbreviated injury scale. Cut-off values of non-linear variables were based on restricted cubic splines

Table 4. Predictors for being transferred: odds ratios of transfer patients (n=301) compared to patients primarily admitted to level II TCs (n=13,076).

	Univariate OR (95% CI)	Multivariable* OR (95% CI)
Gender (male)	2.34 (1.85-2.98)	1.11 (0.83-1.48)
Age <70	1.00 (0.99-1.01)	1.00 (0.99-1.01)
Age ≥70	0.95 (0.94-0.96)	0.96 (0.94-0.97)
GCS	0.74 (0.71-0.77)	0.81 (0.76-0.85)
RR	0.99 (0.96-1.02)	0.99 (0.96-1.02)
SBP <140	1.01 (0.996-1.018)	1.01 (1.00-1.03)
SBP ≥140	0.99 (0.977-0.999)	0.99 (0.98-1.00)
AIS head	2.21 (2.06-2.37)	2.36 (2.04-2.50)
AIS face	1.73 (1.45-2.05)	0.85 (0.68-1.06)
AIS neck	2.26 (1.69-3.01)	1.77 (1.26-2.48)
AIS spine	2.77 (2.54-3.03)	3.20 (2.86-3.59)
AIS thorax	1.37 (1.22-1.53)	1.00 (0.86-1.17)
AIS abdomen	1.57 (1.33-1.87)	1.43 (1.16-1.77)
AIS upper extremities	1.15 (0.997-1.329)	1.06 (0.88-1.26)
AIS lower extremities	0.48 (0.43-0.54)	1.01 (0.87-1.16)
AIS external	1.16 (0.87-1.56)	0.70 (0.47-1.06)
Mechanism of injury		
Traffic: pedestrian	1.93 (0.70-5.34)	1.30 (0.43-3.93)
Traffic: bike	1.14 (0.80-1.64)	0.35 (0.20-0.61)
Traffic: motorised vehicle	0.54 (0.31-0.95)	0.52 (0.30-0.93)
Traffic: scooter/moped	2.14 (1.33-3.44)	0.51 (0.27-0.99)
High energy fall	3.63 (2.46-5.38)	0.46 (0.25-0.83)
Low energy fall	0.34 (0.27-0.44)	0.36 (0.23-0.57)
Other	2.68 (1.94-3.72)	2.63 (1.41-4.93)

*Adjusted for all other predictors in this analysis. OR, odds ratio; 95% CI, 95% confidence interval; GCS, Glasgow coma scale; AIS, abbreviated injury scale. Cut-off values of non-linear variables were based on restricted cubic splines

Discussion

The present study demonstrated no difference for in-hospital mortality between patients that are primarily admitted at level I TCs, patients that are transferred from level II to level I TCs, and patients that are primarily admitted at level II TCs. Furthermore, the present study found several possible predictors regarding type of admission of trauma patients. Compared to patients primarily presented at level I TCs, transferred patients were found more likely to have a higher GCS, a lower SBP, more severe head and spine injuries, and less severe face, thorax, lower extremities and skin injuries. In addition, transferred patients compared to patients primarily presented at level II TCs, were more likely to be younger, have a lower GCS, more severe head, neck, spine and abdominal injuries.

Differences in clinical outcomes measures between level I and level II TCs have been studied in the past[22, 23]. The present study demonstrated similar in-hospital mortality for level I and level II TCs, and transfer patients. These findings were previously reported for general trauma populations[22, 23]. Other studies did find a difference in mortality between level I and level II TCs[6, 11, 24]. A possible explanation for such contradicting results is that trauma systems in high-income countries have matured. Additionally, it is possible that geographical factors play a more prominent role in larger countries in patient allocation. Another possible explanation is that analyses were limited by case-mix differences, therefore not adjusting sufficiently for confounders. The present study found no difference for in-hospital mortality in MT patients. This is not in accordance with findings by other studies[23]. A possible explanation is that while the trauma system in the Netherlands has been maturing, and along with public health in general, mortality rates have steadily been decreasing, also among MT patients. Also Dutch Level II TCs do not have neurosurgery available which explains the high amount of secondary referred neurotrauma patients. Studies often exclude transfer patients, the studies that do include transfer patients are in agreement with the findings of the current study and find no difference in outcomes in patients primarily and secondarily admitted to level I and level II TCs[12, 13, 25, 26].

This study found several possible predictors regarding admission of trauma patients. Compared to patients primarily presented at level I TCs, patients transferred from a level II TC to a level I TC are more likely to have a higher GCS, a lower SBP, more severe head and spine injuries, and less severe facial, thorax, lower extremities and skin injuries. If compliance with prehospital triage is assumed, this demonstrates that patients with unnoticed or not yet apparent signs of TBI are more likely to be transferred when first admitted to a level II TC. This assumption is consistent with previous studies describing that most deaths caused by undertriage are secondary to severe TBI[27].

Compared to patients primarily presented and admitted to level II TCs, transferred patients were more likely to be younger, have a lower GCS and more severe head, neck, spine and abdominal injuries, indicating injuries of the central nervous system. Other studies found similar results, showing that transferred patients presented with more severe head and abdominal injuries and with lower GCS[16, 26]. The findings concerning age could be explained by a study which found nearly half of older trauma patients to be undertriaged[28]. However, another study found transferred patients to be older[26]. These different findings might be due

to undertriage of older trauma patients resulting in these patients staying in non-level I TCs whereas discovery of these undertriaged patients could result in an increase of transfers.

Prehospital identification of MT patients and identification of MT patients at the ED could better focus on specific subgroups that are often undertriaged. The results show that triage leading to admission to a level 1 TC does not always coincide with an ISS >15. This raises the question whether the ISS >15 is a reliable tool regarding the identification of patients that are in need of an admission to level I TCs. A possible alternative suggestion could be a more multidimensional approach by not just taking into account the three body regions with the highest AIS scores as done when calculating the ISS but to also asses which body regions have AIS scores above zero, paying particular attention to head, neck and spine. An example of this is the New Injury Severity Scale (NISS), which takes into account the three highest AIS scores regardless of body region whereas the ISS takes into account the three highest AIS scores from the three different most severely injured body regions. The NISS has been proven to identify more MT patients than the ISS[29]. The trouble with identifying patients that need level I trauma care and patients that need level II trauma care or lower level care is a phenomenon that encompasses many countries and triage protocols, as findings show nearly all triage protocols are unable to properly identify severely injured patients[30].

Limitations

The present study included validated data of a large number of patients records. However, the retrospective design is traditionally limited with several biases. The biggest limitation of our study is that there could be a negative selection bias because transferred patients tend to have worse outcomes than level II TC patients since that is the reason for a transfer to a Level I TC. In non-randomised trials, the observed study results observed may be because of unmeasured factors or variables. There is a chance of confounding bias due to case-mix differences. Additionally, the sample size of the transferred patient group could be too small and therefore lacking in power. Results of the transfer group should be interpreted with caution, especially regarding in-hospital mortality. It is possible there is a statistically significant difference in mortality that was not detected due to the small sample size. Another limitation is focusing on in-hospital mortality only Further research regarding outcomes such as quality of life and functional outcomes could also provide more information about which level of trauma care is appropriate for certain trauma populations.

Conclusions

The current study has provided several possible predictors regarding transfer of trauma patients, most prominent are age and neurotrauma. These findings could have practical implications regarding the triage protocol currently used. Half of the patients transferred to the level I TC have an ISS < 15. It is possible a move away from the ISS >15 and the weight this holds to other parameters could improve triage and therefore admittance of trauma patients to the right level of centre. Focus should better be on specific subgroups that are currently under triaged and primarily admitted to other levels of trauma care.

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PART IV

PATIENT-REPORTED OUTCOME MEASURES IN A TRAUMA NETWORK

CHAPTER 9

Health-related quality of life and return to work one year after major trauma from a network perspective

Highlights

- *Questionnaires on health-related quality of life, cognition, and work resumption were sent one year after trauma.*
- *Most responders experience problems in all health domains and function below population norms.*
- *Level of work resumption was associated with all health domains and cognition.*

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Abstract

Introduction Major trauma very often results in long term disabilities. The aim of this study was to assess health-related quality of life. cognition, and return to work one year after major trauma from a trauma network perspective.

Methods All major trauma patients in 2016 (Injury Severity Score > 15. n=536) were selected from trauma region Southwest Netherlands. Eligible patients (n=365) were sent questionnaires with the EQ-5D-5L and questions on cognition, level of education, comorbidities, and resumption of paid work one year after trauma.

Results A 50% (n=182) response rate was obtained. EQ-US and EQ-VAS scored a median (IQR) of 0.81 (0.62-0.89) and 70 (60-80). respectively. Limitations were prevalent in all health dimensions of the EQ-5D-5L; 90 (50%) responders reported problems with mobility, 36 (20%) responders reported problems with self-care, 108 (61%) responders reported problems during daily activities, 129 (73%) responders reported pain or discomfort, and 70 (39%) responders reported problems with anxiety or depression, 102 (61%) of the patients reported problems with cognition. Return to work rate was 68% (37% full. 31% partial). A median (IQR) EQ-US of 0.89 (0.82-1.00) and EQ-VAS of 80 (70-90) were scored for fully working responders; 0.77 (0.66-0.85, $p < 0.001$) and 70 (62-80, $p = 0.001$) for partial working respondents; and 0.49 (0.23-0.69, $p < 0.001$) and 55 (40-72, $p < 0.001$) for unemployed respondents.

Conclusion The majority experience problems in all health domains of the EQ-5D-5L and cognition. Return to work status was associated with all health domains of the EQ-5D-5L and cognition.

Introduction

In the global burden of disease, trauma is a major contributor to death and disabilities.[1] Surviving trauma can trigger a variety of problems in daily life. Distress and disabilities can have a profound impact on the well-being of the individual, as well as on their social network.[2] Trauma also gives rise to high societal costs due to health care dependence and a partial or complete inability to work.[3]

In the past decades trauma networks have been implemented. Such networks help to improve outcome of trauma care.[4, 5] Primary focus of these networks has long been improving survival. Since mortality has substantially been reduced focus in trauma care has been broadened towards long term functioning after trauma from a functional and psychological perspective.[6, 7] Over the past two decades many studies have been conducted on (health-related) quality of life (QoL) after major trauma (MT, ISS > 15). These publications mainly focus on MT patients admitted to designated (major) Trauma Centres (TC). However, many MT patients also being admitted to non-Trauma Centres (NTC)[8]. Only few cohorts have followed patients from a trauma network perspective.[7, 9, 10]

Most trauma registries identify the severity of injuries with the Injury Severity Score (ISS).[11] which is derived from the Abbreviated Injury Scale (AIS).[12] AIS revisions better reflect contemporary state of the art of trauma care. Few QoL studies focusing on MT have used more recent AIS revisions for calculating ISS in their cohort.[10, 13, 14]

EuroQoL 5D-3L is predominantly used as an instrument to measure QoL in previous studies on MT. Since EQ-5D-5L was introduced, more differentiation is possible in distinguishing between minor levels of impairment. QoL studies focusing on MT that have used EQ-5D-5L in combination with injury coding using recent AIS revision are scarce.[13] The aim of this study was to assess health-related quality of life, cognition, and return to work (RTW) one year after MT from a regional trauma network perspective.

Methods

The local Medical Research Ethics Committee exempted this study. Following review of the protocol, they concluded the study is not subject to the Medical Research Involving Human Subjects Act (MEC-2017-041).

General setting & data collection

Trauma region Southwest Netherlands is a large and diverse trauma region, with a level I TC, eleven level II/III NTC hospitals, a Burn Centre, a dedicated Eye Hospital, and three Emergency Medical Services (EMS). It consists of rural, remote, industrial, urban, and touristic areas with a dense infrastructure inhabited by 2.5 million people. It has an even larger catchment area with the availability of Helicopter Emergency Medical Services (HEMS).

Trauma region Southwest Netherlands participates in the Dutch National Trauma Registry (DNTR)[15] with the Dutch Trauma Registry Southwest (DTR SW) cohort. All major trauma patients (ISS > 15) admitted to an emergency department within 48 hours after trauma following either hospital admission, secondary transfer or death were included, excluding

death on arrival, double registries due to secondary transfers, death within the first year after trauma or residency abroad. Injuries were coded with AIS revision 2005 update 2008 (AIS08).[16] All included MT patients were retrospectively selected form the DNTR. One year after trauma, data from the DTR SW on demographics, injury coding, prehospital setting and clinical outcome measures of the 2016 MT cohort were linked with the results of a questionnaire containing the EQ-5D-5L, questions on cognition, return to (paid) work (RTW) and overall health state compared with pre-injury status (three level answer options nothing changed, worse or better), making it a mixed methods study.

All 12 DTR SW hospitals participated in this study. One year after trauma the municipal base administration was checked whether or not patients had died. Each week, included patient injured twelve months prior were contacted. Non-fatally injured patients living in The Netherlands or the Flemish region of Belgium, were sent a patient information letter, informed consent form, and questionnaire in Dutch. All questionnaires were self-reported, but respondents were allowed to ask for help. If patients lived in the Netherlands but had a language barrier, they were advised to complete the questionnaire with a relative that could help linguistically. For children younger than thirteen it was compulsory to complete the questionnaire and consent together with their parents or legal guardian. Children between thirteen and eighteen years of age were obliged to include consent of a parent or other guardians and allowed to complete the questionnaire themselves. If adult patients were incapacitated, proxies were allowed to sign informed consent. Patients who did not respond after one month were contacted by telephone until contact. All questionnaires contained the adult version of the EQ-5D-5L.

Responder & non-responders

In order to determine whether or not the responders were a representative sample of the population, demographic, injury related parameters, as well as the probability of survival, were compared between responders and non-responders.

Comorbidity & education

Comorbidities were surveyed with a modified version of the Cumulative Illness Rating Scale (CIRS), which is validated as an indicator of health status[17].

Educational level was trichotomised in 'low' (no diploma, primary school, or secondary vocational education), 'middle' (senior secondary or general vocational education , or university preparatory education), and 'high' (university of applied science or academic).

EuroQol-5D-5L & cognition

Health-related QoL was measured by the EQ-5D-5L which is a valid instrument for measuring QoL in healthy, chronically ill, and trauma populations.[18-20] It consists of two summary parts: the EQ-US and the EQ-VAS. The EQ-US is a summed score over five health dimensions that are scored with five levels ('no problems', 'slight problems', 'moderate', 'severe', and 'unable). Health dimensions are mobility, self-care, daily activities, pain or discomfort, and anxiety or depression. Each scored health dimension adds a utility score to a summary score (range -0.33-1.00, higher scores represent better QoL). With the EQ-VAS an

overall health state is scored on a Visual Analogue Scale from the worst imaginable health state to the best imaginable health state (0-100). Since the EQ-5D-5L does not capture cognitive functioning, an extra question was added and considered as a sixth health dimension with the same alteration of the abovementioned five level answer-options as used in the EQ-5D.[21-23] All health dimensions of the EQ-5D-5L and cognition were dichotomised in 'no limitations' ('no problems') and 'limitations' (from 'slight problems' to 'unable'). Subgroup analysis on EQ-US and EQ-VAS were done for gender, age, type of injury, ISS, and Maximum AIS (MAIS, most severe AIS code).

Return to work

Working age population was considered to be 18-65 years. Patients were asked how many days and how many hours per week they had paid work before and one year after trauma. RTW was trichotomised in 'full RTW', 'partial RTW', and 'no RTW'. Subgroup analysis on the level of RTW were done for gender, age, type of injury, ISS, and MAIS. RTW was also analysed in relation to each health domain of the EQ-5D-5L and cognition.

Data analysis

Statistical analyses were done with Statistical Package for Social Sciences version 24.0 (SPSS, Chicago, IL).

Normality of continuous variables was tested using the Shapiro-Wilk test. All continuous variables were non-normally distributed. Descriptive statistics are presented as median (Interquartile Range, IQR) for continuous variables and number (percentage) for categorical variables. A Mann-Whitney-test was used for comparing two groups. A Kruskal-Wallis-test was used for multiple groups, and in case of significant differences groups were tested pairwise with Mann-Whitney-tests. For nominal variables a χ^2-test or Fisher's exact test was used as applicable (both two-sided). A p-value of 0.05 was considered significant.

Results

Study population

Figure 1 shows the selection procedure. In 2016 536 MT patients were registered in the DTR SW. Exclusion criteria were death within the first year (n=139), double registries due to inter hospital referrals (n=13), and residency abroad (n=19). This resulted in a total of 369 patients who were sent questionnaires of whom 185 responded (50% response rate). The median follow-up time was 384 days (IQR 372-414). The responding group was significantly older than the non-responding group with a median age difference of little over a decade (median age 52 versus 41 years, $p = 0.002$). Overall, the responding grouped seemed representative for all included patients that were sent questionnaires (Table 1).

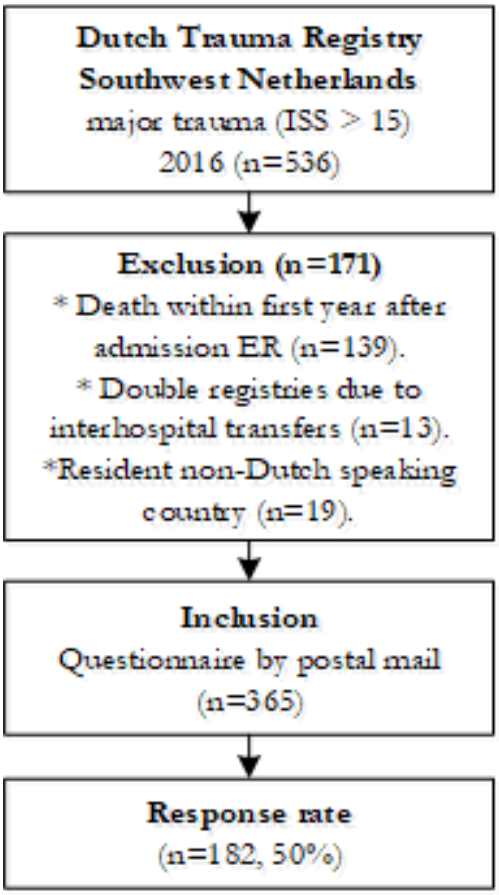

Figure 1. Study flow chart.

Overall health state, EuroQoL-5D-5L, and cognition

Eighty (44%) responders reported to be worse off than before trauma. The median EQ-US and EQ-VAS of all respondents (n=182) were 0.81 (IQR 0.61-0.89) and 70 (IQR 60-80), respectively. Limitations were prevalent in all health dimensions of the EQ-5D-5L; 90 (50%) responders reported limitations with mobility, 36 (20%) responders reported limitations with self-care, 108 (61%) responders reported limitations during daily activities, 129 (73%) responders reported limitations due to pain or discomfort, and 70 (39%) responders reported limitations with anxiety or depression. In the Dutch reference population[22] percentages of limitations in these health domains were 16.5%, 3.2%, 12.5%, 30.8%, and 10.6% respectively. Cognitive limitations were reported by 102 (61%) responders. In the Dutch reference population[22] 7.5% reported cognitive limitations.

Table 1. Comparison of responders with non-responders.

		Inclusion (n=365)	Respondents (n=182)	Non-respondents (n=183)	p-value
Probability of survival		0.95 (0.81-0.98)	0.94 (0.88-0.98)	0.95 (0.77-0.99)	0.554
Age at arrival ED		46 (28-63)	52 (29-67)	41 (26-55)	0.002
Gender – female		124 (34%)	66 (36%)	58 (32%)	0.378
ISS ≥ 25		115 (32%)	54 (30%)	61 (33%)	0.499
ISS		21 (17-25)	20 (17-25)	21 (17-26)	0.548
Penetrating injury		8 (2.2%)	1 (0.5%)	7 (3.8%)	0.067
EIP		67 (18%)	29 (16%)	38 (21%)	0.279
RP		8 (2.2%)	3 (1.6%)	5 (2.7%)	0.724
Hospital LOS		10 (5-19)	10 (5-17)	11 (5-21)	0.587
ICU		219 (60%)	111 (61%)	108 (59%)	0.749
Mechanical ventilation		121 (33%)	55 (30%)	66 (36%)	0.266
Surgery		183 (50%)	91 (50%)	92 (50%)	1.000
Injuries		6 (3-9)	6 (4-9)	5 (3-9)	0.548
Fractures		2 (1-4)	2 (1-4)	2 (1-4)	0.365
Cause	**Violence**	12 (3%)	3 (2%)	9 (5%)	0.381
	Traffic	150 (41%)	79 (43%)	71 (39%)	
	Work	33 (9%)	19 (10%)	14 (8%)	
	Private	119 (33%)	56 (31%)	63 (34%)	
	Sports	29 (8%)	16 (9%)	13 (7%)	
	Self-inflicted	19 (5%)	8 (4%)	11 (6%)	

Data are reported as medians (IQR) or as n (%). There are no missing data. ED, Emergency Department; Endotracheal Intubation Prehospital, EIP; Resuscitation prehospital, RP**;** ISS, Injury Severity Score; LOS, Length of Stay; ICU, combination of admission to an ICU (Intensive Care Unit), High Care Unit (HCU); or Medium Care Unit (MCU).

Table 2 shows the EQ-US, the EQ-VAS, and all health domains of the EQ-5D-5L and cognition for different subgroups. A statistically significant difference between age group 0-17 (n=21) and 18-55 (n=84) was present for EQ-US (0.89 versus 0.76, p =0.005). Age group 0-17 (n=21) scored significantly higher (p < 0.001) than age groups 18-55 (n=84) and 55+ (n=77) on their general health state (EQ-VAS 90 versus 70 and 70, respectively). Having comorbidities was associated with a worse EQ-US (healthy 0.82, one comorbidity 0.81 and >1 comorbidities 0.65, p=0.027) , a worse EQ-VAS (healthy 75, one comorbidity 70 and >1 comorbidities 68 , p=0.002) and more cognitive limitations (healthy 50%, one comorbidity 81% and >1 comorbidities 63 , p=0.002). Educational level was linear associated with cognitive limitation (low 75%, middle 54, high 44%, p=0.008).

Patients with an ISS ≥ 25 (n=54) scored significantly lower than patients with ISS 16-24 (n=128) on EQ-US and EQ-VAS with a median utility sum score of 0.66 and 0.84 respectively ($p < 0.001$), and a median VAS of 60 and 75 respectively ($p < 0.001$). Patients with ISS ≥ 25(n=54) reported cognitive limitations (n=39, 78.0%) significantly ($p = 0.003$) more often than patients with ISS 16-24 (n=63, 53.4%).

Patients with a severe lower extremity injury (MAIS ≥ 3) had significantly lower overall scores (n=33, EQ-US = 0.66, EQ-VAS = 60) than patients with moderate (MAIS 1-2) lower extremity injuries (n=34, EQ-US 0.82, $p = 0.048$) or patients without lower extremity injuries (n=115, EQ-US = 0.82, $p = 0.006$; EQ-VAS = 75, $p = 0.024$). Patients with severe spine injuries (MAIS ≥ 3) scored significantly worse on EQ-US than patients without spine injuries (n=27, EQ-US = 0.73 versus n=130, 0.82, $p = 0.05$). Patients with severe head injuries (MAIS ≥ 3, n=63, 73%) had significantly more often cognitive limitations than patients with moderate (MAIS 1-2, n=8, 36%, $p = 0.001$) or no head injuries (n=31, 52%, $p = 0.008$). Patients with moderate (MAIS 1-2, n=35, 73%) and severe face injuries (MAIS ≥ 3, n=5, 100%) reported significantly ($p = 0.043$ and $p = 0.025$ respectively) more often cognitive limitations than patients with no injuries in the face (n=62, 53%).

Return to work

Although 103 of the 185 respondents stated they had paid work before their trauma, complete data were acquired of 100 patients which could be analysed as working population. One year after trauma, overall RTW rate was 68% (n=68), 37% (n=37) worked as much or more as before trauma, and 31% (n=31) partially resumed work (Table 3). Patients who started working partially again, worked 14 (IQR 7-28) hours per week less than before.

All health domains including cognition are displayed per RTW group in Figure 2. Patients who worked fully again (n=37) had a median (IQR) EQ-US and EQ-VAS of 0.89 (0.82-1.00) and 80 (70-90), respectively. This differed significantly with the partial working group (n=31, EQ-US 0.77 (0.66-0.85), $p < 0.001$; EQ-VAS 70 (62-80), $p = 0.001$) and the unemployed group (n=32, EQ-US 0.49 (0.23-0.69), $p < 0.001$; EQ-VAS 55 (40-72), $p < 0.001$). Partial and no RTW also differed significantly on the EQ-US ($p < 0.001$) and EQ-VAS ($p = 0.002$). Comparing RTW status per health domain gave significant results for all health domains and cognition. A better RTW status, was associated with better scores on all health domains of the EQ-5D-5L and cognition. Patients who returned fully to work, could still experience limitations in health domains (from 5% (n=2) in self-care, up to 65% (n=24) in pain or discomfort).

Table 2. EQ-US. EQ-VAS and cognition one year after MT, in relation to gender, age, type of injury, ISS category, and severity of injuries per body region (MAIS).

		n	EQ-US (n=178)	EQ-VAS (n=174)	Limitations in health domains						
					Mobility (n=180)	Self-care (n=179)	Daily activities (n=179)	Pain & discomfort (n=179)	Anxiety & depression (n=180)	Cognition (n=168)
Respondents		182	0.81 (0.61-0.89; 4)	70 (60-80; 8)	89 (48.9; 3)	36 (19.8; 4)	108 (59.3; 4)	129 (70.9; 4)	70 (38.5; 3)	102 (56.0; 14)
Gender	**Male**	116	0.79 (0.60-0.89; 4)	71 (60-82; 4)	53 (46.9; 3)	24 (21.4; 4)	69 (61.6; 4)	80 (71.4; 4)	45 (39.8; 3)	64 (60.4; 10)
	Female	66	0.81 (0.60-0.89; 0)	70 (59-80; 4)	36 (54.5; 0)	12 (18.2; 0)	39 (59.1; 0)	49 (74.2; 0)	25 (37.9; 0)	38 (61.3; 4)
Age	**0-17**	21	0.89 (0.75-1.00; 0)A	90 (76-99; 1) D	1 (4.8; 0)D	1 (4.8; 0)	7 (33.3; 0)C	11 (52.4; 0)B	7 (33.3; 0)	12 (60.0; 1)
	18-55	84	0.76 (0.56-0.85; 1)	70 (59-80; 2)	44 (53.0; 1)	15 (18.1; 1)	60 (72.3; 1)	68 (81.9; 1)	38 (45.8; 1)	50 (62.5; 4)
	55+	77	0.82 (0.54-94; 3)	70 (55-80; 5)	44 (57.9; 1)	20 (26.7; 2)	41 (54.7; 2)	50 (66.7; 2)	25 (32.9; 1)	40 (59.4; 8)
Education (age 18+)	**Low**	68	0.74 (0.49-0.87; 3)	65 (50-75; 5)	40 (60.6; 2)	18 (29.2; 3)	48 (73,8; 3)	51 (78.5; 3)	32 (48.5; 2)	46 (75.4; 7)B
	Middle	58	0.81 (0.62-0.89; 1)	74 (60-84; 2)	29 (50.9; 1)	9 (15.8; 1)	35 (61,4; 1)	43 (75.4; 1)	22 (38.6; 1)	29 (53.7; 4)
	High	29	0.83 (0.69-0.89; 0)	70 (63-80; 0)	16 (55.2; 0)	5 (17.2; 0)	15 (51.7; 0)	21 (72.4; 0)	8 (27.6; 0)	12 (44.4; 2)
Comorbidity	**None**	99	0.82 (0.66-0.91; 0)A	75 (65-90; 5)C	41 (41.1; 0)B	16 (16.2; 0)A	55 (55.6; 0)	70 (70.7; 0)	34 (34.3; 0)	45 (49.5; 8)D
	1	50	0.81 (0.57-0.92; 2)	70 (60-75; 1)	25 (52.1; 2)	7 (14.6; 2)	31 (64.6; 2)	32 (66.7; 2)	18 (37.5; 2)	39 (81.3; 2)
	>1	33	0.65 (0.41-0.87; 1)	68 (50-75; 1)	23 (69.7; 0)	13 (40.6; 1)	22 (68.8; 1)	27 (84.4; 1)	18 (54.5; 0)	19 (63.3; 3)
ISS	**16-24**	128	0.84 (0.67-.92; 2)D	75 (64-85; 7)D	55 (43.0; 0)B	22 (17.3; 1)	68 (53.5; 1)C	86 (67.7; 1)A	42 (32.8; 0)B	63 (53.4; 10)C
	25+	54	0.66 (0.34-0.84; 2)	60 (48-75; 1)	34 (65.4; 2)	14 (26.9; 2)	40 (76.9; 2)	43 (82.7; 2)	28 (53.8; 2)	39 (78.0; 4)

			1Limitations in health domains							
		n	EQ-US (n=178)	EQ-VAS (n=174)	Mobility (n=180)	Self-care (n=179)	Daily activities (n=179)	Pain & discomfort (n=179)	Anxiety & depression (n=180)	Cognition (n=168)
MAIS										
Head	**None**	62	0.78 (0.48-0.89; 1)	70 (50-84; 2)	31 (50.8; 1)	13 (21.3; 1)	35 (57.4; 1)	49 (80.3; 1)	25 (41.0; 1)	31 (51.7; 2)D
	1-2	27	0.81 (0.60-0.90; 2)	70 (60-83; 1)	15 (57.7; 1)	7 (28.0; 2)	17 (68.0; 2)	19 (76.0; 2)	9 (34.6; 1)	8 (36.4; 5)
	3+	93	0.81 (0.61-0.92; 1)	72 (60-80; 5)	43 (46.2; 0)	16 (17.2; 0)	56 (60.2; 0)	61 (65.6; 0)	36 (38.7; 0)	64 (73.6; 6)
Face	**None**	124	0.81 (0.60-0.89; 3)	71 (55-85; 5)	60 (49.2; 2)	23 (19.0; 3)	70 (57.9; 3)	90 (74.4; 3)	49 (40.2; 2)	62 (53.9; 8)A
	1-2	53	0.79 (0.57-0.91; 1)	71 (60-80; 3)	25 (47.2; 0)	12 (22.6; 0)	34 64.2(; 0)	34 (64.2; 0)	18 (34.0; 0)	36 (73.5; 4)
	3+	5	0.74 (0.44-0.82; 0)	70 (53-73; 0)	4 (80.0; 0)	1 (20.0; 0)	4 (80.0; 0)	5 (100.0; 0)	3 (60.0; 0)	5 (100.0; 0)
Neck	**None**	176	0.81 (0.60-0.89; 4)	71 (60-82; 8)	86 (49.4; 2)	34 (19.7; 3)	102 (59.0; 3)	123 (71.1; 3)	64 (36.8; 2) B	99 (60.7; 13)
	1-2	1	0.74 (0.74-0.74; 0)	65 (65-65; 0)	1 (100.0; 0)	0 (0.0; 0)	1 (100.0; 0)	1 (100.0; 0)	1 (100.0; 0)	0 (0.0; 0)
	3+	5	0.64 (0.59-0.77; 0)	67 (63-73; 0)	2 (40.0; 0)	2 (40.0; 0)	5 (100.0; 0)	5 (100.0; 0)	5 (100.0; 0)	4 (80.0; 0)
Thorax	**None**	92	0.81 (0.53-0.92; 0)	75 (60-85; 4)	46 (50.0; 0)	22 (23.9;)	53 (57.6; 0)	63 (68.5; 0)	30 (32.6; 0)	53 (61.6; 6)
	1-2	21	0.74 (0.46-0.85; 0)	70 (58-83; 0)	12 (57.1; 0)	4 (19.0; 0)	14 (66.7; 0)	16 (76.2; 0)	11 (52.4; 0)	11 (57.9; 2)
	3+	69	0.82 (0.64-0.89; 4)	70 (58-80; 4)	31 (46.3; 2)	10 (15.2; 3)	41 (62.1; 3)	50 (75.8; 3)	29 (43.3; 2)	39 (60.9; 5)
Abdomen	**None**	150	0.81 (0.61-0.89; 2)	71 (60-80; 6)	75 (50.3; 1)	32 (21.5; 1)	92 (61.7; 1)	106 (71.1; 1)	53 (35.6; 1)	88 (62.4; 9)
	1-2	14	0.82 (0.61-0.94; 1)	80 (45-90; 1)	6 (42.9; 0)	1 (7.7; 1)	7 (53.8; 1)	10 (76.9; 1)	8 (57.1; 0)	6 (50.0; 2)
	3+	18	0.72 (0.24-0.94; 1)	65 (50-80; 1)	8 (47.1; 1)	3 (17.6; 1)	9 (52.9; 1)	13 (76.5; 1)	9 (52.9; 1)	9 (56.3; 2)

			Limitations in health domains							
		n	EQ-US (n=178)	EQ-VAS (n=174)	Mobility (n=180)	Self-care (n=179)	Daily activities (n=179)	Pain & discomfort (n=179)	Anxiety & depression (n=180)	Cognition (n=168)
MAIS										
Spine	**None**	130	0.82 (0.65-0.92; 1)A	71 (60-81; 6)	57 (43.5; 0)A	22 (16.9; 0)	72 (55.4; 0)	86 (66.2; 0)A	49 (37.4; 0)	79 (64.2; 7)
	1-2	25	0.75 (0.39-0.85; 2)	70 (55-82; 2)	15 (65.2; 2)	6 (26.1; 2)	16 (69.6; 2)	20 (87.0; 2)	10 (43.5; 2)	13 (61.9; 4)
	3+	27	0.73 (0.46-0.85; 1)	70 (60-80; 0)	17 (65.4; 1)	8 (30.8; 1)	20 (76.9; 1)	23 (88.5; 1)	11 (42.3; 1)	11 (44.0; 2)
Upper Extremity	**None**	106	0.81 (0.59-0.92; 0)	70 (60-85; 1)	55 (51.9; 0)	21 (19.8; 0)A	58 (54.7; 0)	71 (67.0; 0)	39 (36.8; 0)	60 (60.6; 16)
	1-2	74	0.80 (0.60-0.89; 4)	70 (58-80; 7)	33 (45.8; 2)	13 (18.3; 3)	48 (67.6; 3)	56 (78.9; 3)	30 (41.7; 2)	42 (61.8; 6)
	3+	2	0.71 (0.66-0.71; 0)	65 (50-65; 0)	1 (50.0; 0)	2 (100.0; 0)	2 (100.0; 0)	2 (100.0; 0)	1 (50.0; 0)	1 (50.0; 0)
Lower Extremity	**None**	115	0.82 (0.61-1.00; 2) A	75 (60-85; 5)	48 (41.7; 0)D	23 (20.2; 1)	61 (53.5; 0)A	72 (63.2; 0)C	42 (36.5; 0)	62 (57.4; 7)
	1-2	34	0.82 (0.66-0.86; 1)	70 (65-82; 2)	16 (48.5; 1)	4 (12.1; 1)	22 (66.7; 1)	29 (87.9; 1)	12 (36.4; 1)	20 (69.0; 5)
	3+	33	0.66 (0.30-0.84; 1)	60 (50-79; 1)	25 (78.1; 1)	9 (28.1; 1)	25 (78.1; 1)	28 (87.5; 1)	16 (50.0; 1)	21 (65.6; 1)
External	**None**	159	0.81 (0.61-0.89; 4)	71 (60-82; 8)	77 (49.0; 2)	30 (19.2; 3)	97 (62.2; 3)	110 (70.5; 3)	58 (36.9; 2)	86 (58.1; 11)
	1-2	17	0.76 (0.51-0.89; 0)	70 (48-83; 0)	9 (52.9; 0)	4 (23.5; 0)	9 (52.9; 0)	14 (82.4; 0)	9 (52.9; 0)	11 (73.3; 2)
	3+	6	0.76 (0.53-0.90; 0)	60 (39-80; 0)	3 (50.0; 0)	2 (33.3; 0)	2 (33.3; 0)	5 (83.3; 0)	3 (50.0; 0)	6 (100.0; 0)

Data are reported as medians (IQR; no. missing values) or as n (%; no. missing values). [A] $0.05 \leq p<0.01$. [B] $0.01 \leq p<0.005$. [C] $0.005 \leq p<0.001$. [D] $p \leq 0.001$. ISS. Injury Severity Score; MAIS. Maximum Abbreviated Injury Score.

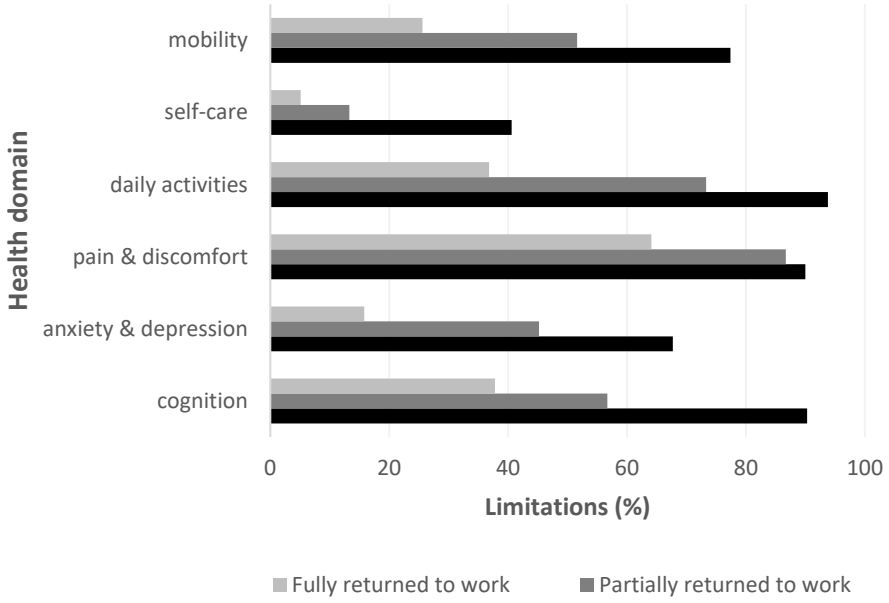

Figure 2. Limitations (%) per health domain of the EQ-5D-5L and cognition per return to work group. In Table 3 fully, partial, and no RTW are shown for different subgroups. Patients with less severe injuries (ISS 16-24, n=68) returned to work more often (p = 0.020). Level of work resumption was unrelated to gender, type of injury, age, level of education, no. of comorbidities and (severity) of specific organ injuries one year after MT.

Table 3. RTW one year after MT, in relation to gender, age, type of injury, ISS category, and maximum AIS per body region (MAIS).

			Level of return to work			
		Overall (n=100)*	**Fully (n=37)**	**Partially (n=31)**	**No return (n=32)**	**p-value**
Female		28 (28%)	7 (19%)	12 (39%)	9 (28%)	0.194
Age 18-55		69 (71%)	25 (36%)	22 (32%)	22 (32%)	0.912
Education	**Low**	39 (40%)	10 (27%)	13 (42%)	16 (53%)	0.107
	Middle	39 (40%)	16 (43%)	11 (36%)	12 (40%)	
	High	20 (20%)	11 (30%)	7 (23%)	2 (7%)	
Comorbidity	**None**	62 (62%)	28 (76%)	16 (52%)	18 (56%)	0.297
	1	26 (26%)	6 (16%)	10 (32%)	10 (31%)	
	>1	12 (12%)	3 (8%)	5 (16%)	4 (13%)	
ISS 16-24		68 (68%)	30 (81%)	22 (71%)	16 (50%)	0.020
MAIS						
Head	**None**	35 (35%)	11 (30%)	12 (39%)	12 (38%)	0.815
	1-2	18 (18%)	8 (22%)	6 (19%)	4 (13%)	
	3+	47 (47%)	18 (49%)	13 (42%)	16 (50%)	

Table 3. RTW one year after MT, in relation to gender, age, type of injury, ISS category, and maximum AIS per body region (MAIS).

		Level of return to work				
		Overall (n=100)*	**Fully (n=37)**	**Partially (n=31)**	**No return (n=32)**	**p-value**
Face	**None**	69 (69%)	26 (70%)	19 (61%)	24 (75%)	0.674
	1-2	26 (26%)	10 (27%)	9 (29%)	7 (22%)	
	3+	5 (5%)	1 (3%)	3 (10%)	1 (3%)	
Neck	**None**	96 (96%)	36 (97%)	30 (97%)	30 (94%)	0.432
	1-2	1 (1%)	-	1 (3%)	-	
	3+	3 (3%)	1 (3%)	-	2 (6%)	
Thorax	**None**	41 (41%)	18 (49%)	10 (32%)	13 (41%)	0.338
	1-2	15 (15%)	3 (8%)	8 (26%)	4 (13%)	
	3+	44 (44%)	16 (43%)	13 (42%)	15 (47%)	
Abdomen	**None**	82 (82%)	30 (81%)	26 (84%)	26 (81%)	0.479
	1-2	8 (8%)	5 (14%)	1 (3%)	2 (6%)	
	3+	10 (10%)	2 (5%)	4 (13%)	4 (13%)	
Spine	**None**	64 (64%)	23 (62%)	21 (68%)	20 (63%)	0.282
	1-2	18 (18%)	9 (24%)	2 (7%)	7 (22%	
	3+	18 (18%)	5 (14%)	8 (26%)	5 (16%)	
Upper Extremity	**None**	58 (58%)	22 (60%)	19 (61%)	17 (53%)	0.819
	1-2	40 (40%)	15 (41%)	11 (36%)	14 (44%)	
	3+	2 (2%)	-	1 (3%)	1 (3%)	
Lower Extremity	**None**	60 (60%)	23 (62%)	18 (58%)	19 (60%)	0.881
	1-2	20 (20%)	8 (22%)	7 (23%)	5 (16%)	
	3+	20 (20%)	6 (16%)	6 (20%)	8 (25%)	
External	**None**	87 (87%)	35 (95%)	28 (90%)	24 (75%)	0.138
	1-2	10 (10%)	2 (5%)	2 (7%)	6 (19%)	
	3+	3 (3%)	-	1 (3%)	2 (6%)	

Data are reported as n (%). * Three responders reported work. but did not state how many hours and were left out of the analysis. ISS, Injury Severity Score; MAIS, Maximum Abbreviated Injury Score.

Discussion

This study assessed functional limitations by the means of health-related QoL and RTW in patients one year after MT (ISS > 15) from a trauma network perspective. The median overall utility score was 0.81 and the median general health state 70. Over 60% reported cognitive problems and less than 40% fully returned to work. If patients reported limitations, the majority scored little or moderate problems on all health domains. Severe problems or 'not able' was scored less (4.4-20.7%). Limitations within the five health domains of the EQ-5D or cognition were reported by 87% of all responders. In contrast, 44% of the respondents reported to be worse off after their trauma. Many respondents might have had functional

limitations before their trauma. Trauma populations are associated with higher pre-existing morbidity, compared with non-injured populations, which might be prone to an overestimation of problems post injury.[24] In addition, recall bias could have caused responders to overconfidently report their overall health state. A mean overall utility score of 0.88 has been reported for the Dutch population.[22] Dutch non-hospitalised trauma patients have a comparable health status five months after trauma (0.87).[25] A mean overall utility score of ≈ 0.84 has been reported for a Dutch hospitalised trauma population one year after trauma (taken from graph).[26] For the majority of the respondents in the present study. QoL was below population norms one year after MT.

Dutch studies[27-29] comparable to the current study were done on adult MT populations in a single level I trauma centre with the usage of EQ-5D-3L. A mean EQ-US of 0.69 was reported by two studies[27, 28] and a median of 0.73 in the remaining study.[29] A recent regional study[30] reported an mean overall utility score with EQ-5D-3L on adults of 0.77 one year after MT trauma. The adult population in the current study had an median EQ-US of 0.81 (IQR 0.61-0.89), and for comparing purposes a mean of 0.70 (SD 0.30). Prevalence of limitations in most health domains remain high and yields a similar pattern compared to previous mentioned single centre studies. Despite improvements in trauma care, health domains mobility, daily activities, and pain or discomfort even display increased prevalence of limitations. Future research should focus on interventions that reduce common chronic complaints that impact QoL after MT. Such interventions should not only be addressed to hospitals, but in collaboration with revalidation trajectories on all levels. Prevention of trauma by wearing helmets in traffic by people on (motor driven) bicycles, separating cycle roads from major roads, fall prevention for the elderly, and reducing substance abuse and psychiatric disorders are some examples of favorable strategies over cure and care.

A straightforward comparison of the present study with international publications on (health-related) QoL after MT is difficult due to the use of different questionnaires, reporting the same instruments differently, variability in inclusion criteria, and the usage of different AIS revisions for injury coding. Studies that used unknown or older AIS revisions reported a mean EQ-US range of 0.60-0.69 or a median EQ-US range of 0.60-0.73, within a response time range of six to eighteen months after trauma. The current study combined injury coding and inclusion on the basis of AIS08 with the EQ-5D-5L. Only one MT study[13] with AIS08 injury coding that reported QoL and had general inclusion criteria used the 5L version (median EQ-US ≈ 0.80, taken from graph). MT patients have higher mortality rates and more frequently need intensive care and urgent surgery when the ISS is derived from AIS08 compared to older AIS revisions.[31] One would also expect a worse QoL compared to previous studies with injury coding on the basis of AIS98, however this was not the case. Two factors could have been a major contributor to better QoL in the current cohort. First, the EQ-5D with a 5-level answer option might have had a moderating effect compared to the 3-level version. Secondly, (major) trauma networks have matured.

Especially international studies handling QoL after MT from a regional trauma network perspective are scarce.[7, 9, 10] Most studies on QoL of MT patients included adult populations admitted to a single TC. In 2015-2018 around one third of all MT patients in the DTR SW cohort were directly admitted to NTC's. The current study looked at all MT patients captured in one TC and eleven NTC's, a truly representative national sample.

Patients with an ISS ≥ 25 scored worse on EQ-US, EQ-VAS, and cognition than patients with an ISS 16-24. A similar association was found between RTW and ISS. These results suggest that being able to return to work has a positive impact on the perceived QoL one year after MT, or that improved QoL may facilitate RTW. QoL and RTW are associated. Even though RTW can indicate a certain health status, the question is whether it is a reliable parameter to evaluate trauma outcome since it can be affected by many other factors (*e.g.* economic).[32]

Limitations

First, a response rate of 50% might have resulted in a non-response bias. A part of the patients will not have been able to respond due to (severe) problems with *e.g.* hand writing, post-traumatic stress, depression, or level of consciousness. MT patients that have had fewer problems post injury, might have been more likely to respond because they have fewer attention consuming activities around their recovery or found participating not that confronting. These biases will result in an overestimation of the recovery status of the studied cohort one year after MT. However, during reminder calls, statements on not participating due to no experienced problems were also not uncommon. Recall bias could have resulted in an underestimation of the overall health state of the responders. In general, reliable information on pre-injury is lacking in this study. Such information is appropriate in compensating for attribution bias. Second, the EuroQOL-group advises a proxy version for ages 0-7, the EQ-5D-Y for ages 8-11, and for ages 12-18 the adult version can be used (for ages 12-15 the EQ-5D-Y is recommended). These versions are developed on the basis of the EQ-5D-3L and at present a utility value set for the EQ-5D-Y is lacking. In the present study the adult version of the EQ-5D-5L was used for children, which probably resulted in an overestimation of the QOL of children aged 15 years and younger.[33] Third, the definition of MT has always been under the debate, we used a threshold of ISS > 15. The ISS was calculated following AIS08, while the most recent version being AIS15. It is unclear what the effects of the AIS15 are on a MT cohort with an ISS > 15. In addition, a certain part of injuries are wrongly coded due to inter-rater agreement and reliability limitations of the AIS.[34] Adding patients to the current cohort with a significant trauma mechanism but an ISS < 16 in combination with AIS15 could have created a more comprehensive and contemporary overview of QoL after MT.

The extent of problems people experience one year after MT stresses the necessity of a long multicentre follow-up. More insight can be gained in the long term recovery status of MT patients. Physical and mental recovery take a long time, but social integration might take much longer. Especially when not just considering the effect of traumatic events on individuals, but also on their social environment and relatives.

Conclusion

One year after major trauma, the majority of patients experience problems in all health domains of the EQ-5D-5L and cognition, and function below population norms. Trauma care should focus on these health domains in collaboration with other revalidation disciplines. Return to work status was associated with all health domains of the EQ-5D-5L and cognition, showing that focus on health status of trauma patients in recovery trajectories can potentially have many positive effects.

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CHAPTER 10

Comparing health status after major trauma across different levels of trauma care

Highlights

- *Health-related quality of life of major trauma patients admitted to a level I trauma centre was below population norms, when admitted to a non-level I trauma centre scores were similar as populations norms.*
- *After adjusting, general health status of respondents one to two years after trauma did not differ across levels of trauma care.*
- *Fewer limitations in mobility, self-care, and pain and discomfort were reported in level II facilities in adjusted analysis.*
- *Trauma populations differ across levels of trauma care, making it an important factor in analysing quality of trauma care.*

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Abstract

Introduction Mortality due to trauma has reduced the past decades. Trauma network implementations have been an important contributor to this achievement. Besides mortality, patient-reported outcome parameters should be included in evaluation of trauma care. While concentrating major trauma care, hospitals are designated with a certain level of trauma care following specific criteria.

Objective Comparing health status of major trauma patients after two years across different levels of trauma care in trauma networks.

Methods Multicentre observational study comprising a secondary longitudinal multilevel analysis on prospective cohorts from two neighbouring trauma regions in the Netherlands. Inclusion criteria: patient aged ≥ 18 with an ISS > 15 surviving their injuries at least one year after trauma. Health status was measured one and two years after trauma by EQ-5D-5 L, added with a sixth health dimension on cognition. Level I trauma centres were considered as reference in univariate and multivariable analysis.

Results Respondents admitted to a level I trauma centre scored less favourable EQ-US and EQ-VAS in both years (0.81–0.81, 71–75) than respondents admitted to a level II (0.88–0.87, 78–85) or level III (0.89–0.88, 75–80) facility. Level II facilities scored significantly higher EQ-US and EQ-VAS in time for univariate analysis (β 0.095, 95% CI 0.038–0.153, $p = 0.001$, and β 7.887, 95% CI 3.035–12.740, $p = 0.002$), not in multivariable analysis (β 0.052, 95% CI -0.010–0.115, $p = 0.102$, and β 3.714, 95% CI -1.893–9.321, $p = 0.193$). Fewer limitations in mobility (OR 0.344, 95% CI 0.156–0.760), self-care (OR 0.219, 95% CI 0.077–0.618), and pain and discomfort (OR 0.421, 95% CI 0.214–0.831) remained significant for level II facilities in multivariable analysis, whereas significant differences with level III facilities disappeared.

Conclusion Major trauma patients admitted to level I trauma centres reported a less favourable general health status and more limitations compared to level II and III facilities scoring populations norms one to two years after trauma. Differences on general health status and limitations in specific health domains disappeared in adjusted analysis. Well-coordinated trauma networks offer homogeneous results for all major trauma patients when they are distributed in different centres according to their need of care.

Introduction

The global trauma burden is substantial.[1, 2] Health care and productivity costs are considerable, physical trauma can have a psychological impact, a large group reports social dysfunction and quality of life is below populations norms one year after major trauma.[3-8] In order to reduce that burden, many countries and regions have successfully implemented trauma systems the past decades.[9] Such trauma systems have been an important contributor to a reduction in mortality.[10-12] With a focus on concentrating major trauma care, management of prehospital and in-hospital trauma care, and volume-outcome associations are getting more attention recent years.[13-15]

Focus in trauma outcome analysis has also shifted to non-fatal outcome with longitudinal analysis of large cohorts.[16-18] Studies relating health status or non-fatal clinical outcome measures to different levels of trauma care in a network are limitedly available or display inconsistencies in the body of evidence.[19] The only available study comparing patient-reported outcome measures across different levels of trauma care in a trauma network, reported similar health status for major trauma patients admitted to level I and level II facilities.[20]

Regionalised trauma care in the Netherlands is organised as an inclusive system. Trauma centres in the Netherlands have designated levels of care based on criteria established by the Dutch Trauma Society. Level I trauma centres deliver most extensive trauma care with immediate availability of specialists around the clock and are required to treat a minimum of 240 major trauma (Injury Severity Score (ISS) > 15) patients annually. Level II facilities are able to stabilise major trauma patients, but, do not have all neurosurgical facilities and other (damage control) resources immediately available. Patients with minor or isolated injuries should be admitted to a level III facility. Despite trauma networks, many major trauma patients are still admitted to a level II and level III facilities.[21] In level I trauma centres, major trauma populations might differ typically in composition of patient profiles from those admitted to level II and level III facilities. Especially for multivariable analysis of health status, it is relevant to gain knowledge on case mix by adjustment for the right variables. Local health care context, such as trauma networks with different levels trauma care facilities, can be an important factor in analysing quality of trauma care provided. This study aimed to determine health status of major trauma patients across different levels of trauma care at one and two years after trauma.

Methods

Following review of the protocol, the local Medical Research Ethics Committee concluded this study was not subject of the Medical Research Involving Human Subjects Act (MEC-2022-0136). Previous data collection in Southwest Netherlands was approved by the local Medical Ethics Committee (MEC-2017-041), and in Brabant by the local Medical Ethics Committee (NL50258.028.14) and registered at ClinicalTrials.gov (NTC02508675). Data are reported in line with strengthening the reporting of observational studies in epidemiology (STROBE).[22]

This multicentre observational study comprised a secondary longitudinal multilevel analysis on data from prospective cohorts from two large neighbouring trauma regions in the Netherlands, Brabant and Southwest Netherlands. The combined trauma regions have 20 hospitals (two level I trauma centres), one dedicated Burn Centre, one dedicated Eye Hospital, six Emergency Medical Services (EMS), and the availability of Helicopter Emergency Medical Services (HEMS). Geographically, the catchment area is diverse with rural, remote, industrial, urban and touristic parts, inhabited by 5 million people.

Data of the Brabant cohort were extracted from a larger cohort (Brabant Injury Outcome Surveillance, BIOS).[23] This cohort included all acute (within 48 hours after trauma) hospitalised adult (≥18years) major trauma (ISS > 15) patients who survived to discharge. Patients were followed throughout six follow up moments from 1 week up to 24 months. The Southwest cohort included all acute (within 48 hours after trauma) hospitalised adult (≥18years) major trauma (ISS > 15) patients from the Dutch National Trauma Registry (DNTR)[24], and invited participants one year and two years after trauma.[7] The inclusion period of the Brabant cohort ran from August 1, 2015 to July 31, 2016, the inclusion period for the Southwest cohort was January 1, 2016 to December 31, 2016 (Figure 1). All persons or legal proxies gave written consent, before participating. Non-response bias was reduced to a minimum by sending reminders and allowing legal sequelae to help incapacitated persons.

Demographics and clinical variables

For descriptive characteristics of the cohorts and useful predictors of health status, age, sex, level of trauma care, cause of trauma, type of injury (blunt or penetrating), Revised Trauma Score (RTS)[25] at ED, Hospital Length of Stay (LOS), ICU admitted, mechanical ventilation, all injuries coded with the Abbreviated Injury Scale 2008[26] (AIS08), derived Injury Severity Score[27, 28] (ISS08), as well as the number of fractures were extracted from the DNTR. Both trauma regions have a 100% participation rate in the DNTR.

From AIS08 coded injuries a Prehospital Trauma Triage Protocol (PTTP) variable was created. In the Netherlands, specific injuries are mentioned in a national protocol for prehospital trauma care for (H)EMS, whether a patient should be allocated to a level I trauma centre or a non-level I trauma centre. The following injury codes are specifically mentioned in the PTTP; 'flail chest', 'cervical, thoracic, lumbar cord contusion', 'brachial plexus', 'pelvic instability', 'penetrating head, thoracic or abdominal injuries', 'two or more fractures of tibia, humerus or femur', and 'hypothermia ≤ 33 Celsius'. For hypothermia, AIS08 codes have a cut-off point of 32° Celsius or 34° Celsius, the latter was chosen. PTTP was dichotomised in 'yes' and 'no'. PTTP is also based on vital signs, which are represented In the RTS as a covariate.

Comorbidities present before trauma were surveyed with a modified version of the Cumulative Illness Rating Scale (CIRS), which is validated as an indicator of health status.[29] First available reported comorbidities were used for analysis. Educational level was categorised in 'low' (no diploma, primary school, or secondary vocational education), 'middle' (senior secondary or general vocational education, or university preparatory education), and 'high' (university of applied science or academic).

Outcome

Health status was measured by EuroQol-5D (EQ-5D)[30], which is a valid instrument for measuring health-related quality of life.[31-33] Five health dimensions are scored on a Likert scale: 'mobility', 'self-care', 'daily activities', 'pain or discomfort', and 'anxiety or depression'. Each scored health dimension adds a utility score to a summary EuroQol utility score (EQ-US, range 3L-version -0.329-1.000, range 5L-version -0.446-1.00, higher scores represent better health status). The second part of the EQ-5D is the EuroQol visual analogue scale (EQ-VAS). The EQ-VAS represents an overall health state and is scored from 'worst imaginable' to 'best imaginable' health state (0-100).

The Brabant cohort used EQ-5D-3L, and the Southwest cohort used the 5L version. In the 3L version all health dimensions are scored on a 3 point Likert scale ('no problems', 'moderate problems', 'severe problems'), and for the 5L version answer options on a 5 point Likert scale are 'no problems', 'slight problems', 'moderate', 'severe', and 'unable'. An EQ-5D-5L Index Value Calculator[34] was developed by the EuroQol Group and used to convert EQ-US based on EQ-5D-3L to EQ-5D-5L, based on the Dutch value set.

Since EQ-5D does not capture cognitive functioning, an extra question was added and considered as a sixth health dimension with the same alteration of the above mentioned 3L and 5L answer-options as used in EQ-5D.[35-37]

All health dimensions of EQ-5D-3L and EQ-5D-5L and cognition were dichotomised in 'no limitations' ('no problems') and 'limitations' (from 'moderate to severe' for EQ-5D-3L and 'slight problems' to 'unable' for the EQ-5D-5L).

Data analysis

Statistical analyses were done with Statistical Package for Social Sciences version 25.0 (SPSS, Chicago, IL). Normality of continuous variables was tested using the Shapiro-Wilk test (p-value < 0.05 was considered significant). All continuous variables were non-normally distributed. Descriptive statistics are presented as median with 25th and 75th percentiles (P_{25}-P_{75}) for continuous variables and number (percentage, %) for categorical variables.

A Mann-Whitney-test was used for comparing two groups. A Kruskal-Wallis-test was used for multiple groups. For categorical variables a χ^2-test or Fisher's exact test was used, as applicable. All statistical tests were two-sided. A p-value of <0.05 was considered significant.

Linear mixed models with random intercepts for subject and trauma region were performed with level of trauma care as covariate and EQ-US and EQ-VAS as outcome measures (univariate, unadjusted). Linear mixed models were also used in multivariable analysis with EQ-US and EQ-VAS as outcome variables, and independent variable level of trauma care combined with age, sex, comorbidities, educational level, PTTP, mechanical ventilation, ISS, RTS at the ED, and time. Estimates per covariate were reported with 95% confidence interval (CI) and p-value. Logistic mixed models were performed with the same procedure (univariate and multivariable with the same covariates) on all dichotomised (limitations 'yes' and 'no') health dimensions of EQ-5D and cognition as outcome measures. The following reference categories were taken: sex (male), level of trauma care (level I), comorbidities (none),

educational level (high), measurement (year 1). Odds ratio's with 95% CI and significance level were reported per independent variable.

Results

This study included 765 major trauma patients, of which 377 (49%) responded at either one year and/or two years after trauma (Figure 1). One year after trauma 335 (44%) responded, and 269 (36%) responded at two years after trauma. Two third (n=230) responded at both time points.

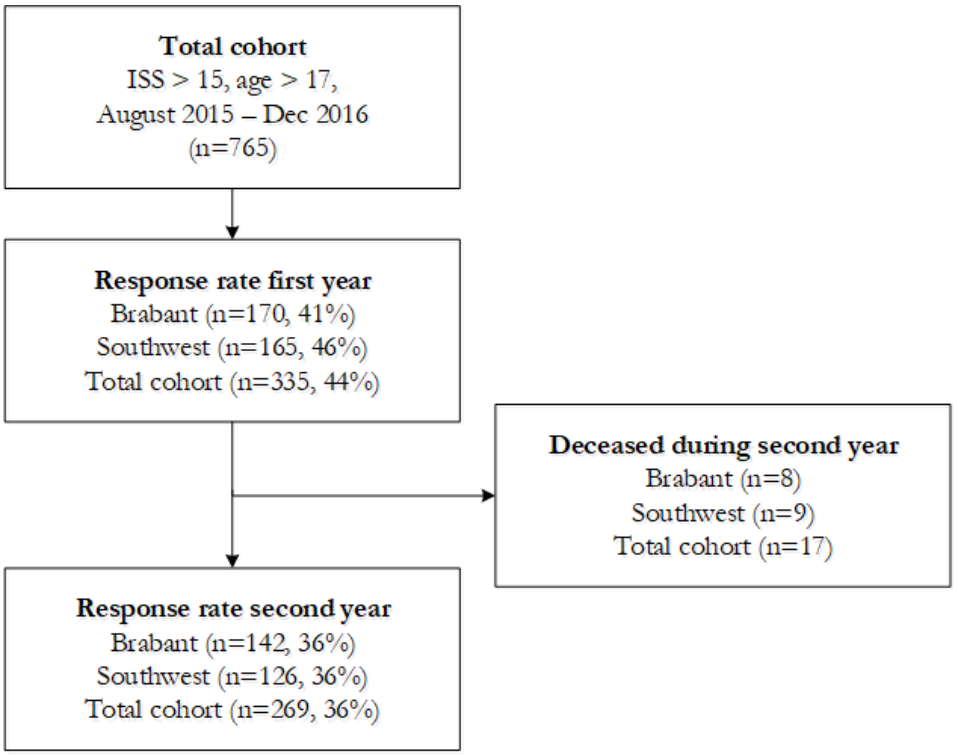

Figure 1. Study flow chart.

Descriptive analysis

Table 1 displays that respondents were significantly older (55 years, P_{25}-P_{75} 40-68, p =0.034), had a longer hospital LOS (11 days, P_{25}-P_{75} 9-19, p = 0.022) and were more frequently ICU admitted (n=242, 64%, p =0.024) than non-respondents (50 years, P_{25}-P_{75} 31-66; LOS 9, P_{25}-P_{75} 4-18; n=218 (56%), respectively). One of the 12 included patients with penetrating injuries responded. Trauma settings differed significantly between respondents and non-respondents; a smaller percentage sustained their injuries due to violence (2%), traffic (36%) or were self-inflicted (3%) in the responding group than non-respondents (4%, 41%, and 5% respectively), and a larger percentage had work (9%) or sports (8%) related injuries in the responding group than non-respondents (6% and 3%, respectively).

Table 1. Characteristics of the total cohort one year after non-fatal trauma and epidemiological comparison between respondents at one or two years post trauma and non-respondents.

		Total cohort missing (n)	Total cohort (n=765)	Respondents missing (n)	Respondents* (n=377)	Non-respondents missing (n)	Non-Respondents (n=388)	p-value
Age at arrival ED (year)		-	53 (36-68)	-	55 (40-68)	-	50 (31-66)	0.034
Females		-	257 (33.6%)	-	118 (30.4%)	-	139 (36.9%)	0.059
Level of trauma care I	**I**	-	533 (69.7%)	-	267 (70.8%)	-	266 (68.6%)	0.299
	II	-	186 (24.3%)	-	84 (22.3%)	-	102 (26.3%)	
	III	-	45 (5.9%)	-	26 (6.9%)	-	19 (4.9%)	
ISS		-	20 (17-25)	-	20 (17-25)	-	20 (17-25)	0.452
Hospital LOS (days)		3	10 (5-18)	2	11 (9-19)	1	9 (4-18)	0.022
Admission ICU		-	460 (60.1%)	-	242 (64.2%)	-	218 (56.2%)	0.024
Mechanical ventilation		-	194 (25.4%)	-	100 (26.5%)	-	94 (24.2%)	0.465
Number of fractures		4	2 (1-4)	3	2 (1-4)	1	2 (1-4)	0.128
Penetrating injury		36	12 (1.6%)	16	1 (0.3%)	20	11 (2.8%)	0.004
Cause	**violence**	22	23 (3.0%)	5	6 (1.6%)	17	17 (4.4%)	0.007
	traffic		311 (40.7%)		153 (35.8%)		158 (40.7%)	
	work		58 (7.6%)		34 (9.0%)		24 (6.2%)	
	home/leisure		273 (35.7%)		135 (35.8%)		138 (35.6%)	
	sports		42 (5.5%)		31 (8.2%)		11 (2.8%)	
	self-inflicted		28 (3.7%)		10 (2.7%)		18 (4.6%)	

Data are shown as median (P_{25}-P_{75}) or as n (%). *Respondents either at one year, two years or at both measurements. ED, Emergency Department; ISS, Injury Severity Score; LOS, Length Of Stay; ICU, Intensive Care Unit.

Table 2. Characteristics and epidemiological comparison between respondents for different levels of trauma care.

		Level I missing (n)	Level I n=267	Level II missing (n)	Level II (n=84)	Level III missing (n)	Level III (n=26)	p-value
Age at arrival ED (year)		-	53 (36-66)	-	64 (51-75)	-	58 (41-74)	< 0.001
Females		-	88 (33%)	-	41 (49%)	-	10 (39%)	0.031
ISS		-	21 (17-26)	-	18 (17-21)	-	20 (17-23)	< 0.001
PTTP level I injuries		-	106 (40%)	2	23 (27%)	-	7 (27%)	0.093
RTS ED		85	7.84 (6.90-7.84)	13	7.84 (7.84-7.84)	6	7.84 (7.84-7.84)	< 0.001
Mechanical ventilation		-	97 (36%)	-	3 (4%)	-	0 (0%)	< 0.001
Educational level	**High**	7	55 (21%)	2	19 (23%)	1	6 (23%)	0.663
	Low		92 (35%)		22 (26%)		7 (27%)	
	Middle		113 (42%)		41 (49%)		12 (46%)	
Comorbidity	**None**	-	131 (49%)	-	43 (51%)	-	14 (54%)	0.058
	1		88 (33%)		20 (24%)		3 (12%)	
	> 1		48 (18%)		21 (25%)		9 (35%)	
Response time	**1 year**	35	374 (366-391)	8	370 (363-392)	4	389 (371-414)	0.013
	2 years	72	737 (726-753)	28	733 (722-747)	10	762 (739-796)	0.002

Data are shown as median (P_{25}-P_{75}) or as n (%). ED, Emergency Department; ISS, Injury Severity Score; PTTP, Prehospital Trauma Triage Protocol; RTS, Revised Trauma Score.

Respondents to a level I centre were younger (53, P_{25}-P_{75} 36-66) than respondents admitted to a level II (64, P_{25}-P_{75} 51-75) or a level III centre (58, P_{25}-P_{75} 41-74) (Table 2). The percentage responding females was lower in level I trauma centres than level II and III facilities (49% and 39%, respectively). Respondents admitted to a level I centre were more severely injured (ISS 21, P_{25}-P_{75} 17-26) than respondents admitted to a level II (18, P_{25}-P_{75} 17-21) or level III (ISS 20, P_{25}-P_{75} 17-23) facility. Respondents admitted to the ED of a level II or a level III facility, had an equal RTS (7.84, P_{25}-P_{75} 7.84-7.84), which was lower based on P_{25}-P_{75} for respondents admitted to a level I trauma centre (7.84, P_{25}-P_{75} 6.90-7.84). A larger part of the respondents

was mechanically ventilated in a level I trauma centre (36%) than in a level II (4%) or level III (0%) facility.

Health status: EQ-US and EQ-VAS

The crude median EQ-US was 0.83 (P_{25}-P_{75} 0.71-0.81) at one year after trauma and 0.82 (P_{25}-P_{75} 0.71-1.00) at two years after trauma (Figure 2). For respondents who completed the questionnaire at both time points, an increase was reported from 0.83 (P_{25}-P_{75} 0.71-1.00) to 0.84 (P_{25}-P_{75} 0.72-1.00) (Supplemental Figure S1). Respondents admitted to a level I trauma centre scored lower on crude EQ-US in both years (0.81-0.81) than respondents admitted to a level II (0.88-0.87) or level III (0.89-0.88) facility.

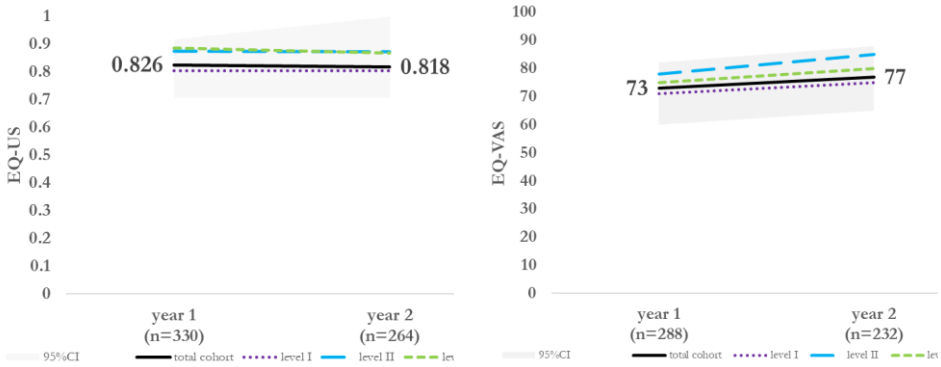

Figure 2. EQ-US and EQ-VAS at one and two years after major trauma for the total cohort. Missing values EQ-US: year 1 n=8 (2%), year 2 n=5 (2%). Missing values EQ-VAS: year 1 n=50 (15%), year 2 n=37 (14%).

The crude median EQ-VAS increased from 73 (P_{25}-P_{75} 60-82) in the first year to 77 (P_{25}-P_{75} 65-88) in the second year after trauma, for the total cohort. When looking at complete cases only, crude medians did not differ and P_{25}-P_{75} were 60-85 and 65-89, respectively (Supplemental Figure S1). Respondents admitted to a level I trauma centre scored lower on crude EQ-VAS in both years (71-75) than respondents admitted to a level II (78-85) or a level III (75-80) facility.

Health dimensions and cognition

Limitations with mobility were experienced by 49% (n=164) of the respondents at one year after trauma, and by 47% (n=126) at two years after trauma (Figure 3). Limitations in self-care were reported by 18% (n=61) of the respondents at 1 year after trauma and by 22% (n=59) of the respondents at 2 years after trauma. Limitations in daily activities were reported by 55% (n=181) of the respondents after one year and after two years by 57% (n=152) of the respondents. Pain and discomfort were reported by 63% (n=210) of the respondents one year after trauma and by 60% (n=161) of the respondents after two years. Of the respondents 36% (n=119) reported limitations due to anxiety and depression after one year, which was 38% (n=100) two years after trauma. Cognitive limitations were reported by 48% (n=156) of the respondents one year after trauma, which was 50% (n=134) after two years. Overall, a larger part of the respondents admitted to a level I trauma centre reported limitations than respondents admitted to a level II or a level III facility (Figure 3). In general, respondents

reported in both years less limitations in year two on all health dimension of the EQ-5D and cognition for all levels of trauma care (Supplemental Figure S2).

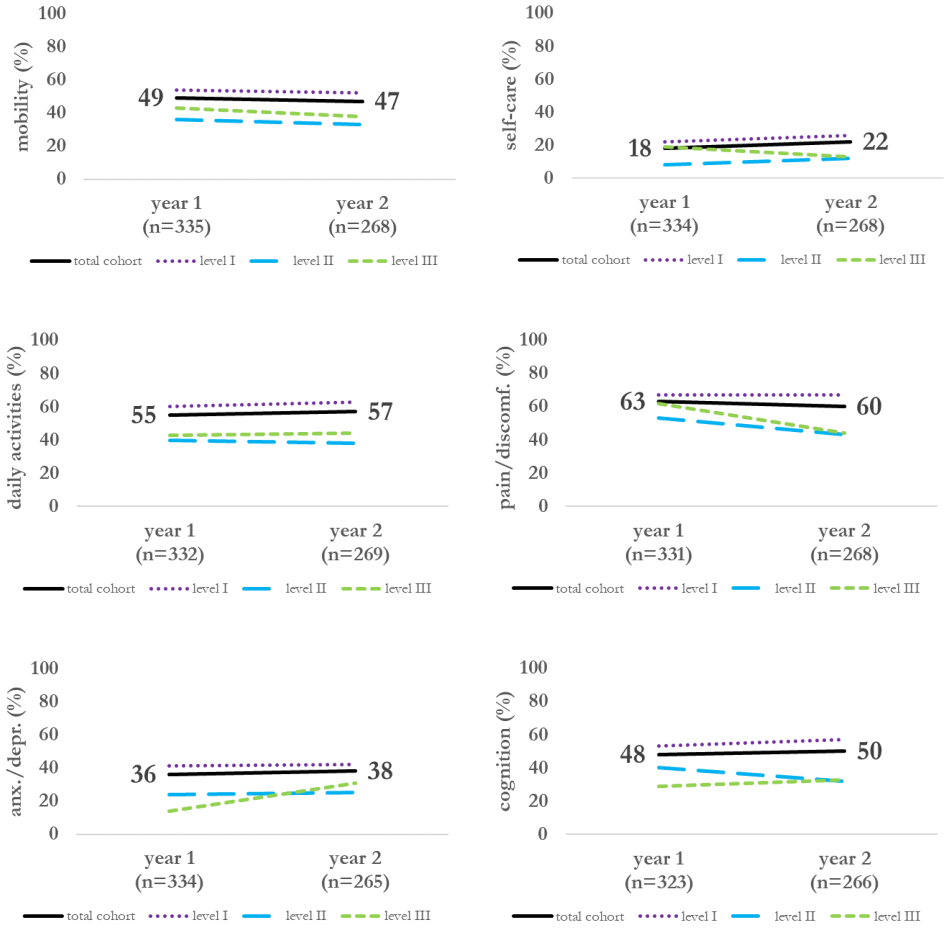

Figure 3. Limitations in all health dimensions of the EQ-5D and cognition one and two years after major trauma. Missing values mobility: year 1 n=3 (1%), year 2 n=1 (0%). Missing values self-care: year 1 n=4 (1%), year 2 n=1 (0%). Missing values daily activities: year 1 n=6 (2%), year 2 n=0 (0%). Missing values pain/discomfort: year 1 n=7 (2%), year 2 n=1 (0%). Missing values anxiety/depression: year 1 n=4 (1%), year 2 n=4 (1%). Missing values cognition: year 1 n=15 (4%), year 2 n=3 (1%).

EQ-US

Univariate analysis resulted in a statistically significant higher EQ-US over time (β 0.095, 95% CI 0.038-0.153, $p = 0.001$) for level II facilities than for level I trauma centres (Table 3). EQ-US in level III facilities did not differ from level I trauma centres in univariate analysis, over time (β 0.058, 95% CI -0.037-0.154, $p = 0.228$). Multivariable analysis of EQ-US revealed no

statistically significant differences over time in level II (β 0.052, 95% CI -0.010-0.115, p = 0.102) and level III (β 0.010, 95% CI -0.089-0.108, p = 0.844) facilities, relative to level I trauma centres.

EQ-VAS

Univariate analysis resulted in a statistically significant higher EQ-VAS over time in level II (β 7.887, 95% CI 3.035-12.740, p = 0.002) and level III (β 7.986, 95% CI 0.374-15.598, p = 0.040) facilities, relative to level I trauma centres (Table 3). Multivariable analysis of EQ-VAS revealed no statistically significant differences over time in level II (β 3.714, 95% CI -1.893-9.321, p = 0.193) and level III (β 4.837, 95% CI -3.571-13.246, p = 0.258) facilities, relative to level I trauma centres.

Table 3. Univariate (unadjusted) and multivariable (adjusted) linear mixed models for EQ-US and EQ-VAS and multivariable logistic mixed models for all health dimensions of the EQ-5D-5L and cognition, focusing on level of trauma care.

Linear Mixed Models		**Unadjusted***		**Adjusted°**	
	level	**β (95% CI)**	***p-value***	**β (95% CI)**	***p-value***
EQ-US	II	0.095 (0.038-0.153)	***0.001***	0.052 (-0.010-0.115)	0.102
	III	0.058 (-0.037-0.154)	0.228	0.010 (-0.089-0.108)	0.844
EQ-VAS	II	7.887 (3.035-12.740)	***0.002***	3.714 (-1.893-9.321)	0.193
	III	7.986 (0.374-15.598)	***0.040***	4.837 (-3.571-13.246)	0.258
Logistic Mixed Models		**Unadjusted***		**Adjusted°**	
Limitations	**level**	**OR (95% CI)**	***p-value***	**OR (95% CI)**	***p-value***
Mobility	II	0.430 (0.243-0.762)	***0.004***	0.344 (0.156-0.760)	***0.008***
	III	0.589 (0.227-1.531)	0.277	0.511 (0.143-1.830)	0.302
Self-care	II	0.368 (0.177-0.767)	***0.008***	0.219 (0.077-0.618)	***0.004***
	III	0.679 (0.222-2.075)	0.497	0.466 (0.086-2.515)	0.374
Daily activities	II	0.380 (0.225-0.642)	***0.000***	0.584 (0.294-1.160)	0.124
	III	0.455 (0.188-1.106)	0.082	0.722 (0.235-2.212)	0.567
Pain	II	0.442 (0.267-0.731)	***0.002***	0.421 (0.214-0.831)	***0.013***
	III	0.564 (0.241-1.320)	0.186	0.567 (0.189-1.704)	0.311
Anxiety	II	0.438 (0.255-0.753)	***0.003***	0.570 (0.275-1.178)	0.129
	III	0.387 (0.148-1.012)	0.053	0.626 (0.189-2.070)	0.441
Cognition	II	0.459 (0.262-0.802)	***0.006***	0.714 (0.338-1.506)	0.375
	III	0.339 (0.128-0.897)	***0.029***	0.618 (0.179-2.134)	0.446

*Unadjusted: univariate model including level of trauma care. °Adjusted: multivariable model adjusting for age, sex, ISS, PTTP, RTS at ED, Mechanical Ventilation, level of trauma care, educational level, comorbidity and time. β, linear regression coefficients; OR, Odds Ratio; CI, Confidence Interval. In unadjusted and adjusted models for all outcome measures level I trauma centres are the reference category.

Health dimensions and cognition

Univariate analysis displayed statistically significant fewer limitations in patients admitted to a level II facility, than major trauma patients admitted to a level I trauma centre, in all health

dimensions of the EQ-5D and cognition (Table 3) over time; Mobility (OR 0.430, 95% CI 0.243-0.762), self-care (OR 0.369, 95% CI 0.177-0.767), daily activities (OR 0.380, 95% CI 0.225-0.642), pain and discomfort (OR 0.442, 95% CI 0.267-0.731), anxiety and depression (OR 0.438, 95% CI 0.255-0.753), cognition (OR 0.459, 95% CI 0.262-0.8025).

Multivariable analysis resulted in statistically significant differences over time between level II and level I trauma centres for mobility (OR 0.344, 95% CI 0.156-0.760), self-care (OR 0.219, 95% CI 0.077-0.618), and pain and discomfort (OR 0.421, 95% CI 0.214-0.831). No statistically significant differences over time were found for daily activities (OR 0.584, 95%CI 0.294-1.160), anxiety and depression (OR 0.570, 95%CI 0.275-1.178), and cognition (OR 0.714, 95%CI 0.338-1.506).

Univariate analysis displayed statistically significant less cognitive limitations (OR 0.339, 95% CI 0.128-0.897) in patients admitted to a level III facility than their counterparts admitted to a level I trauma centre over time. They did not score statistically significant different over time on mobility (OR 0.589 (0.227-1.531), 95% CI), self-care (OR 0.679, 95%CI 0.222-2.075), daily activities (OR 0.455, 0.188-1.106), pain and discomfort (OR 0.564, 95%CI 0.241-1.320), and anxiety and depression (OR 0.387, 95%CI 0.148-1.012).

Multivariable analysis did not result in statistically significant differences between level III and level I trauma centres in all health dimensions of the EQ-5D and cognition over time; Mobility (OR 0.511, 95%CI 0.143-1.830), self-care (OR 0.466, 95%CI 0.086-2.515), daily activities (OR 0.722, 95%CI 0.235-2.212), pain and discomfort (OR 0.567, 95%CI 0.189-1.704), anxiety and depression (OR 0.626, 95%CI 0.189-2.070), cognition (OR 0.618, 95%CI 0.179-2.134).

Discussion

Two large Dutch major trauma cohorts of neighboring inclusive trauma networks were merged for this study. A response rate of 44% (n=335) was obtained one year after trauma, and 36% (n=269) two years after trauma. Respondents scored an EQ-US of 0.83 and 0.82 at one and two years after trauma, respectively. This is below the population norm of 0.88.[36] One and two years after trauma, respondents admitted to level II (EQ-US 0.88-0.87 resp.) and level III (EQ-US 0.89-0.87 resp.) facilities scored similar to abovementioned population norms. Major trauma patients admitted to level I trauma centres reported a lower general health status at one and two years after trauma (EQ-US 0.81-0.81 resp.). Differences in general health status of major trauma patients admitted to level I trauma centres and level II facilities disappeared, after adjusting for age, sex, ISS, PTTP, RTS, mechanical ventilation, level of trauma care, educational level, comorbidity, and time. Similar, major trauma patients admitted to level I trauma centres reported more limitations in all health domains of the EQ-5D and cognition, than major trauma patients admitted to level II facilities. With adjusted analysis this difference disappeared for health domains daily activities, anxiety, and cognition, while differences in health domains mobility, self-care, and pain remained. General health status or limitations in specific health domains of major trauma patients admitted to level III facilities did not differ significantly from level I trauma centres in all crude and adjusted analysis. "Composition of trauma populations admitted to different levels of trauma care differ. Responders of major trauma patients admitted to level I trauma centres were younger and had

more severe injuries due to high impact trauma, whereas responders of non-level I trauma centres were older and had less severe injuries due to low energy trauma." Overall, major trauma care appears to be of high quality, independently of level of trauma care.

Angerpointer et al.[20] published similar results comparing level I and level II facilities in a certified trauma network in southern Germany. Crude analysis displayed higher EQ-US and EQ-VAS up to 2 years after trauma for level II facilities. After adjusting for injury severity, revised injury severity classification II[38], and functional capacity index[39], no significant difference was present for general health status. Level I (mean EQ-US ≈ 0.65-0.69) and II (mean EQ-US ≈ 0.75-0.78) facilities scored lower one and two years after trauma than the German reference population (EQ-US 0.90). This deviates from the present study; non-level I trauma centres score similar, and level I trauma centres score lower than the Dutch reference population.

When analysing health status of major trauma patients across different levels of trauma care, an ISS > 15 cut-off point is questionable. First, this threshold is internationally accepted, but mortality based[40] and with limitations.[41, 42] Severely injured can also be defined by an ISS < 15, deviating physiological parameters, a long clinical length of stay, or trauma team activation for instance. Second, health status of severely injured patients with an ISS < 15 can be very much affected. Injuries like amputations, multiple long bone fractures, or complex panfacial fractures result in an ISS < 15, but can heavily impact daily life and recovery trajectories. Third, patients at risk for impaired health status can be identified by symptoms of anxiety or depression, acute stress disorder, post-traumatic stress disorder, neuroticism, and trait anxiety, and in general not on sociodemographics or clinical outcome measures.[43] Fourth, level I trauma centres might not have reached their optimal volume of major trauma patients for an ideal exposure/skills and ownership/coordination ratio.[44] When analysing health status of severely injured patients on a broader spectrum of patient profiles, an optimal learning/feedback curve in contemporary major trauma care might developed. Regionalisation of major trauma care has created a high level of trauma care in all trauma facilities. Merging trauma centres on a supraregional scale could be the next step for trauma care in the Netherlands.

Limitations

Many major trauma patients are prehospitally undertriaged and over time scattered with small volumes over level II and III facilities.[45] Major trauma profiles are heterogeneous and when considered in such small proportions possibly not a reliable comparison with volumes of regional level I trauma centres. Even though we merged two large trauma regions, sample sizes of respondents in level I trauma centres were well above 100 per centre, this was 6 per centre for level II and level III facilities. With level I trauma centres having many injury patterns across their major trauma population, and non-level I trauma centres having very small incidences of specific injury patterns, chances are that not all injury profiles are represented throughout each level of trauma care. Especially major trauma patients admitted to level III facilities had very few respondents, resulting in non-significant findings a priori. Merging multiple major trauma cohorts can create a dataset with all patient profiles fully represented, and increases power and the use of statistical tools for longitudinal subgroup and multilevel analysis.

Due to combining health dimensions of the 3L and the 5l version of the EQ-5D, we did not compensate for ceiling effect, thereby ignoring internal validity issues by combining two cohorts. The ceiling effect has been reported to be around 4% lower for the 5L version. The ceiling effect in the Dutch population has been reported to be low for both EQ-5D versions.

With a response rate of 44% one year after trauma and response rate of 36% two year after trauma, this study is prone to non-response bias. Non-response bias was reduced to a minimum by sending reminders and allowing legal sequelae to help incapacitated persons, however it seems reasonable to expect some overestimation of health status by a lower response rate under incapacitated persons and younger persons (Table 1) still recovering. Complete case analysis displays an increase of EQ-US between year one and year two after trauma, and the percentage of respondents experiencing limitations decreases between year one and year two after trauma. When looking at all responses, EQ-US displays a decrease and several health dimensions display an increase of experienced limitations. An overestimation of health status one year after trauma and an underestimation of health status after two years is probable.

Strengths

Two large major trauma cohorts have been merged, creating a representative Dutch cohort. Analyses were done with pre-injury demographics, on scene prehospital trauma triage protocol, emergency department vital signs, clinical parameters and injury coding. With regionalised trauma care being a complex and team performance, all phases in acute trauma care are represented.

Conclusion

Major trauma patients admitted to level I trauma centres reported a less favorable general health status and more limitations in all health dimension of the EQ-5D at one and two years after trauma than major trauma patients admitted to level II or level III facilities. After adjusting, health status of respondents one to two years after trauma did not differ significantly between levels of trauma care. Level II admitted major trauma patients reported less limitations in mobility, self-care and pain/discomfort than major trauma patients admitted to level I trauma centres. Differences are most probably present due to more severely injured patients with high energy trauma admitted to level I trauma centres, and older low energy major trauma patients admitted to non-level I trauma centres. A well-coordinated trauma network can offer homogeneous results to all major trauma patients when they are distributed in different centres according to their need of care.

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Supplemental Table S1. Multivariable linear mixed models for EQ-US and EQ-VAS.

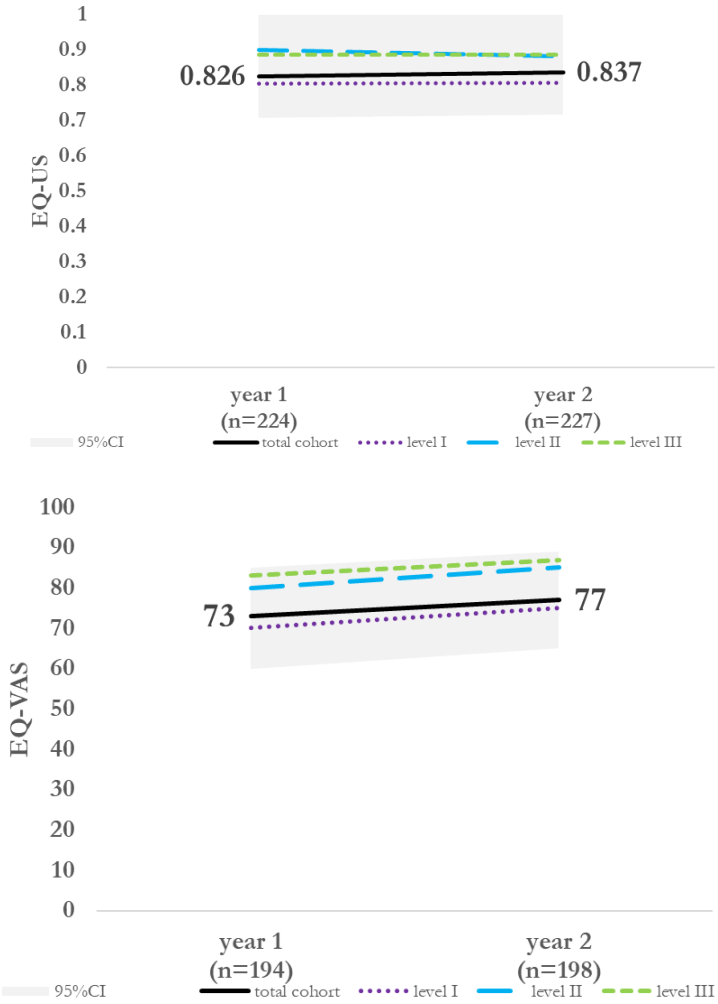
		Linear regression coefficients (95% CI)	
		EQ-US	**EQ-VAS**
Intercept		0.81 (0.58-1.04)[D]	78.35 (58.75-97.96)[D]
Age at arrival ED		0.00 (-0.28-0.24)	0.05 (-0.09-0.18)
Sex (male)		-0.04 (-0.09-0.01)	-1.39 (-6.04-3.26)
ISS		-0.00 (-0.01-0.00)	-0.30 (-0.63-0.04)
PTTP level I		0.06 (0.01-0.11)[A]	2.54 (-2.02-7.10)
RTS ED		-0.00 (-0.03-0.02)	-0.53 (-2.69-1.64)
Mech. ventilation		0.07 (-0.02-0.15)	5.50 (-1.89-12.89)
Level trauma care	**II**	0.05 (-0.01-0.12)	3.71 (-1.89-9.32)
	III	0.01 (-0.10-0.11)	4.84 (-3.57-13.25)
Education	**Low**	-0.09 (-0.15- -0.02)[B]	-4.21 (-10.01-1.59)
	Middle	-0.02 (-0.09-0.05)	-0.25 (-6.21-5.72)
Comorbidities	**> One**	-0.13 (-0.20- -0.06)[D]	-13.05 (-19.34- -6.76)[D]
	One	-0.05 (-0.11-0.01)	-5.46 (-10.70- -0.21)[A]
Response	**Year 2**	-0.00 (-0.03-0.02)	1.79 (-0.38-3.97)

ED, Emergency Department; ISS, Injury Severity Score; PTTP, Prehospital Trauma Triage Protocol; RTS, Revised Trauma Score. [A] $0.05 \leq p<0.01$, [B] $0.01 \leq p<0.005$, [C] $0.005 \leq p<0.001$, [D] $p \leq 0.001$.

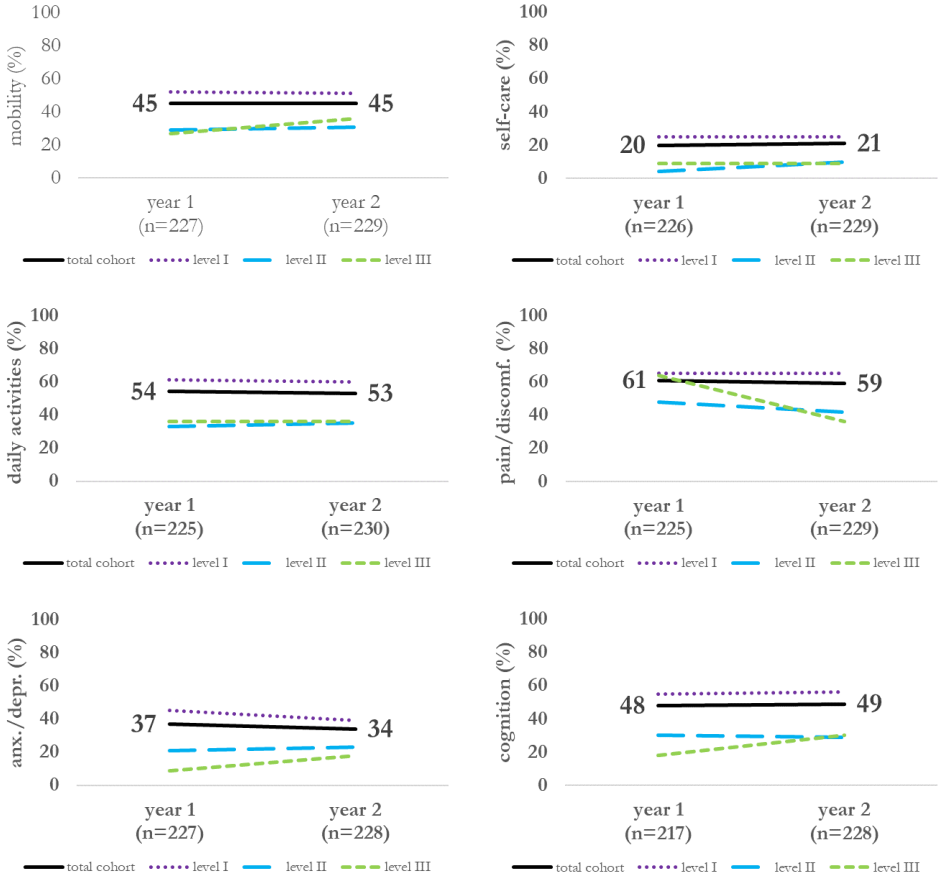
Supplemental Table S2. Multivariable logistic mixed models for all health dimensions of the EQ-5D-5L and cognition.

		Odds Ratio (95% CI) for limitations					
		Mobility	Self-care	Daily activities	Pain/discomfort	Anxiety/depression	Cognition
Intercept		0.04 (0.00-0.78)A	0.01 (0.00-0.39)A	2.32 (0.17-32.12)	1.67 (0.12-22.51)	2.88 (0.23-36.41)	1.75 (0.11-29.36)
Age at arrival ED		1.02 (0.10-1.04)	1.04 (1.01-1.06)C	0.99 (0.97-1.01)	0.99 (0.98-1.01)	0.97 (0.95-0.99)D	0.98 (0.96-0.99)A
Sex (male)		2.53 (1.30-4.93)B	2.11 (0.99-4.48)	1.84 (1.02-3.33)A	1.55 (0.86-2.79)	1.46 (0.81-2.65)	1.55 (0.82-2.91)
ISS		1.01 (0.96-1.06)	1.03 (0.98-1.09)	1.00 (0.96-1.05)	1.00 (0.95-1.04)	1.02 (0.98-1.07)	1.03 (0.98-1.08)
PTTP level I		0.44 (0.22-0.85)A	0.28 (0.13-0.61)D	0.46 (0.25-0.84)A	0.41 (0.23-0.74)C	0.69 (0.38-1.26)	1.25 (0.66-2.38)
RTS ED		1.43 (1.04-1.99)A	0.94 (0.67-1.30)	1.05 (0.76-1.36)	1.11 (0.83-1.49)	0.87 (0.66-1.14)	0.88 (0.65-1.21)
Mech. ventilation		0.23 (0.07-0.70)A	0.90 (0.28-2.89)	0.41 (0.15-1.10)	0.77 (0.29-2.07)	0.76 (0.29-1.96)	0.40 (0.14-1.12)
Level trauma care	**II**	0.34 (0.16-0.76)B	0.22 (0.08-0.62)C	0.58 (0.29-1.16)	0.42 (0.21-0.831)A	0.57 (0.275-1.18)	0.71 (0.34-1.51)
	III	0.51 (0.14-1.83)	0.47 (0.09-2.52)	0.72 (0.25-2.21)	0.57 (0.19-1.70)	0.63 (0.19-2.07)	0.62 (0.18-2.13)
Education	**Low**	2.53 (1.11-5.78)	3.84 (1.35-10.97)A	2.45 (1.19-5.05)A	2.15 (1.06-4.39)A	2.85 (1.33-6.14)B	3.95 (1.76-8.85)D
	Middle	1.40 (0.58-3.41)	2.40 (0.75-7.69)	1.62 (0.75-3.52)	1.14 (0.54-2.42)	1.36 (0.60-3.07)	2.05 (0.87-4.81)
Comorbidity	**> One**	4.08 (1.70-9.77)C	2.71 (1.050-6.97)A	3.10 (1.41-6.81)B	3.65 (1.62-8.22)C	3.63 (1.64-8.03)C	2.67 (1.15-6.23)A
	One	1.67 (0.79-3.51)	0.88 (0.36-2.17)	1.23 (0.66-2.56)	0.88 (0.45-1.70)	1.72 (0.87-3.42)	2.72 (1.30-5.70)B
Response	**Year 2**	0.85 (0.51-1.40)	1.06 (0.58-1.95)	1.11 (0.70-1.75)	1.00 (0.634-1.58)	1.02 (0.64-1.634)	1.22 (0.75-2.00)

ED, Emergency Department; ISS, Injury Severity Score; PTTP, Prehospital Trauma Triage Protocol; RTS, Revised Trauma Score. [A] $0.05 \leq p<0.01$, [B] $0.01 \leq p<0.005$, [C] $0.005 \leq p<0.001$, [D] $p \leq 0.001$.



Supplemental Figure S1. EQ-US and EQ-VAS one and two years after major trauma, complete cases only.



Supplemental Figure S2. Limitations in all health dimensions of the EQ-5D and cognition one and two years after major trauma, complete cases only.

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CHAPTER 11

Psychological health status after major trauma across different levels of trauma care: a multicentre secondary analysis

Highlights

- *Major trauma patients admitted to a level I trauma centre have more depressive, anxious, and post-traumatic stress symptoms than major trauma patients admitted to a non-level I trauma centre.*
- *Symptoms of depression, anxiety, and post-traumatic stress were differently reported across trauma regions, which might indicate that populations differ across trauma regions.*
- *Psychological health status should also be part of designing trauma networks and concentrating trauma care.*

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Abstract

Introduction Concentration of trauma care in trauma network has resulted in different trauma populations across designated levels of trauma care.

Objective Describing psychological health status, by means of the impact event scale (IES) and the hospital anxiety and depression scale (HADS), of major trauma patients one and two years post-trauma across different levels of trauma care in trauma networks.

Methods A multicentre retrospective cohort study was conducted. Inclusion criteria: aged ≥ 18 and an Injury Severity Score (ISS) > 15, surviving their injuries one year after trauma. Psychological health status was self-reported with HADS and IES. Subgroup analysis, univariate, and multivariable analysis were done on level of trauma care and trauma region for HADS and IES as outcome measures.

Results Psychological health issues were frequently reported (likely depressed n=31, 14.7%); likely anxious n=32, 15.2%; indication of a post-traumatic stress disorder n=46, 18.0%). Respondents admitted to a level I trauma centre reported more symptoms of anxiety (3, P_{25}-P_{75} 1-6 vs. 5, P_{25}-P_{75} 2-9, p=.002), depression (2, P_{25}-P_{75} 1-5 vs. 5, P_{25}-P_{75} 2-9, p<0.001), and post-traumatic stress (6, P_{25}-P_{75} 0-15 vs. 13, P_{25}-P_{75} 3-33, p=0.001), than patients admitted to a non-level I trauma centre. Differences across trauma regions were reported for depression (3, P_{25}-P_{75} 1-6 vs. 4, P_{25}-P_{75} 2-10, p=0.030) and post-traumatic stress (7, P_{25}-P_{75} 0-18 vs. 15, P_{25}-P_{75} 4-34, p<0.001).

Conclusions Major trauma patients admitted to a level I trauma centre have more depressive, anxious, and post-traumatic stress symptoms than when admitted to a non-level I trauma centre. These symptoms differed across trauma regions, indicating populations differences. Level of trauma care and trauma region are important when analysing psychological health status.

Keywords 'Trauma Centres', 'Multiple Trauma', 'Trauma and Stressor Related Disorders', 'Depression', 'Anxiety', 'Stress Disorder, Post-Traumatic'

Introduction

With many more trauma patients without than with fatal injuries, mortality is not the main concern of trauma care professionals and public health care policy makers. Measuring trauma outcome is changing from fatal to clinical non-fatal and patient-reported outcome measures. Impaired quality of life, difficulties with return to work, health care consumption, post-traumatic stress, and impact on families are important factors in daily recovery trajectories and can be considerable in life after (major) trauma. A large group reports social dysfunctioning, and quality of life is below population norms at one year after major trauma [1-7] Monitoring physical, mental, and social outcome measures can be important for health care workers and patients during recovery trajectories, providing discernment in expectation- and self-management.

Dutch trauma care is organised by inclusive trauma networks, hospitals are designated with a specific level of trauma care based on criteria established by the Dutch Trauma Society [8]. Level I trauma centres provide most extensive trauma care with immediate availability of specialists around the clock and are required to treat a minimum of 240 major trauma (Injury Severity Score (ISS) > 15) patients annually. Level II trauma centres are able to stabilise major trauma patients, but do not have all neurosurgical facilities, extra-corporal life support, or multidisciplinary limb sparing techniques immediately available around the clock. Patients with minor or isolated injuries can also be admitted to a level III trauma centre. (Major) trauma populations across levels of trauma care differ, making it an important factor when analysing outcome measures in a trauma network [8]

Pre-injury assessment of health status is of importance when estimating impact of physical trauma [9] Major trauma has also been linked to a higher incidence of psychological issues after and before physical trauma [10, 11] Psychological risk factors and personality have been associated with less favourable health status, psychological complaints and stress disorders [12, 13] With a high societal prevalence of mental disorders and additional use of psychotropic medications [14-16] In combination with the impact of trauma, limitations in psychological health status might be more prevalent within trauma patients than society in general. If trauma populations across different levels of trauma care and trauma region differ it is of value to what extent they differ on psychological outcome measures and risk factors. This will provide insight into how psychosocial health care of trauma patients in different type of hospitals and across trauma regions should be organised. This study described psychological health status, by means of the impact event scale (IES) and the hospital anxiety and depression scale (HADS) one and two years after major trauma, across trauma regions and different level of trauma care.

Methods

Following review of the protocol, the local Medical Research Ethics Committee concluded this study was not subject to the Medical Research Involving Human Subjects Act (MEC-2023-0695), and provided a waiver of consent. Previous data collection by Trauma Centre Southwest Netherlands was approved by the local Medical Research Ethics Committee (MEC-2017-041). Data collection by Network Emergency Care Brabant was approved by the local Medical Research Ethics Committee (NL50258.028.14) and registered at ClinicalTrials.gov (NTC02508675).

Study setting

This multicentre retrospective cohort study comprised a secondary longitudinal multilevel analysis on data from prior cohorts from two large neighbouring trauma regions in the Netherlands (Trauma Centre Southwest Netherlands and Network Emergency Care Brabant). The combined trauma regions have 20 hospitals (each trauma region has one level I trauma centre), one dedicated Burn Centre, one dedicated Eye Hospital, six Emergency Medical Services (EMS), and the availability of one Helicopter Emergency Medical Service (HEMS). Geographically, the catchment area is diverse with rural, remote, industrial, urban and touristic parts, inhabited by 5 million people.

Data on major trauma patient (ISS > 15) of the cohort in Network Emergency Care Brabant (trauma region I) were extracted from a larger cohort (Brabant Injury Outcome Surveillance, BIOS) [17] This cohort included all adult (≥18 years) patients with an unplanned hospital admission within 48 hours after trauma who survived to discharge. Patients were followed throughout six follow up moments from 1 week up to 24 months. The cohort of Trauma Centre Southwest Netherlands (trauma region II) included all patients with the same inclusion criteria from the Dutch National Trauma Registry (NTR), and invited major trauma patients one year and two years after trauma [1, 18] The inclusion period of trauma region I ran from August 1, 2015 to July 31, 2016, the inclusion period for trauma region II was January 1, 2016 to December 31, 2016 (Figure 1). All patients or legal proxies gave written consent, before participating in the study. Non-response bias was reduced to a minimum by sending two reminders and allowing legal sequelae to help incapacitated persons.

Demographics and clinical variables

For descriptive characteristics of the cohorts and useful predictors of psychological health status, age, sex, level of trauma care, cause of trauma, type of injury (blunt or penetrating), Hospital Length of Stay (LOS), ICU admitted, mechanical ventilation, and all injuries coded with the Abbreviated Injury Scale 2008 (AIS08), derived Injury Severity Score (ISS08) were extracted from the DNTR.[19-21]

Comorbidities present before trauma were surveyed with a modified version of the Cumulative Illness Rating Scale (CIRS), which is validated as an indicator of health status [22] First available reported comorbidities were used for analysis. Pre-existing psychological disorders are part of CIRS, and was separately dichotomised in 'yes' and 'none'.

Outcome measures

Psychological health status was assessed using the hospital anxiety and depression scale (HADS) and the impact event scale (IES), which are valid instrument for measuring symptoms of anxiety, depression, and posttraumatic stress disorder (PTSD) [23, 24] All items of both questionnaires are scored on a four point Likert scale (HADS six items positively scored (0-3) and 8 items negatively scored (3-0), IES 0 (not at all), 1 (rarely), 3 (sometimes), 5 (often)). The HADS consists of two 7 item parts on anxiety and depression. For each part a score from 0-21 is obtained, which is categorised from 0-7 (no anxiety/depression), 8-10 (possible anxiety/depression), and 11-21 (likely anxious/depressed). The IES consists of 15 items assessing subjective distress set off by a life event, and split up by seven items on intrusive symptoms and eight on avoidance. All items relate to a specific stressor. The intrusive subset sum score ranges from 0-35, the avoidance subset sum score from 0-40, and the sum of both subsets is the total posttraumatic stress reaction score. Higher scores indicate a greater frequency of intrusion, avoidance, or a potential PTSD (0-8 subclinical, 9-25 mild, 26-43 moderate, ≥ 44 , respectively).

Data analysis

Statistical analyses were done using Statistical Package for Social Sciences version 25.0 (IBM, Chicago, IL) and R Software Environment (version 4.1.1, the R Foundation for Statistical Computing, Vienna Austria). Data are reported in line with strengthening the reporting of observational studies in epidemiology (STROBE) [25]

Normality of continuous variables was tested using the Shapiro-Wilk test. All continuous variables were non-normally distributed. Descriptive statistics are presented as median with 25^{th} and 75^{th} percentiles (P_{25}-P_{75}) for continuous variables and number (percentage, %) for categorical variables. For continuous data a Mann-Whitney-test was used for comparing two groups. A Kruskal-Wallis-test was used for multiple groups, followed by a pairwise comparison with the Mann-Whitney U test as applicable. For categorical variables a χ^2-test or Fisher's exact test was used, as applicable. All statistical tests were two-sided. A p-value of <0.05 was considered significant in all tests. Linear mixed models with random intercepts for subject and trauma region were performed with level of trauma care and time as covariate and HADS (subset anxiety and depression) and IES (subset intrusive and avoidance and sum score PTSD) as outcome measures (univariate, unadjusted). All procedures for univariate analysis were repeated with trauma region and time as covariate. Linear mixed models were also used in multivariable analysis with random intercepts for subject and trauma region, and HADS (subset anxiety and depression) and IES (subset intrusive and avoidance and sum score PTSD) as outcome measures, and independent variable level of trauma care adjusted for age, sex, ISS, ICU admission, trauma region, comorbidity, Pre-existing psychological disorders and time. Estimates per covariate were reported with 95% confidence interval (CI) and p-value. The following reference categories were taken: sex (male), level of trauma care (level I), trauma region (trauma region I), comorbidities (none), Pre-existing psychological disorders (no), ICU (no), measurement (year 1). Odds ratio's with 95% CI and significance level were reported per independent variable. In univariate and multivariable models level I trauma centres or trauma region I are the reference category.

Results

The total cohort included 765 major trauma patients, of whom 335 (44%) responded at one year and 269 (36%) responded two years after trauma (Figure 1), of which n=230 (30%) responded at both time points.

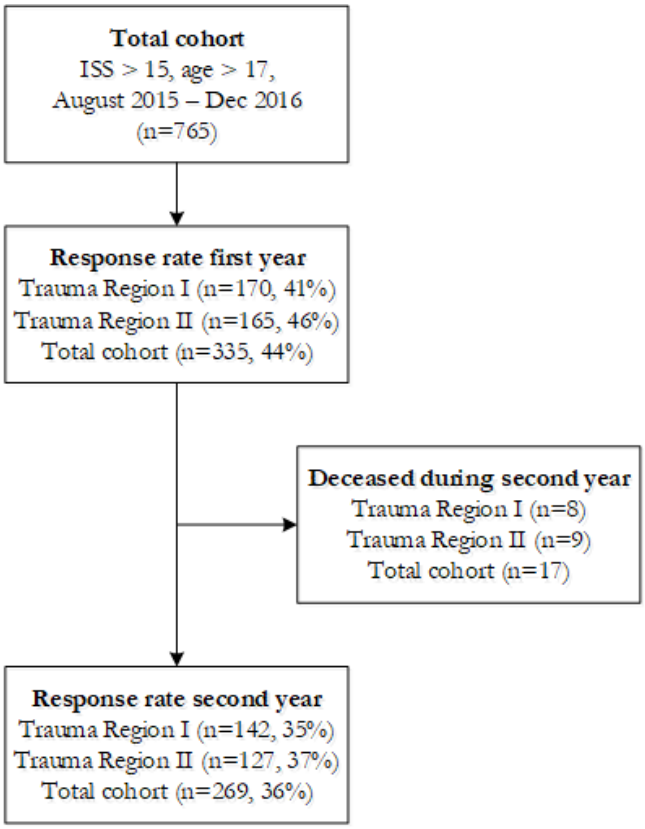

Figure 1. Study flow chart.

Table 1 shows that respondents were significantly older (50 years, P_{25}-P_{75} 31-66 vs. 55 years, P_{25}-P_{75} 40-68; p=0.033), had a longer hospital LOS (9 days, P_{25}-P_{75} 4-18 vs. 11 days, P_{25}-P_{75} 9-19; p=0.017) and were more frequently ICU admitted (n=217, 56% vs. n=243, 64%; p=0.020) than non-respondents. Trauma settings differed significantly between respondents and non-respondents; a smaller percentage sustained their injuries due to violence (n=6, 1.6% vs. n=17, 44%), traffic (n=153, 40.5% vs. n=158, 40.8%), or were self-inflicted (n=10, 2.6% vs. n=18, 4.7%) in the responding group, and a larger percentage had work related (n=34, 9.0% vs. n=24, 6.2%) or sports related (n=31, 8.2% vs. n=11, 2.8%) injuries in the responding group. In addition, respondents with penetrating injuries were underrepresented compared with non-respondents (n=1, 0.4% vs. n= 11, 2.8%).

Table 1. Characteristics of the total cohort one year after non-fatal trauma and epidemiological comparison between respondents at one or two years post trauma and non-respondents.

		Total cohort (n=765)	Respondents* (n=378)	Non-Respondents (n=387)	p-value
Age (year)		53 (36-68)	55 (40-68)	50 (31-66)	0.033
Females		257 (33.6%)	118 (30.5%)	139 (36.8%)	0.066
Level of trauma care	**I**	533 (69.7%)	268 (70.9%)	265(68.5%)	0.291
	II	186 (24.3%)	84 (22.2%)	103(26.7%)	
	III	45 (5.9%)	26 (6.9%)	19 (4.9%)	
ISS		20 (17-25)	20 (17-25)	20 (17-25)	0.398
Hospital LOS (days)		10 (5-18)	11 (6-19)	9 (4-18)	0.017
ICU admission		460 (60.1%)	243 (64.3%)	217 (56.1%)	0.020
Mechanical ventilation		194 (25.4%)	101 (26.7%)	93 (24.0%)	0.393
Penetrating injury		12 (1.6%)	1 (0.3%)	11 (2.8%)	0.004
Type of trauma	**violence**	23 (3.0%)	6 (1.6%)	17 (4.4%)	0.007
	traffic	311 (40.7%)	153 (40.5%)	158 (40.8%)	
	work	58 (7.6%)	34 (9.0%)	24 (6.2%)	
	home/leisure	273 (35.7%)	136 (36.0%)	137 (35.4%)	
	sports	42 (5.5%)	31 (8.2%)	11 (2.8%)	
	self-inflicted	28 (3.7%)	10 (2.6%)	18 (4.7%)	

Data are shown as median (P_{25}-P_{75}) or as n (%). Missing values: Hospital LOS respondents n=2, non-respondents n=1; penetrating injury respondents n=16, non-respondents n=20; type of trauma respondents n=8, non-respondents n=22.*Respondents either at one year, two years or at both measurements. ED, Emergency Department; ISS, Injury Severity Score; LOS, Length Of Stay; ICU, Intensive Care Unit.

Table 2 displays that, compared with respondents admitted to a non-level I trauma centre, respondents admitted to a level I trauma centre are younger (53 years, P_{25}-P_{75} 63-66 vs. 63 years, P_{25}-P_{75} 49-74; p<0.001), had more often no comorbidities (n=131, 48.9% vs. n=57, 51.8%), more pre-existential psychological disorders (n=47, 17.5% vs. n=16, 14.5%), have a higher ISS (21, P_{25}-P_{75} 17-26 vs. 19, P_{25}-P_{75} 17-21, p<0.001), a longer hospital LOS (13 days, P_{25}-P_{75} 7-21 vs. 7 days, P_{25}-P_{75} 4-11; p<0.001), are more frequently ICU admitted (n=197, 73.5% vs. n=46, 41.8%; p<0.001), were more frequently mechanically ventilated (n=98, 36.6% vs. n=3, 2.7%; p<0.001), and type of trauma was more traffic related (n=115, 42.9% vs. n=38, 34.5%), work related (n=29, 10.8% vs. n=5, 4.5%) and self-inflicted (n=9, 3.4% vs. n=1, 0.9%). Responders admitted to a hospital in trauma region I were, compared with respondents admitted to a hospital in trauma region II, older (58 years, P_{25}-P_{75} 45-70 vs. 53 years, P_{25}-P_{75} 37-67; p=0.007), were more frequently admitted to an ICU (n=127, 69.4% vs. n=116, 59.5%), were more frequently injured in private settings (n=80, 43.7% vs. n=56, 28.7%), and we less frequently injured during work (n=12, 6.6% vs. n=22, 11.3%), in traffic (n=70, 38.3% vs. n=83, 42.6%) and due to self-harm (n=1, 0.5% vs. n=9, 4.6%).

Table 2. Characteristics and epidemiological comparison between respondents admitted to a level I trauma centre and respondents admitted to a non-level I trauma centre, and between respondents admitted to trauma region I or trauma region II.

		Level I (n=268)	Non-level I (n=110)	p-value	Trauma Region I (n=183)	Trauma Region II (n=195)	p-value
Age (year)		53 (36-66)	63 (49-74)	<0.001	58 (45-70)	53 (37-67)	0.007
Females		88 (32.8%)	51 (46.4%)	0.013	69 (37.7%)	70 (35.9%)	0.716
Comorbidities	**None**	131 (48.9%)	57 (51.8%)	0.027	86 (47.0%)	102 (52.3%)	0.469
	1	88 (32.8%)	23 (20.9%)		55 (30.1%)	56 (28.7%)	
	>1	48 (17.9%)	30 (27.3%)		42 (23.0%)	36 (18.5%)	
PEPD*		47 (17.5%)	16 (14.5%)	0.469	29 (15.8%)	34 (17.4%)	0.662
ISS		21 (17-26)	19 (17-21)	<0.001	20 (17-25)	21 (17-26)	0.112
Hospital LOS		13 (7-21)	7 (4-11)	<0.001	12 (6-19)	10 (6-19)	0.414
Admission ICU		197 (73.5%)	46 (41.8%)	<0.001	127 (69.4%)	116 (59.5%)	0.044
MV		98 (36.6%)	3 (2.7%)	<0.001	41 (22.4%)	60 (30.8%)	0.066
Type of trauma	**Violence**	4 (1.5%)	2 (1.8%)	0.157	2 (1.1%)	4 (2.1%)	0.008
	Traffic	115 (42.9%)	38 (34.5%)		70 (38.3%)	83 (42.6%)	
	Work	29 (10.8%)	5 (4.5%)		12 (6.6%)	22 (11.3%)	
	Home/Leisure	88 (32.8%)	48 (43.6%)		80 (43.7%)	56 (28.7%)	
	Sports	20 (7.5%)	11 (10.0%)		11 (6.0%)	20 (10.3%)	
	Self-inflicted	9 (3.4%)	1 (0.9%)		1 (0.5%)	9 (4.6%)	

Data are shown as median (P_{25}-P_{75}) or as n (%). Missing values level I: comorbidities n=1, PEPD n=1, education n=8, Hospital LOS n=1, type of trauma n=1. Missing values non-level I: education n=3, type of trauma n=5. Missing values trauma region I: education n=6, Hospital LOS n=2, type of trauma n=6. Missing values trauma region II: comorbidities n=1, PEPD n=1, education n=5, type of trauma n=1. Respondents either at one year, two years or at both measurements. ED, Emergency Department; ISS, Injury Severity Score; PEPD, Pre-Existential Psychological Disorders; LOS, Length Of Stay; ICU, Intensive Care Unit; Mechanical Ventilation, MV.

Table 3. Univariate (unadjusted) and multivariable (adjusted) linear mixed models for the Impact Event Scale and Hospital Anxiety and Depression Scale, and subset scores per level of trauma care (upper) and per trauma region (lower).

	Unadjusted*		Adjusted°	
	β (95% CI)	p-value	β (95% CI)	p-value
Level of Trauma Care				
HADS anxiety	-1.41 (-2.51 - -0.31)	0.012	-1.12 (-2.17 - -0.06)	0.038
HADS depression	-1.65 (-2.76 - -0.54)	0.004	-1.42 (-2.53 - -0.32)	0.011
IES intrusion	-3.07 (-5.02 - -1.12)	0.002	-2.31 (-4.30 - -0.32)	0.023
IES avoidance	-3.45 (-5.47 - -1.44)	<0.001	-2.93 (-5.00 - -0.86)	0.006
IES PTSD	-6.45 (-10.20 - -2.69)	<0.001	-5.17 (-8.99 - -1.34)	0.008
Trauma Region				
HADS anxiety	-0.56 (-1.58 - 0.45)	0.274	-0.51 (-1.43 – 0.41)	0.273
HADS depression	-1.56 (-2.57 - -0.55)	0.003	-1.57 (-2.53 - -0.61)	0.001
IES intrusion	-2.78 (-4.56 - -0.99)	0.002	-2.11 (-3.86 - -0.32)	0.018
IES avoidance	-2.76 (-4.61 - -0.91)	0.004	-2.67 (-4.48 - -0.86)	0.004
IES PTSD	-5.51 (-8.95 - -2.06)	0.002	-4.72 (-8.07 - -1.37)	0.006

*Unadjusted: univariate model including level of trauma care and time or trauma region and time. °Adjusted: multivariable model adjusting for age, sex, ISS, ICU, level of trauma care, trauma region, comorbidity, PEPD and time. ISS, Injury Severity Score; ICU, Intensive Care Unit; PEPD, Pre-Existential Psychological Disorders; β, linear regression coefficients; CI, Confidence Interval; HADS, Hospital Anxiety and Depression Scale; IES, Impact Event Scale; PTSD Post Traumatic Stress Disorder. In unadjusted and adjusted models for all outcome measures level I trauma centres or trauma region I are the reference category.

Psychological Health status: HADS & IES

When comparing year one and year two for scores on subsets anxiety and depression of HADS and PTSD, intrusive, and avoidance of IES, results were not significantly different (Figure 2 and 3, additional numbers in Supplemental Table 2). Comparing trauma regions in year one, scores on PTSD, intrusive, and avoidance of IES were significantly higher in trauma region II than in trauma region I (PTSD 8, P_{25}-P_{75} 0-23 and 14, P_{25}-P_{75} 5-33; p 0.002; intrusive 4, P_{25}-P_{75} 0-11 and 8, P_{25}-P_{75} 2-15; p=0.009; avoidance 4, P_{25}-P_{75} 0-11 and 6, P_{25}-P_{75} 1-14; p=0.002), which held for year two (PTSD 7, P_{25}-P_{75} 0-18 and 15, P_{25}-P_{75} 4-34; p<0.001; intrusive 3, P_{25}-P_{75} 0-8 and 8, P_{25}-P_{75} 2-15; p<0.001; avoidance 3, P_{25}-P_{75} 0-10 and 8, P_{25}-P_{75} 1-18; p<0.001). In year two scores on depression were significantly higher in trauma region II than trauma region I (3, P_{25}-P_{75} 1-6 and 4, P_{25}-P_{75} 2-10; p=0.030). Scores on anxiety and depression of HADS and scores on PTSD, intrusive, and avoidance of IES were significantly higher in level I trauma centres than in non-level I trauma centres (anxiety 4, P_{25}-P_{75} 2-8 and 3, P_{25}-P_{75} 1-6; p=0.035; depression 4, P_{25}-P_{75} 2-9 and 3, P_{25}-P_{75} 1-7; p=0.005, PTSD 14, P_{25}-P_{75} 3-33 and 7, P_{25}-P_{75} 1-17; p=0.005; intrusive 7, P_{25}-P_{75} 1-16 and 4, P_{25}-P_{75} 0-8; p=0.011; avoidance 6, P_{25}-P_{75} 0-17 and 3, P_{25}-P_{75} 0-8; p=0.002), which held for year two (anxiety 5, P_{25}-P_{75} 2-9 and 3, P_{25}-P_{75} 1-6; p=0.002; depression 5, P_{25}-P_{75} 2-9 and 2, P_{25}-P_{75} 1-5; p<0.001, PTSD 13, P_{25}-P_{75}

3-33 and 6, P_{25}-P_{75} 0-15; p=0.001; intrusive 5, P_{25}-P_{75} 1-15 and 3, P_{25}-P_{75} 0-8; p=0.011; avoidance 6, P_{25}-P_{75} 0-16 and 1, P_{25}-P_{75} 0-8; p<0.001), respectively.

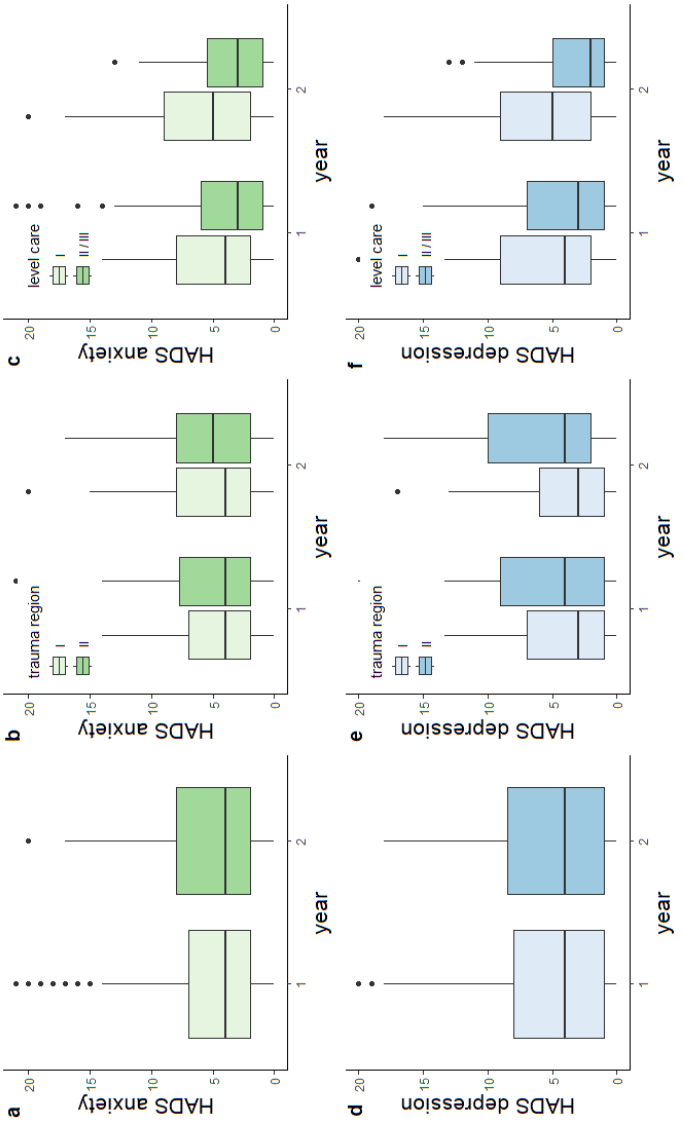

Figure 2. Sum scores of the Hospital Anxiety and Depression Scale (HADS, subscales anxiety and depression) one year and two years after major trauma (a and d), per trauma region (b and e), and for level I trauma centres and non-level I trauma centres (c and f).

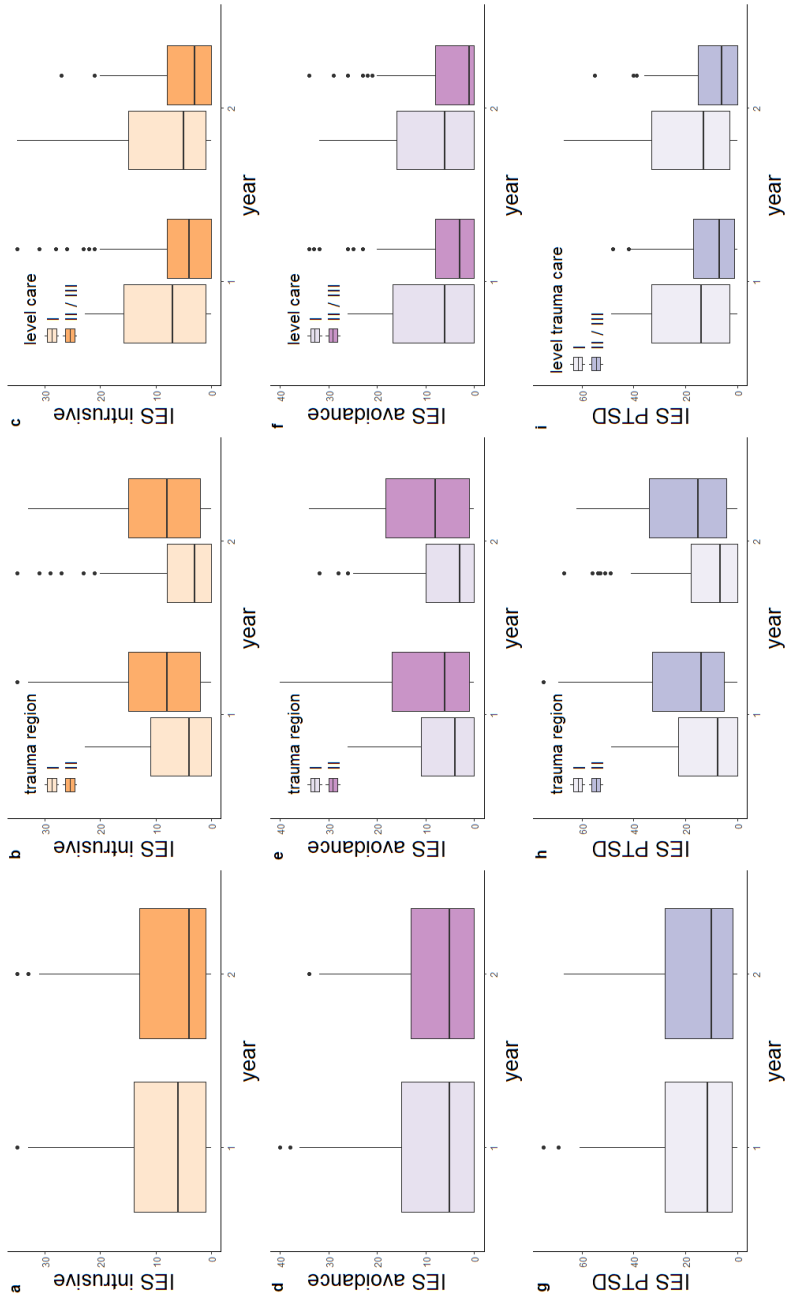

Figure 3. Sum scores of the Impact Event Scale (Post Traumatic Stress Disorder (PTSD) and subscales avoidance and intrusive) one year and two years after major trauma (a,d,g), per trauma region (b,e,h) and for level I trauma centres and non-level I trauma centres (c,f,i).

Regression: Level of trauma care

Univariate analysis resulted in a statistically significant lower anxiety score (β -1.41 95% CI -2.51--0.31, p=0.012) and depression score (β -1.65 95% CI -2.76--0.54, p=0.004) for respondents admitted to a non-level I trauma centre than for respondents admitted to a level I trauma centre (Table 3). Likewise, scores on intrusion, avoidance, and PTSD were all significantly lower for respondents admitted to a non-level I trauma centre than for respondents admitted to a level I trauma centre (β -3.07 95% CI -5.02--1.12, p=0.002 ; β -3.45 95% CI -5.47--1.44, p<0.001; β -6.45 95% CI -10.20--2.69, p<0.001, respectively).

In multivariable analysis, respondents admitted to a non-level I trauma centre scored statistical significantly lower than respondents admitted to a level I trauma centre on all subsets of HADS (anxiety β -1.12 95% CI -2.17--0.06, p=0.038; depression β -1.42 95% CI -2.53--0.32, p<0.011) and IES (intrusion β -2.31 95% CI -4.30--0.32, p=0.023; avoidance β -2.93 95% CI -5.00--0.86, p=0.006; PTSD β -5.17 95% CI -8.99--1.34, p<0.008).

Regression: Trauma region

Univariate analysis resulted in a statistically significant lower depression score (β -1.56 95% CI -2.57--0.55, p=0.003) for respondents admitted to a trauma centre in trauma region I than for respondents admitted to a trauma centre in trauma region II (Table 3). Scores on intrusion, avoidance, and PTSD were all significantly lower for respondents admitted to a trauma centre in trauma region I than for respondents admitted to a trauma centre in trauma region II (β -5.51 95% CI -8.95--2.06, p=0.002; β -2.76 95% CI -4.61--0.91, p<0.004; β -2.78 95% CI -4.56--0.99, p=0.002, respectively).

In multivariable analysis, results were similar as univariate analysis. Respondents admitted to a trauma centre in trauma region I scored significantly lower on depression than respondents admitted to a trauma centre in trauma region II (β -1.57 95% CI -2.53--0.61, p=0.001). Scores on intrusion, avoidance, and PTSD were also significantly lower for respondents admitted to a trauma centre in trauma region I than for respondents admitted to a trauma centre in trauma region II (β -4.72 95% CI -8.07--1.37, p=0.006; β -2.67 95% CI -4.48--0.86, p=0.004; β -2.11 95% CI -3.86--0.36, p=0.018, respectively).

Discussion

Combining two major trauma cohorts of two trauma regions, resulted in response rate of 44% at one year after trauma, a response rate of 36% two years after trauma, and 30% responded at both time points (Figure 1). Overall, major trauma patients scored subclinical on depression (4, P_{25}-P_{75} 2-8), subclinical on anxiety (4, P_{25}-P_{75} 1-9), and mild post-traumatic stress symptoms (10, P_{25}-P_{75} 2-28), two years after trauma (Supplemental Table 2). Still, 15% of major trauma patients scored to be likely depressed (n=31, 14.7%) or likely anxious (n=32, 15.2%), two years after trauma. A little less than one out of five (n=46, 18.0%) major trauma patients reported symptoms of post-traumatic stress indicative for PTSD[26, 27], two years after trauma (Supplemental Table 3).

Differences between level I trauma centres and non-level I trauma centres were reported, as well as differences between trauma regions. Two years after major trauma, respondents reported more symptoms of anxiety, depression, and post-traumatic stress when admitted to a level I trauma centre (5, P_{25}-P_{75} 2-9; 5, P_{25}-P_{75} 2-9; 13, P_{25}-P_{75} 3-33, respectively) than major trauma patients admitted to a non-level I trauma centre (3, P_{25}-P_{75} 1-6; 2, P_{25}-P_{75} 1-5; 6, P_{25}-P_{75} 0-15, respectively). Similar, major trauma patients admitted to trauma region Southwest reported more symptoms of anxiety (5, P_{25}-P_{75} 2-8), depression (4, P_{25}-P_{75} 2-10), and post-traumatic stress (15, P_{25}-P_{75} 4-34), two years after trauma, than major trauma patients admitted to trauma region I (4, P_{25}-P_{75} 2-8; 3, P_{25}-P_{75} 1-6; 7, P_{25}-P_{75} 0-18, respectively). Nearly all results, were consistent over time, as well as across trauma regions and across level of trauma care. In addition, comorbidities and pre-existential psychological disorders were also indicative for a higher score on anxiety, depression, and post-traumatic stress symptoms (Supplemental Table 1). Demographic and clinical differences across level of trauma care and across trauma regions were related to age, sex, high impact trauma mechanisms, intentional trauma, injury severity, a longer length of stay and ICU admission. Overall, major trauma patients admitted to a level I trauma centre were more severely injured than major trauma patients admitted to a non-level I trauma centre, this was also the case for major trauma patients admitted to trauma region II. However, both trauma regions and both level of trauma care had the same prevalence of pre-existing psychological disorders , and the trauma region and level of trauma care having the lowest score on depression, anxiety, and post-traumatic stress also had the lowest prevalence of multi-comorbidity, whereas the variables are indicative for more depression, anxiety, and post-traumatic stress. This seems to be contra-dictionary and is probably due to different patient profiles, based on unmeasured variables. This could partly be explained by subgroups with specific injuries. Sample sizes were too small to do sensitivity analysis on subgroups with specific injuries.

Pre-existential psychological disorders have been reported to result in a lower health-related quality of life, more inpatient (psychological) morbidity, and a longer hospital length of stay, but do not independently predict health-related quality of life [28, 29] An association of post-traumatic stress and health-related quality of life has also been reported previously [27] In addition, post-traumatic stress disorders dysregulate hypothalamus-pituitary-adrenal axis and the hypothalamus-pituitary-thyroid axis [30] Increased activity of the hypothalamus-pituitary-thyroid axis results in hyper arousal symptoms part of PTSD. The effect of PTSD on the hypothalamus-pituitary-adrenal axis is either excessive glucocorticoid activity mobilising bodily resources for survival, or insufficient glucocorticoid signaling, leading to stress related pathology like inflammation. The latter is in line with poor wound healing, resulting in infections or other complications [31] Especially for major trauma patients with multiple injured body regions this mechanism can result in poor outcome [32, 33] Finally, a combination of pre-existential psychological disorder and pre-injury traumatic events have been reported to result in a risk factor for the intentional and unintentional injury [34] Physical trauma, resulting in PTSD affecting physiological healing processes having an impact of quality of life, which in return can keep psychological health status impaired, making people prone to unhealthy behavior, potentially leading to new physical trauma.

Physical trauma, psychological health status and quality of life are interconnected, as they are part of a complex interplay between medical history, stress regulation, hormonal axis alterations, immunology, and daily functioning. Societal pressure is most likely contra productive, and should not be part of recovery programs. On the other hand, psychological treatment can reduce symptoms of stress disorders later on when provided in the emergency department, and organising psychological after-care post discharge will be of great value to reduce post-concussion-like symptoms and post-traumatic stress which will positively impact on quality of life [35] Providing point on care with regard to psychological disorders, should also be part of concentrating and spreading specific acute health care pathways. For instance, hospital length of stay is partly based on psychiatric comorbidity, and around two third of admitted trauma patients have a delayed discharge plan [29] Providing psychological monitoring and acute psychological health care, during admission and post-discharge, will not only be beneficial for quality of life and psychological health status, but can also be of great value for capacity planning and reducing re-admission rates. By concentrating major trauma care, not just efficiency will be optimised, this way major trauma care will be able to keep her multidisciplinary character and will be able to innovate beneficial to people having to deal with high impact injuries.

Limitations & Strengths

Even though major trauma care is supposedly concentrated in level I trauma centres, many major trauma patients are undertriaged prehospitally and admitted to non-level I trauma centres [36] Due to the regional function of level I trauma centres it seems logical that in level I trauma centres major trauma profiles are more diverse. With small numbers of major trauma patients scattered over non-level I trauma centres, possibly not all major trauma profiles are represented in non-level I trauma centres, let alone responded. For instance, of two major trauma patients with the same ISS, one with a low energetic trauma mechanism and one with a high energetic trauma mechanism, the major trauma patient with the high energetic trauma mechanism is more likely to be admitted to a level I trauma centre. Such phenomena could have resulted in incomparable cohorts between different levels of trauma care, and maybe across trauma regions . Population differences were possibly not corrected for enough in multivariable analysis, Combining more major trauma cohorts or cohorts on a longer study period, could increase power for subgroup analysis.

This study is prone to selection bias, with a response rate of 44% and 36%, one year and two years after trauma, respectively. We have tried to reduce selection bias by sending many reminders, also by telephone, and allowed legal sequelae to help incapacitated persons. As mentioned above, type of trauma setting differed between respondents and non-respondents. This could have added to non-response bias as well.

PTSD is a tripartite model with symptoms clusters intrusive, avoidance, and hyperarousal following Diagnostic and Statistical Manual of Mental Disorders. In the revised impact event scale, all three clusters are represented, whereas the version of the impact event scale used for this study lacked the symptom cluster hyperarousal. More profound into depth analysis could have been possible if the revised version of the impact event scale was used.

Two large major trauma cohorts from two trauma regions were combined, creating a large Dutch cohort, in which all type of hospitals participated. Adjusted analyses were done with pre-injury demographics, and pre-existing psychological disorders in combination with questionnaires on psychological health status as outcome measures, compensating for the most relevant covariates.

Conclusion

Major trauma patients admitted to a level I trauma centre have more depressive, anxious, and post-traumatic stress symptoms, than major trauma patients admitted to a non-level I trauma centre, which held over time. Similar, the intensity of depressive, anxious, and post-traumatic stress symptoms were also different across trauma regions. These differences are probably due to different patient profiles in major trauma populations across level of trauma care and trauma regions, based on unmeasured variables. Level of trauma care and trauma region are important factors when addressing psychological health status one and two years after major trauma. A well-coordinated trauma networks could benefit from implementing a trauma care pathway in which psychological support at various time points is incorporated from the acute phase to long term recovery trajectories. Psychological health status should also be part of designing trauma networks and concentrating trauma care.

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Supplementary Table 1.

		IES PTSD		HADS anxiety		HADS depression	
		Year 1	Year 2	Year 1	Year 2	Year 1	Year 2
Sex	**Females**	9 (2-24.5; 200)A	8 (1-25; 163)	4 (1-7; 179)A	4 (2-8; 140)	4 (1-8; 179)	4 (1-9; 140)
	Male	15 (3-33.8; 120)	14 (3-31; 93)	5 (2.3-8; 96)	5 (2-9; 71)	4 (1-8; 97)	4 (2-8; 71)
Age	**18-65**	12 (4-29; 206)	9.5 (3-31.3; 166)	4 (2-8.3; 190)	4 (2-9; 147)	4 (1-8; 190)	4 (1-9; 147)
	>65	8.5 (0.8-28; 114)	100.5 (0-24.3; 90)	4 (1.5-7; 85)	4 (2-6; 64)	4 (1-8; 86)	4 (1.3-7.8; 64)
Comorbidities	**None**	9.5 (2-22.3; 162)	6.5 (0-21; 134)B	3 (1-7; 146)D	3 (1-6.5; 121)D	3 (1-7; 146)C	2 (1-6; 121)D
	1	12 (1.5-29; 93)	15 (3-33; 69)	4 (2-7; 81)	5 (3-9; 57)	4 (1-8; 81)	5 (2-9; 57)
	>1	14 (4.5-35; 65)	15.5 (3-34; 52)	7 (3-11; 48)	7.5 (4-12; 32)	7 (2.5-10; 49)	7 (5-10; 32)
PEPD*	**Yes**	25.5 (7.5-41; 54)D	19 (12-40; 37)D	9 (5-12.5; 49)D	11 (6-13; 33)D	8 (4-11.5; 227)D	7 (4-12.5; 177)D
	No	10 (1-24.3; 266)	8 (1-23; 218)	3 (1-6; 226)	4 (2-6; 177)	3 (1-7; 49)	3 (1-8; 33)
ICU	**Yes**	12 (3-31.8; 200)	10 (2-29; 167)	4 (2-8; 175)	4 (2-8; 143)	4 (1-8; 175)	4 (1-8; 143)
	No	10 (1.3-25; 120)	10 (0.5-26; 89)	3 (1-7; 100)	4 (2-7.8; 68)	3 (1-8; 101)	4 (1-9; 68)
Trauma region	**I**	14 (4.8-33; 162)C	15 (4-34; 124)D	4 (1.8-8; 154)	5 (2-8; 111)	4 (1-9; 155)	4 (2-10; 111)A
	II	7.5 (0-23.5; 158)	6.5 (0-18; 132)	4 (2-7; 121)	4 (2-8; 100)	3 (1-7; 121)	3 (1-6; 100)
Level of care	**L1**	14 (3-33; 223)C	13 (3-33; 183)D	4 (2-8; 195)B	5 (2-9; 156)C	4 (2-9; 195)C	5 (2-9; 156)D
	non-LI	7 (1-17; 97)	6 (0-16; 73)	3 (1-6; 80)	3 (1-6; 55)	3 (1-7; 81)	2 (1-5; 55)

Significance level between subgroups. [A] $0.05 \leq p < 0.01$, [B] $0.01 \leq p < 0.005$, [C] $0.005 \leq p < 0.001$, [D] $p \leq 0.001$. For IES PTSD, IES avoidance, IES intrusive year 1 and year 2 measurements were non-significantly different. HADS, Hospital Anxiety and Depression Scale; IES, Impact Event Scale; PEPD, Pre-existing psychological disorders; ICU, Intensive Care Unit; LI, Level I.

Supplementary Table 2. Additional numbers to Figure 2 and 3.

		HADS anxiety	p-value	HADS depression	p-value	IES PTSD	p-value	IES intrusive	p-value	IES avoidance	p-value
Year 1		4 (2-7)	0.643	4 (1-8)	0.861	12 (2-28)	0.486	6 (1-14)	0.333	5 (0-15)	0.717
Year 2		4 (2-8)		4 (1-9)		10 (2-28)		4 (1-13)		5 (0-13)	
Year 1	**trauma region I**	4 (2-7)	0.85	3 (1-7)	0.064	8 (0-23)	0.002	4 (0-11)	0.009	4 (0-11)	0.002
	trauma region II	4 (2-8)		4 (1-9)		14 (5-33)		8 (2-15)		6 (1-17)	
Year 2	**trauma region I**	4 (2-8)	0.367	3 (1-6)	0.03	7 (0-18)	0	3 (0-8)	0	3 (0-10)	0
	trauma region II	5 (2-8)		4 (2-10)		15 (4-34)		8 (2-15)		8 (1-18)	
Year 1	**trauma region I**	4 (2-8)	0.035	4 (29)	0.005	14 (3-33)	0.005	7 (1-16)	0.011	6 (0-17)	0.002
	trauma region II	3 (1-6)		3 (1-7)		7 (1-17)		4 (0-8)		3 (0-8)	
Year 2	**trauma region I**	5 (2-9)	0.002	5 (2-9)	0	13 (3-33)	0.001	5 (1-15)	0.014	6 (0-16)	0
	trauma region II	3 (1-6)		2 (1-5)		6 (0-15)		3 (0-8)		1 (0-8)	

HADS, Hospital Anxiety and Depression Scale; IES, Impact Event Scale; PTSD Post Traumatic Stress Disorder.

Supplementary Table 3. Respondents who reported to be likely anxious, reported to be likely depressed, or reported moderate to severe symptoms of PTSD.

		HADS anxiety	HADS depression	IES PTSD
Year 1		41 (14.9%)	42 (15.2%)	63 (19.7%)
Year 2		31 (14.7%)	32 (15.2%)	46 (18.0%)
Year 1	**trauma region I**	13 (10.7%)	10 (8.3%)	24 (15.2%)
	trauma region II	28 (18.2%)	32 (20.6%)	39 (24.1%)
Year 2	**trauma region I**	10 (10.0%)	7 (7.0%)	18 (13.6%)
	trauma region II	21 (18.9%)	25 (22.5%)	28 (22.6%)
Year 1	**trauma region I**	33 (16.9%)	34 (17.4%)	53 (23.8%)
	trauma region II	8 (10.0%)	8 (9.9%)	10 (10.3%)
Year 2	**trauma region I**	29 (18.6%)	28 (17.9%)	40 (21.9%)
	trauma region II	2 (3.6%)	4 (7.3%)	6 (8.2%)

HADS, Hospital Anxiety and Depression Scale; IES, Impact Event Scale; PTSD Post Traumatic Stress Disorder.

PART V

DISCUSSION AND SUMMARY

CHAPTER 12

Discussion and future perspectives

Discussion

The aim of this thesis was to evaluate network performance for major trauma patients, which was introduced in **Part I**. In **Part II** this was done by starting at the basis, getting feeling for the number of missed registrations when relying only on automation and classification of injury severity, with data as represented in the Dutch National Trauma Registry. **Part III** assessed major trauma network performance by analysing different levels of care in the light of survival and non-fatal outcome measures. **Part IV** also analysed network performance across different levels of trauma care, using patient-reported outcome measures on health-related quality of life and psychological health status. The findings of each main part will consecutively be presented, completed with a discussion and future perspectives of major trauma care in a regional network.

Part II – Registry validation and injury classification

Missed registrations, when relying on automation only, are common and a potential source of information bias resulting in an ecological fallacy.[1-4] This was confirmed in **chapter 2**, a little over seven percent registrations were flagged as missed, which was 16 percent for the subset with major trauma patients (Injury Severity Score (ISS) > 15). Analyses on automated registration datasets are likely to be valid, although volume outcome measures and quality indicators might be biased for certain subgroups, such as major trauma. Missed patients in a registry might also be problematic for administration of finances, in-house trauma management, and integral health care packages. In addition, throughout the registry process a lot of effort is also put into falsely included registrations. Checking for missed registrations is time consuming, automated registration lists need a human touch for validation and completeness.[5] Despite uniform software, the range of potentially missed registrations was large across participating hospitals, opting for custom attention per hospital. On the other hand, it is also indicated that close contact with software companies that provide electronic patient health records is beneficial for future perspectives. Finally, use of text mining, registration bots, and forms of artificial intelligence should be explored in order to keep registration loads as low as possible.

Injury coding is an important element for quality benchmarking of trauma care and classifying patient groups within trauma registries.[6-10] Lacking uniformity of injury reporting in electronic health records was hypothesised to negatively impact classifying trauma populations. For **chapter 3**, a standardised radiologic reporting template for head scans compatible with the Abbreviated Injury Scale (AIS) was implemented in daily clinical practice. This displayed a change in classification of traumatic brain injury (TBI) severity in 30% of the patients, a reduction of the number of missed TBI, more detailed injury codes, an increased number of patients classified as 'major trauma', and an increased inter-centre coding consistency. With major trauma quality indicators in the Netherlands currently focusing on volume and proportion of patients directly admitted to a regional level I trauma centre these indicators are seen in new light. Coding traumatic brain injury with the abbreviated injury scale following a standardised radiologic template will improve the reliability of classification of trauma populations. Such templates could also be implemented for other body regions, like thorax and abdomen. The largest effect on severely injured populations is probably for the head

region. However, multiple templates combined might also give a more significant effect than the effect of a template regarding one body region.

Worldwide, the AIS is used for injury coding, of which the ISS is derived. The most commonly used definition for major trauma is an Injury Severity Score (ISS) > 15. This threshold was adopted following evaluation of mortality rates in the North American Major Trauma Outcome Study in the 1980s.[17, 18] Several AIS revisions have taken place since then, however the definition of major trauma by ISS > 15 has remained untouched, and has served as a gold standard of injury coding, even though the ISS has substantial limitations.[11-16] In **chapter 4,** the effect of different AIS revisions (1998, 2008 and 2015) has been described; ISS08 > 10 and ISS15 > 11 thresholds perform similarly to a threshold ISS98 > 15 for in-hospital mortality and intensive care unit admission rate. Adjusted ISS thresholds for major trauma populations determined for use with AIS08 and AIS15 coded data provide ongoing comparability within registries that previously used AIS98, or across registries using different AIS revisions. This assumes that the ISS remains an objective 'gold standard', instead of the de facto standard for measuring injury severity, assessing in-hospital mortality risk and providing quality indicators for measuring trauma network performance. However, this is not the case. Various studies have included other anatomical summary scores by distinguishing between severe isolated injuries and polytrauma, or by adding physiological parameters and biomarkers to registries, to define major trauma populations or risk-adjust when evaluating outcomes.[15, 19-25] Modifying or selectively using ISS thresholds for defining major trauma should therefore be seen as an important, but temporary measure when comparing data collected across more than one AIS revision. Defining major trauma using appropriate ISS thresholds is important for quality indicators, comparing datasets, and adjusting for injury severity.

Part III – Clinical outcome measures in a trauma network

In the pursuit of optimal care for trauma patients, regional systems have been implemented worldwide, showing significant improvement in outcomes.[26-30] Hospitals in trauma networks are commonly categorised by level of care based on criteria developed by professionals. Higher level trauma centres have more, immediate and 24/7 available resources for the most severely injured patients, lower level facilities are designed for patients with less severe injuries and do not need to have materials and personnel permanently prepared.[30, 31] Studies on outcome differences between levels of trauma care showed inconsistent results.[27, 32] The underlying rationale seems complex due to case mix differences and local health care context; outcome measures are dependent on complex clinical and process factors, and the time factor of maturing or the impact of implementing regional systems.

The meta-analyses in **chapter 5** and **chapter 6** display that major trauma patients admitted to a level I centre have a survival benefit and a higher resource demand compared with their counterparts admitted to a non-level I centre. In addition, severely injured patients admitted to a level I trauma centre require a longer clinical length of stay, more intensive care, and a greater need for post-hospital rehabilitation trajectories, compared to their counterparts admitted to a non-level I trauma centre. With an external validation of these results on local data, **chapter 7** and **chapter 8** did not confirm the results of the two systematic reviews on in-hospital mortality, but did confirm results on non-fatal clinical outcome measures.

A possible explanation for discrepancies between international literature and an evaluation of a single trauma network is that the volume-outcome relationship of major trauma populations and mortality is convergent over time, and changes in volume over time did not affect outcome measures either.[33, 34] Two main arguments could apply here; Outcome measures of major trauma patients are dependent on multiple factors, for which not all can be compensated for in analysis (e.g. public or local health care context); Trauma care in high-income countries have developed to a transition point in which the law of diminished returns has made its entrance.

Another plausible reason for divergent results could be that an ISS > 15 threshold for major trauma, is not a contemporary definition for major trauma any more in the Dutch trauma system. Originally, this threshold was considered by the Major Trauma Outcome Study based on a mortality rate of twenty percent.[18] Nowadays, mortality rates for major trauma populations are somewhere between nine and 16 percent.[3, 35] Alternative definitions for the severely injured to be admitted to a level I centre have been described previously with the Berlin polytrauma definition.[19, 24, 36] These studies consider a higher ISS threshold (maximum AIS >2 in at least two separate body regions, resulting in an ISS > 17) in combination with physiological parameters that are associated with mortality (Glasgow Coma Scale, Systolic Blood Pressure, Base Excess, International Normalised Ratio). Mortality rates in populations defined with the Berlin polytrauma definition are around 30 percent, setting the bar more progressively. Using the Berlin polytrauma definition will result in around twenty percent less severely injured patients admitted to a level I centre, compared with the classic definition. In addition, patients with two severe injuries are more prone to physiological derangement through a systemic inflammatory response syndrome, resulting in poor outcome.[22, 23] It could be that the number of patients with specific severe injuries that have a survival benefit by being admitted to a level I centre were too small in regional data to be statistically significant.

In our regional analysis, transport times were not compensated for. Adherence to a prehospital major trauma triage protocol might not be adequately selecting major trauma patients in the Netherlands, with many major trauma patients being under triaged to a non-level I trauma centre. However, when looking at the results on clinical outcome measures in a single regional network, one might also conclude that most patients were correctly triaged. This does not mean, that no more effort in admitting as much as possible major trauma patients primarily to a level I centre needs to be undertaken. Clinical outcome measures such as length of stay or mortality do not necessarily represent quality of care. Health care in the Netherlands has structural problems with emergency department crowding, clinical capacities and long throughput times because of a lack of beds in the aftercare setting. And for some major trauma patients, there is a near-certainty they will die. Whereas, quality of care could also be measured with a complication rate, or end-of-life treatment. Such analyses were not part of this thesis.

Part IV – Patient-reported outcome measures in a trauma network

With a relatively low fatality rate in the Netherlands, mortality is not the main concern of trauma care professionals and public health care policy makers. Evaluation of trauma outcome measurements will create more emphasis on patient-reported outcome measures. Impaired quality of life, difficulties with return to work, health care consumption, post-traumatic stress, and impact on families are of importance in daily recovery trajectories and can be considerable in life after (major) trauma. A large group reports social dysfunctioning and quality of life below populations norms one year after major trauma.[37-43]

In **chapter 9**, a median overall utility score of the EQ-5D-5L of 0.81 and a median general health state of 70 was reported. Over 60% reported cognitive limitations and less than 40% fully returned to work. These health-related quality of life scores are below population levels, and the return to work rate was conform international literature on major trauma patients.[44, 45] A better return to work status was associated with better scores on all health domains of the EQ-5D-5L and cognition. These results suggest that being able to return to work has a positive impact on perceived quality of life one year after major trauma, or that improved quality of life may facilitate return to work. Even though return to work can indicate a certain health status, the question is whether it is a reliable parameter to evaluate trauma outcome, since it can be affected by many other factors (e.g. economic).[46] Ten percent of all global disability-adjusted life-years come from injuries, with a significant part affecting work.[45, 47, 48] Trauma care should also focus on health-related quality of life and return to work in collaboration with other rehabilitation disciplines, to start with restoring self-identity and social connections in order to avoid unnecessary pressure, thus stress negatively impacting on their recovery.

Concentration of major trauma care in a network has resulted in different populations across designated levels care. Major trauma patients admitted to a level I centre reported a less favourable general health status and more limitations than patients admitted to a non-level I centre, scoring populations norms one to two years after trauma (**chapter 10**). Well-coordinated networks offer homogeneous results for all major trauma patients when they are distributed in different centres according to their need of care. When analysing health status of major trauma patients across different levels of care, an ISS > 15 cut-off point is questionable. Health status of severely injured patients with an ISS < 15 can be very much affected.[49, 50] Injuries like amputations, multiple long bone fractures, or complex panfacial fractures result in an ISS < 15, but can heavily impact daily life and rehabilitation programmes. In addition, patients at risk for impaired health status can be identified by symptoms of anxiety or depression, acute stress disorder, post-traumatic stress disorder'(PTSD), neuroticism, and trait anxiety, and in general not on sociodemographics or clinical outcome measures.[39, 40, 51]

Chapter 11 displays that major trauma patients admitted to a level I centre were more severely injured and had more depressive, anxious, and post-traumatic stress symptoms, than major trauma patients admitted to a non-level I centre, which held over time. Similar, severity of injuries and the intensity of depressive, anxious, and post-traumatic stress symptoms were also different across regions. These differences are probably due to different patient profiles in major trauma populations across levels of care and networks, based on unmeasured variables.

Pre-existential psychological disorders have been reported to result in a lower health-related quality of life, more inpatient (psychological) morbidity, and a longer hospital length of stay, but do not independently predict health-related quality of life.[52, 53]

An association of post-traumatic stress and health-related quality of life has also been reported previously.[54] PTSD dysregulates the hypothalamus-pituitary-adrenal axis and the hypothalamus-pituitary-thyroid axis.[55] Increased activity of the hypothalamus-pituitary-thyroid axis results in hyper arousal symptoms as a part of PTSD. The effect of PTSD on the hypothalamus-pituitary-adrenal axis is either excessive glucocorticoid activity utilising bodily resources for survival, or insufficient glucocorticoid signaling, leading to stress related pathology like inflammation. The latter is in line with poor wound healing, resulting in infections or other complications.[56] Especially for major trauma patients with multiple injured body regions this mechanism could result in poor outcome.[22, 23] Physical trauma, psychological health status, and quality of life are interconnected, as they are part of a complex interplay between medical history, stress regulation, hormonal axis alterations, immunology, and daily functioning. Societal pressure is most likely contra productive, and should not be part of rehabilitation programs. Focusing on strength instead of on pathology and disabilities will positively impact experienced health status; Personal development, social interactions, and positive psychology will ameliorate resilience and post-traumatic growth.[57, 58] A well-coordinated network could benefit from implementing a trauma care pathway in which psychological support at various time points is incorporated from the acute phase to long term recovery trajectories.[40, 59-61] Psychological health status should also be part of designing trauma networks and concentrating trauma care.

Future Perspectives

Evaluating trauma care begins by asking with which values, parameters, and outcomes can we gauge at the usefulness and quality of delivered trauma care, thus, how would we like it to be in the future? All studies in this thesis, except the two systematic reviews, were based on the variables collected for the Dutch National Trauma Registry. Of those eight performed studies, six needed extra data collection to be able to answer the formulated questions in the introduction. This is where the DNTR of the future begins. To be able to optimally use DNTR data, the trauma field needs to ask itself, what data do we need to evaluate trauma care performance, and what information is available? And to be able to efficiently use trauma data, to what expense are we collecting data for this evaluation?

Suggestions have been made on the first question recently. Geo-spatial analysis is essential when analysing performance of the acute care chain. For resources to be used efficient and primarily to minimise health damage. The DNTR is currently putting effort in getting reliable data from emergency medical services. This will not only reduce missing values on location and the pace of trauma care, but also on availability of emergency medical services. Recommendations have also been made on collecting physiological parameters and biomarkers, for their prognostic value and usage for classification of the severely injured. Once again other data sources might come of hand. Not in the least place, the availability of big data will reduce registration loads. Such linkage with other related databases are potentially a source of further development of the DNTR and a further decrease of registration load.

Examples of data sources that can be linked with the DNTR are, electronic health records of (helicopter) emergency medical services, Netherlands Emergency department Evaluation Database (NEED), Dutch National Intensive Care Evaluation (NICE), and the Dutch National Hospital Registration (LBZ).

Diagnosis Related Groups (in Dutch, Diagnose Behandel Combinatie) are used in the Netherlands for registration and reimbursement of hospital care. Diagnosis treatment combinations are based on the Dutch version of the International Classification of Diseases, version 10. A mapping structure from ICD to AIS exists, mapping injury codes containing general information. Mapping from AIS to ICD is also possible, with the AIS having a higher detail level. If injury coding following the AIS would be done by medical specialists, the registration load would remain similar (now they are coding with the ICD) and the financial administration would have less omissions. Injury coding following the AIS could be supported by radiologic imaging and templates for radiologic reports. Previously mentioned templates will make AIS coding easier by reducing registration loads and results in more reliable injury coding. Potentially, artificial intelligence techniques can be used to directly derive radiologic reports from radiologic images, thus AIS coding, in the future. All abovementioned requires less hands-on registrations, and more hands-off data managing. This does not mean, validation of data is useless. Data of the future will heavily rely on automation, but is still user generated, and definitely not flawless. While this thesis focusses on severely injured populations, in general, discipline specific diagnostic codes with the highest possible detail level should be leading in multidisciplinary care and accessory administration. Disciplines like radiology, pathology, and microbiology should base their diagnosis on disease specific fields in medicine, not for administrative or financial purposes. That way, the standardised radiologic template discussed in this thesis can be an example for less registration load of all kinds resulting in better communication, thus care.

Patient-reported outcome measures (PROMs) are also part of the next generation data. This type of data is generated by the patients themselves. PROMs can support patients and caregivers in their awareness of progress and expectation management of recovery trajectories. Patients know best to express their abilities and limitations in daily life. Trauma surgeons consider PROMs to positively facilitate shared decision-making. Generic information about a patients' physical , mental and social health status is considered relevant within daily trauma surgical practice. To generate PROMs data, the implementation can be automated as well. Automation of questionnaires will most likely result in a very low response rate. For the response rate to go up, paper correspondence and telephone communication will ask for a lot of effort, of both sender and receiver. It would be of great value to dig into forms of automation in the likes of applications and short message services with hyperlinks. Such digital services could be presented to patients before each outpatient clinical visit. Another possibility is looking for other partners in the trauma chain with overlapping target populations, who will be interested in presenting patient-reported outcome measures. This could result in more collaboration between different disciplines in a network. A Dutch national working group advised to implement generic PROMs, and add disease specific questionnaires wherever considered relevant.[62] Disease specific questionnaires might be more useful for standalone projects, or directed on specific subgroups only. Generic PROMs can be used to evaluate and compare health abilities and limitations across trauma and other (sub)populations. Looking at

the heterogeneity of trauma populations represented in the DNTR, generic PROMs seem to be a logical first step of collecting data not themed with clinical and process information.

Implementation of designated trauma regions has been successful in organising trauma care. To remain innovative and optimally use resources with a benefit for major trauma patients, it seems to be time for an out of the box approach. A discussion about the degree of concentration of trauma care is ongoing. Too what extent should major trauma care be regionalised over all acute health care regions? Looking at Helicopter Emergency Medical Services (HEMS), providing on-scene specialist care for the most unstable patients, a different concentration of acute health care has been chosen. Also a different concentration of care for patients in need of endovascular treatment of ischemic stroke has been arranged. What do trauma surgeons think of contemporary concentration of trauma care, besides the scientific evidence? If fewer trauma centres are designated to provide care for the most severely injured patients, the pre- and posthospital care could also potentially be more innovative on many concerns, like pre-hospital treatment or resources that would normally be not affordable for small groups of patients. Trauma care is a very multidisciplinary and holistic field of medicine. A stronger link with post-clinical rehabilitation trajectories could be constructed, with for instance an integral health care package per patient. Health care pathways in superregional trauma centres could also be imbedded with medical psychological care units. And last but not least, these centres could also develop expertise in ethical aspects in the treatment of trauma patients on topics like comatose survivors, withdrawal of treatment, and participation of families in these settings. Although much has improved in the organisation of trauma care, many relevant open ends deserve attention in the (near) future.

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CHAPTER 13

Summary

Part I – Introduction and outline

Modern society faces an ongoing challenge with five millions of trauma-related deaths annually, and approximately 10 percent loss of disability adjusted life years due to injuries worldwide. On a national level in the Netherlands, the incidence of medical treatment after unintentional trauma is around 1.5 million per year, which is approximately 900 per 10,000 inhabitants. Around five percent involves clinical admission to a hospital which is somewhat more than 40 per 10,000 inhabitants. Trauma can result in impaired quality of life, difficulties with return to work, health care consumption, post-traumatic stress, and long-term social limitations. Trauma can have a profound impact on the social environment as well. In the Netherlands, care for persons with injuries requiring acute admission to a hospital is organised in networks nested in trauma regions, with hospitals having designated levels of trauma care. Trauma networks were originally designed to respond adequately during high impact disasters and care for the most severely injured.

In this thesis major trauma care from a network perspective was evaluated: In **part II**, validation of trauma data on and classification of major trauma patients was assessed, in **part III** different levels of trauma care were compared on mortality and non-fatal clinical outcome measures for major trauma populations, closing with **part IV**, in which long-term patient-reported outcome measures of major patients were compared across different level of trauma care.

Part II – Registry validation and injury classification

Missed registrations can be potential source of information bias resulting in false interpretation of statistical data. **chapter 2** displays that automated registration lists in clinical electronic health records are not complete, based on a multicentre retrospective cohort study. Missed registrations occur frequently (a little over seven percent were flagged as missed), and the amount differs greatly across hospitals. It does not necessarily need to be the case in other trauma regions, but there was a high prevalence of major trauma patients (Injury Severity Score (ISS) > 15) classified as missing in retrospect (15% of all missed registration). Checking for missed registrations can be time consuming because automated registration lists need a human touch for validation and to be complete.

Injury coding with the Abbreviated Injury Scale (AIS) is an important element for benchmarking, trauma registries and research. Various studies have shown variability between injury coders and between hospitals in injury coding. In **chapter 3**, lacking uniformity of injury reporting in electronic health records was hypothesised to negatively impact classifying trauma populations.A standardised radiologic template was implemented in two level I trauma centres, featuring all AIS coding elements of the head. Traumatic brain injuries (TBI) were AIS coded without and with the availability of an standardised radiologic template. Injury coding based on a radiologic template changed the classification of TBI severity in 29.9% of the patients (underestimated 22.9% and overestimated 7.0% of the cases). Coding traumatic brain injuries with the AIS based on a standardised radiologic template resulted in more injuries being coded, the injury codes were more specific, and the number of major trauma patients increased with 14.6%. Traumatic brain injury coding with a standardised radiologic template improves classification of patient specific injuries and the trauma population in

general'.. Specifically, it adds to a more accurate indicator major trauma on volume as well as the percentage major trauma patients primarily admitted to a level I trauma centre.

An ISS > 15 threshold is common in classifying major trauma, although the AIS has been extensively revised over time. An association of classifying major trauma patients based on injury severity and clinical outcome measures was evaluated in **chapter 4**, with an multicentre retrospective cohort study. By using three revisions of the Abbreviated Injury Scale, this chapter demonstrated that an ISS > 15 threshold for major trauma will potentially result in difficulties comparing datasets containing injury codes from different revisions of the Abbreviated Injury Scale across the datasets. When coding injuries using AIS08 or AIS15, thresholds of ISS08 ≥ 11 and ISS15 ≥ 12 respectively, perform similarly to a threshold of ISS ≥ 16 in AIS98 in terms of in-hospital mortality and ICU admission. Mapping datasets with different ISS thresholds for major trauma is possible and useful, but should not replace efforts in developing more appropriate major trauma definitions in contemporary care.

Part III – Clinical outcome measures in a trauma network

With the implementation of trauma systems, levels of trauma care were introduced. Working with such a system has been linked to significant improvements in survival and other outcomes. Two systematic reviews in **chapter 5** and **chapter 6** confirmed a survival benefit for major trauma populations, when admitted to a level I trauma centre. This result was found by combining studies of major trauma populations as a whole (adjusted OR 0.77; CI 95% 0.69-0.87), as well as when combining studies focusing on major trauma populations with specific severe injuries (adjusted OR 0.87; 95% CI 0.80-0.94). The literature indicated that major trauma populations have a higher ISS, a longer length of stay, longer intensive care, and a smaller percentage of being discharged home, after being admitted to a level I trauma centre. Similar results were found in the Dutch National Trauma Registry of Southwest Netherlands in **chapter 7** and **chapter 8**, based on two multicentre retrospective cohort studies. A survival benefit for major trauma patients after being admitted to a level I trauma centre was not found (adjusted OR 1.06; 95% CI 0.73-1.53), also not after transferring the severely wounded from a level II hospital to the regional level I trauma centre (adjusted OR 0.72; 95% CI 0.40-1.31). With patients admitted to the level I TC being the most severely injured, this is quite a network performance. Most major trauma patients with a high mortality probability, are adequately triaged to the level I trauma centre, resulting in homogeneous mortality rates throughout the trauma network.

Part IV – Patient-reported outcome measures in a trauma network

Mortality due to trauma has reduced in the past decades. The implementation of trauma networks has contributed a lot to this achievement. Besides mortality, patient-reported outcome parameters should be included in evaluation of trauma care, while major trauma very often results in long term disabilities. The aim of **chapter 9** was to assess health-related quality of life, cognition, and return to work one year after major trauma from a network perspective. Questionnaires containing the EQ-5D-5L and questions on cognition, level of education, comorbidities, and resumption of paid work were sent one year after trauma, and combined with data from the Dutch National trauma registry. Major trauma patients perform below population norms regarding health-related quality of life one years after trauma (median

overall utility score 0.81 versus 0.88). Limitations were prevalent in all health dimensions of the EQ-5D-5L and cognition. The return to work rate was 68% (37% full. 31% partial), and was associated with all health domains of the EQ-5D-5L and cognition suggesting that being able to return to work has a positive impact on perceived health-related quality of life, or that health-related quality of life may facilitate return to work.

Concentration of trauma care in a network has resulted in different trauma populations across designated levels of care. In **chapter 10** and **chapter 11** a multicentre observational cohort study comprising secondary longitudinal multilevel analysis on prospective cohorts from two neighbouring trauma regions was conducted. With chapter 9 health status was reported one and two years after trauma by EQ-5D-5L, added with a sixth health dimension on cognition. Major trauma patients admitted to level I trauma centres reported a less favourable general health status and more limitations compared to level II and III facilities (median overall utility score 0,81 versus 0,88 and 0.89 after one year). Patients admitted to a level II or III hospital scored conform populations norms with these results. Differences on general health status and limitations in specific health domains disappeared in adjusted analysis. Similar in chapter 10, psychological health status was self-reported with the hospital anxiety and depression scale and the impact event scale. Respondents admitted to a level I trauma centre reported in comparison with respondents admitted to a non-level I trauma centre more symptoms of anxiety (3, P_{25}-P_{75} 1-6 vs. 5, P_{25}-P_{75} 2-9, p=.002), depression (2, P_{25}-P_{75} 1-5 vs. 5, P_{25}-P_{75} 2-9, p<0.001), and post-traumatic stress (6, P_{25}-P_{75} 0-15 vs. 13, P_{25}-P_{75} 3-33, p=0.001). These symptoms also differed across trauma regions, indicating populations differences. Level of trauma care and trauma region are important when analysing health-related quality of life and psychological health status.

Part V – Discussion and future perspectives

Registrations and classification of major trauma patients can be done based on higher quality of data and more efficient injury coding. Checking for missed registrations and implementing a standardised radiologic template are examples that reduce registration load and improve financial administration, quality of data analysis on major trauma populations, and expediency of the quality indicators on major trauma. Major trauma patients admitted to level I trauma centres are more severely injured, require more intensive care, resulting in a longer clinical stay and are more often discharged to rehabilitation facilities, than those admitted to a non-level I trauma centre. Major trauma patients admitted to a level I trauma centre reported a health-related quality of life that is below populations norms, and a large part reports elements of depression, anxiety, and post-traumatic stress, two years post trauma. With a relatively low fatality rate in the Netherlands, mortality remains a concern of trauma care professionals and public health care policy makers, however is less discriminative for quality of care as it was and creates space for non-fatal outcome measures in quality surveillance systems. Other parameters and classifications with which care for major trauma patients can be evaluated should be explored. In addition, composition of trauma populations differ across levels of trauma care, making it an important factor in analysing quality of trauma care in a network, of which patient-reported outcome measures on health-related quality of life and psychological health status should be a part. Well-coordinated networks offer homogeneous results for all major trauma patients when they are distributed in different hospitals according to their need of care. Not all patients with severe injuries are identified based on automated registration lists. In addition, not all patients with severe injuries are injury coded and classified as such.

This creates an incomplete overview on the volume-outcome relationship and benchmarking major trauma care.

Scientific literature tells us that major trauma patients primarily admitted to a level I trauma centre, require more intensive care and have a survival benefit over being primarily admitted to a non-level I trauma centre. Similar results were also seen in trauma region Southwest Netherlands, besides a survival benefit comparable over all trauma levels. Long term follow-up of major trauma patients also shows long-term limitations in health-related quality of life and psychological health status, being more present for major trauma patients admitted in a level I trauma centre. Adjusted analysis displayed more homogeneous health-related quality of life and psychological health status, which is a network performance of a matured network ready for further development in the near-future.

CHAPTER 14

Samenvatting

Deel I – Introductie en doelstelling

De mensheid staat voor een continue uitdaging met jaarlijks vijf miljoen trauma-gerelateerde sterfgevallen en ongeveer 10 procent verlies van 'levensjaren gecorrigeerd voor beperkingen' door letsel, wereldwijd. In Nederland is de incidentie van een medische behandeling na niet-intentioneel trauma ongeveer anderhalf miljoen per jaar, wat neerkomt op ongeveer 9.000 per 100.000 inwoners. Om en nabij vijf procent van alle mensen met een traumatisch letsel wordt klinisch opgenomen in een ziekenhuis. Dat is iets meer dan 400 per 100.000 inwoners. Fysiek trauma kan leiden tot een verminderde kwaliteit van leven, moeilijkheden bij terugkeer naar werk, bovengemiddelde zorgconsumptie, posttraumatische stress en langdurige sociale beperkingen. Een ongeval kan ook een aanzienlijke impact hebben op de sociale omgeving. In Nederland, is zorg voor traumapatiënten die acute opname in een ziekenhuis vereisen, georganiseerd in netwerken verdeeld over 10 traumaregio's. De ziekenhuizen hebben een niveau van zorg op basis van levelcriteria opgesteld door de Nederlandse Vereniging voor Traumachirurgie. Traumanetwerken zijn oorspronkelijk ontworpen om adequaat te reageren tijdens rampen en crises met grote impact en zijn ontworpen om zorg te bieden aan meervoudig ernstig gewonde patiënten, ook wel multitraumapatiënten genoemd.

In dit proefschrift werd de zorg voor patiënten met ernstig trauma vanuit een netwerkperspectief geëvalueerd op uitkomstmaten: In deel II werd de validatie van letselgegevens en de classificatie van patiënten met ernstig letsel beoordeeld, in deel III werden verschillende niveaus van traumazorg vergeleken op mortaliteit en niet-fatale klinische uitkomstmaten voor patiëntpopulaties met ernstig letsel, afrondend met deel IV, waarin patiënt-gerapporteerde uitkomstmaten van multitraumapatiënten op lange termijn werden vergeleken tussen verschillende niveaus van traumazorg.

Deel II – Validatie en letselclassificatie

Gemiste registraties kunnen een potentiële bron van informatiebias zijn, wat resulteert in een onvolledig beeld van patiëntpopulaties en een verkeerde interpretatie van statistische data. **hoofdstuk 2** toont aan dat geautomatiseerde registratielijsten in elektronische patiëntendossiers niet volledig zijn, gebaseerd op een multicentrische retrospectieve cohortstudie. Gemiste registraties komen frequent voor (iets meer dan zeven procent werd gemarkeerd als gemist), en het aantal gemiste registraties kan sterk verschillen per ziekenhuis. Dit hoeft niet per se het geval te zijn in alle traumaregio's. Er was een hoge prevalentie van patiënten met ernstig letsel (Injury Severity Score (ISS) > 15), die achteraf als gemist werden geclassificeerd (15% van de gemiste registraties). Het controleren op gemiste registraties kan tijdrovend zijn omdat geautomatiseerde registratielijsten een menselijke hand nodig hebben voor validatie en om compleet te zijn.

Letselcodering met de Abbreviated Injury Scale (AIS) is een belangrijk element voor traumaregistraties, standaardrapportages en onderzoek. Verschillende studies hebben variabiliteit aangetoond tussen letselcodeurs van één ziekenhuis en ook tussen ziekenhuizen in het coderen van letsels. In **hoofdstuk 3** werd verondersteld dat het ontbreken van uniformiteit in het radiologisch rapporteren van letsel in elektronische patiëntendossiers een negatieve invloed heeft op de classificatie van traumapopulaties. Een gestandaardiseerd radiologisch sjabloon werd geïmplementeerd in twee level I ziekenhuizen, met alle AIS-

coderingsonderdelen van het hoofdstuk hoofd. Traumatisch hersenletsel werd AIS-gecodeerd met en zonder de beschikbaarheid van een ingevuld gestandaardiseerd radiologisch sjabloon. Letselcoderingen op basis van een radiologisch sjabloon veranderde de classificatie van neurologische letselernst bij 29,9% van de patiënten (een onderschatting bij 22,9% en een overschatting bij 7,0% van de gevallen). Letselcoderingen van traumatisch hersenletsel met de AIS op basis van een gestandaardiseerd radiologisch sjabloon resulteerde in meer gecodeerde letsels, de letselcodes waren specifieker en het aantal patiënten met een ISS > 15 nam toe met 14,6%. Uniforme letselcodering van niet aangeboren hersenletsel met een gestandaardiseerd radiologisch sjabloon verbetert de classificatie van patiënt-specifiek letsel en traumapopulaties in het algemeen. Specifiek draagt het bij aan een nauwkeurigere kwaliteitsindicator multitrauma op volume en het percentage multitraumapatiënten dat primair wordt opgenomen in een level I ziekenhuis.

Geruime tijd is een ISS > 15 afkappunt gebruikelijk voor het classificeren van multitraumapatiënten, hoewel de AIS in dit tijdsbestek veelvuldig is gereviseerd. Een associatie van de classificatie van patiënten op basis van letselernst via de AIS en klinische uitkomstmaten werd geëvalueerd in **hoofdstuk 4**, met een multicentrische retrospectieve cohortstudie. Door gebruik te maken van drie revisies van de Abbreviated Injury Scale, toonde dit hoofdstuk aan dat het gebruik van een afkappunt ISS > 15 voor ernstig trauma mogelijk zal resulteren in moeilijkheden bij het vergelijken van datasets die letselcodes uit verschillende revisies van de Abbreviated Injury Scale gebruikt hebben. Indien letsel gecodeerd wordt met de AIS08 of AIS15, zijn een afkappunt van ISS08 ≥ 11 en ISS15 ≥ 12 respectievelijk, vergelijkbaar met een ISS ≥ 16 wanneer AIS98 gebruikt wordt, wanneer gekeken wordt naar de hoogte van ziekenhuis mortaliteit en IC-opname. Het in kaart brengen van datasets met verschillende ISS-drempels voor ernstig trauma is mogelijk nuttig, en zou inspanningen om meer geschikte definities van ernstig trauma te ontwikkelen niet moeten vervangen.

Deel III – Klinische uitkomstmaten in een traumanetwerk

Met de implementatie van traumasystemen werd tevens een niveau van traumazorgclassificatie geïntroduceerd. Het werken met een dergelijk systeem wordt in verband gebracht met significante verbeteringen in overleving en andere uitkomstmaten. Twee systematische literatuurstudies in **hoofdstuk 5** en **hoofdstuk 6** bevestigden een overlevingsvoordeel voor patiëntpopulaties met ernstig letsel, wanneer ze werden opgenomen in een level I ziekenhuis. Dit resultaat werd gevonden door studies van patiëntpopulaties met alle soorten ernstig letsel te combineren (aangepaste OR 0,77; 95% CI 0,69-0,87), evenals bij het combineren van studies die zich richten op patiëntpopulaties met specifiek ernstig letsels (aangepaste OR 0,87; 95% CI 0,80-0,94). De literatuur gaf aan dat patiëntpopulaties met ernstig letsel een hogere ISS hebben, een langere opnameduur, langere intensive care, en een kleiner percentage dat naar huis wordt ontslagen, na opname in een level I ziekenhuis. Vergelijkbare resultaten werden gevonden in de landelijke traumaregistratie van Zuidwest-Nederland in **hoofdstuk 7** en **hoofdstuk 8**, gebaseerd op twee multicentrische retrospectieve cohortstudies. Een overlevingsvoordeel voor patiënten met ernstig letsel na opname in een level I ziekenhuis werd niet gevonden (gecorrigeerde OR 1.06; 95% CI 0.73-1.53), ook niet na het secundair overplaatsen van een patiënt van een level II ziekenhuis naar het level I ziekenhuis in de betreffende regio (gecorrigeerde OR 0.72; 95% CI 0.40-1.31). Aangezien patiënten met de meest ernstige letsels opgenomen worden in een level I traumacentrum, is dit is een behoorlijke netwerkprestatie. De meeste patiënten met een a priori hoge kans op overlijden,

worden adequaat getrieerd prehospitaal, resulterend in homogene overlevingskansen door het traumanetwerk heen.

Deel IV – Patiëntgerapporteerde uitkomstmaten in traumanetwerken

Sterfte door trauma is de afgelopen decennia verminderd. De implementatie van traumanetwerken heeft een belangrijke bijdrage geleverd aan deze ontwikkeling. Naast sterfte zouden patiënt-gerapporteerde uitkomstparameters van toegevoegde waarde kunnen zijn in de evaluatie van traumazorg, aangezien ernstig letsel vaak resulteert in langdurige beperkingen. Het doel van **hoofdstuk 9** was om de gezondheid-gerelateerde kwaliteit van leven, cognitie en terugkeer naar werk, één jaar na ernstig trauma, vanuit een traumanetwerkperspectief te beoordelen. Vragenlijsten bestaande uit de EQ-5D-5L en vragen over cognitie, opleidingsniveau, medische voorgeschiedenis en hervatting van werk werden één jaar na trauma verzonden en gecombineerd met gegevens uit de landelijke traumaregistratie. Patiënten met ernstig letsel scoren beneden populatienormen wat betreft gezondheid-gerelateerde kwaliteit van leven één jaar na trauma (mediaan algemene utiliteitsscore 0,81 versus 0,88). Beperkingen waren aanwezig in alle gezondheidsdomeinen van de EQ-5D-5L en cognitie. Het percentage patiënten dat terugkeerde naar werk was 68% (37% volledig, 31% gedeeltelijk), en was geassocieerd met alle gezondheidsdomeinen van de EQ-5D-5L en cognitie. Dit suggereert dat het kunnen terugkeren naar werk een positieve invloed heeft op de waargenomen gezondheid-gerelateerde kwaliteit van leven, of dat gezondheid-gerelateerde kwaliteit van leven de terugkeer naar werk kan vergemakkelijken.

Concentratie en spreiding van traumazorg in een netwerk heeft geresulteerd in verschillende traumapopulaties over aangewezen zorgniveaus. In **hoofdstuk 10** en **hoofdstuk 11** werd een multicentre observationele cohortstudie uitgevoerd op data voortkomend uit prospectieve cohorten van twee aangrenzende traumaregio's. In hoofdstuk 9 werd door patiënten hun gezondheidstoestand één en twee jaar na trauma gerapporteerd met de EQ-5D-5L, aangevuld met een zesde gezondheidsdimensie over cognitie. Patiënten met ernstig letsel die werden opgenomen in een level I ziekenhuis, rapporteerden een minder gunstige algemene gezondheidstoestand en meer beperkingen dan patiënten die werden opgenomen in een level II of III ziekenhuis (mediaan algemene utiliteitsscore 0,81 versus 0,88 en 0.89 na één jaar). Patiënten opgevangen in een level II of een level III ziekenhuis rapporteerden hiermee **conform** populatienormen. Verschillen in algemene gezondheidstoestand en beperkingen in specifieke gezondheidsdomeinen over de verschillende levels van zorg verdwenen in gecorrigeerde analyses. Vergelijkbaar in hoofdstuk 10 werd de psychologische gezondheidstoestand zelf gerapporteerd met de 'Hospital Anxiety and Depression Scale' en de 'Impact Event Scale'. Patiënten met ernstig letsel die werden opgenomen in een level I ziekenhuis rapporteren in vergelijking tot patiënten die werden opgenomen in een level II of een level III ziekenhuis meer tekenen van depressie (2, P_{25}-P_{75} 1-5 vs. 5, P_{25}-P_{75} 2-9, $p<0.001$), angst (3, P_{25}-P_{75} 1-6 vs. 5, P_{25}-P_{75} 2-9, $p=.002$) en posttraumatische stress (6, P_{25}-P_{75} 0-15 vs. 13, P_{25}-P_{75} 3-33, $p=0.001$). Deze symptomen verschilden ook tussen traumaregio's, wat wijst op populatieverschillen. Het niveau van traumazorg en de traumaregio, of het traumanetwerk, waar zorg plaats heeft gevonden, zijn belangrijk elementen bij het analyseren van gezondheid-gerelateerde kwaliteit van leven en ervaren psychologische gezondheidstoestand in breder verband.

Deel V – Discussie en toekomstperspectief

Registraties en classificatie van patiënten met ernstig letsel kunnen worden gedaan op basis van hogere kwaliteit van gegevens en efficiëntere letselcodering. Het controleren op gemiste registraties en het implementeren van een gestandaardiseerd radiologisch sjabloon zijn voorbeelden die registratielast verminderen, de financiële administratie verbeteren, en bijdragen aan de kwaliteit van data-analyse van patiëntpopulaties met ernstig letsel en de bruikbaarheid van de kwaliteitsindicator multitrauma. Patiënten met ernstig letsel opgenomen in een level I ziekenhuis zijn ernstiger gewond, en hebben intensievere zorg nodig, wat resulteert in een langere klinische opname, en worden ook vaker ontslagen naar revalidatiefaciliteiten, dan degenen opgenomen in een non-level I ziekenhuis. Patiënten met ernstig letsel opgenomen in een level I ziekenhuis rapporteerden een gezondheid-gerelateerde kwaliteit van leven die beneden populatienormen ligt, en een groot deel rapporteerde elementen van depressie, angst en posttraumatische stress, twee jaar na trauma. Met een relatief laag sterftecijfer in Nederland is mortaliteit nog steeds een belangrijk doel van zorg voor traumazorgprofessionals en beleidsmakers in de gezondheidszorg, echter is steeds minder discriminatief voor de kwaliteit van zorg en er komt ook steeds meer ruimte voor niet-fatale uitkomstmaten als onderdeel van kwaliteitsbewaking. Andere parameters en classificaties waarmee de zorg voor patiënten met ernstig letsel kan worden geëvalueerd, moeten worden verkend om kwaliteit van zorg weer te geven. Bovendien verschilt de samenstelling van patiëntpopulaties tussen de niveaus van traumazorg, wat een belangrijke factor is bij het analyseren van kwaliteit van traumazorg in een netwerk. Patiënt-gerapporteerde uitkomstmaten over gezondheid-gerelateerde kwaliteit van leven en psychologische gezondheidstoestand zouden hier ook een onderdeel van moeten zijn. Goed gecoördineerde traumanetwerken bieden homogene resultaten voor alle traumapatiënten wanneer ze worden verdeeld over verschillende ziekenhuizen naar hun zorgbehoefte.

Niet alle patiënten met ernstig letsel worden geïdentificeerd op basis van geautomatiseerde registratielijsten, en niet alle patiënten met ernstig letsel worden correct geclassificeerd als dusdanig. Dit geeft mogelijk een onvolledig beeld van het volume patiënten met ernstig letsel, en een vertekend beeld van de kwaliteitsindicator multitrauma. De wetenschappelijke literatuur verteld ons dat patiënten met ernstig letsel die primair aangeboden worden aan een level I ziekenhuis, meer intensieve zorg nodig hebben en een hogere overlevingskans hebben dan wanneer aangeboden aan een non-level I ziekenhuis. In de traumaregio Zuidwest-Nederland waren deze resultaten ook te zien, behalve de overlevingskans, deze was vergelijkbaar over de verschillende ziekenhuizen. Naast meer intensieve zorg voor patiënten met ernstig letsel, werd gezien dat ernstig letsel op lange termijn voor beperkingen blijft zorgen in de ervaren kwaliteit van leven en psychologische gezondheidsstatus, welke het grootst waren voor de patiëntengroepen opgevangen in een level I ziekenhuis. Na gecorrigeerde analyses verdween het verschil tussen de ziekenhuizen, wat met recht een prestatie van een ontwikkeld traumanetwerk genoemd mag worden, klaar voor verdere innovaties.

PART VI

APPENDICES

CHAPTER 15

Thankōjanan

A

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Zoals gezegd, onderzoek is een groepsproces. Zonder coauteurs gaat het niet. **Ed,** jij was mijn begeleider tijdens de NIHES-studie en bracht mij onder andere op het pad van de vragenlijsten. Daar heb ik onwijs veel van geleerd. **Charlie**, de gehele middenpijler van deze thesis had waarschijnlijk of heel lang geduurd, of had er compleet anders uit gezien. Jij bracht **Leonne** en **Claire** als masterstudenten binnen. Jullie gingen alle drie heel gemakkelijk op in het datamanagement van het Traumacentrum Zuidwest Nederland. Jullie brachten op het vlak van onderzoek een leuke dynamiek. Ik wens jullie een hele mooie loopbaan toe. Dear **Cameron**, your expertise on the Abbreviated Injury Scale was very inspirational. Your willingness to participate in one of my first publications gave me a boost that launched me towards better scientific writing. This is highly appreciated. Beste **Menco**, wij hebben heel wat momenten gehad online, of telefonisch, waarin we heel strategisch vervolgstappen doornamen. Jij en ik zijn veelpotigen en zijn daardoor gedwongen tot efficiëntie van tijdsbesteding. Dat neemt niet weg dat wij elkaars wetenschappelijke reis op een bijna vriendschappelijke manier hebben mogen volgen. Ik wens jou het allerbeste in het Hoge Noorden. Beste **Mariska,** het aansluiten van de data die ik verzamelde met data uit de BIOS-studie heeft een mooie samenwerking tot stand gebracht. Met al jouw ervaring ben je steeds nog heel benaderbaar en je gelooft overduidelijk in samenwerking. Dat doe je op een voor mij heel prettige manier. De laatste pijler van deze thesis is overduidelijk mede tot stand gekomen door jouw inbreng. Ik ben erg benieuwd hoe nieuwe projecten vorm gaan krijgen.

Beste **Els**, jij durfde het aan mij te laten studeren aan het NIHES. Toen wij in dat kartonnen Ha-gebouwtje zaten, dat meedeinde op de wind, telde het Traumacentrum Zuidwest Nederland enkele medewerkers, en toch durfde jij vooruit te kijken. Je hebt een degelijk basis neergelegd voor persoonlijke en professionele groei. Daar ben ik je heel dankbaar voor. Toen je stopte bij het Traumacentrum heb je gekozen voor een nieuwe indeling in het leven, daar heb ik altijd veel bewondering voor gehad. En dan kwamen we elkaar ook nog in een nieuwe functie tegen bij MMT Nederland, dat voelde direct goed. Ik hoop dat we ook daar iets moois kunnen neerzetten.

Beste **Nienke**, onder jouw veren explodeerde de acute zorg tak van het stafbureau en kregen we te maken met pandemische paraatheid. Jouw energie, en wil om zaken voor elkaar te krijgen was voelbaar op de vloer. Onder unieke omstandigheden, een enorme groei van medewerkers, en een omdoping van Traumacentrum naar Acute Zorgnetwerk, waren jouw ambities aanstekelijk. Soms had ik twijfels of onderzoek wel paste bij het Traumacentrum, toch voelde ik mij altijd gesteund door jou, waarvoor dank.

Met de komst van **Anneloes** kon ik op het gebied van onderzoek direct rekenen op een gelijkgestemde. Wij kennen elkaar nog niet lang, wel heb je nu al overduidelijk interesse laten zien in het gedane werk en nieuwe ideeën. Hopelijk kunnen wij wat betreft onderzoek structuur gaan aanbrengen voor de toekomst, en ik wens jou heel veel plezier in het afronden van jouw eigen promotietraject.

Datamanagers, registratiemedewerkers, en studenten voor de landelijke traumaregistratie. Ik zou gerust vijftig namen kunnen opnoemen. Dat lijkt wat overdadig, de meeste van jullie lezen dit namelijk niet. Toch wil ik jullie allen danken voor de inzet. Zonder valide data geen onderzoek. Enkelen hebben een meer blijvende indruk achtergelaten. Il**se**, **Amin**, **Maurits**,

Urmi, **Anneloes**, **Julia**, het was een waar genoegen. **Sonja**, we hadden wel eens spanning onderling, we keken elkaar ook weer recht aan. Er viel een overduidelijk gat toen jij met pensioen ging. Het was niet voor niets dat wij van jou op een fijne manier afscheid hebben mogen nemen. **Nadine**, jij gaat met het vertrek van Tea een heel mooi nieuw hoofdstuk toevoegen aan jouw werk. Dank voor jouw collegialiteit, en ik hoop dat we samen met de nieuwe verdeling nieuwe successen kunnen boeken. Jij lijkt er helemaal klaar voor. **Lydia**, zo lang werken we ook nog niet samen, en toch voelt het wel zo. Ik denk dat we een mooie driehoek kunnen vormen met Nadine wat betreft de traumatak. Ik wens je veel geluk met jouw nieuwe stek en de nieuwe telg.

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Lieve oud collega's van **Hotel de Goudfazant**. Hoe fijn voelde het niet om een nutteloze van de nacht te zijn. Met zielenpijn keerde ik terug van Amsterdam naar Rotterdam. Ik ga er geen proza van maken, echter, er gaan nooit veel dagen voorbij totdat ik moet denken aan een bepaalde situatieschets met jullie. Jullie weten wie jullie zijn. Ik voel mij oprecht bevoorrecht met jullie ziel en zaligheid te hebben mogen delen.

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de tijd van een jong gezin, krankzinnig of een mogelijkheid in tijden van huiselijkheid? In die zin waren die gesprekken het vlindereffect voor deze thesis.

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A

CHAPTER 16

Statements

Statements

Analyses on automated registration datasets are likely to be valid, however volume outcome measures might be biased. (this thesis)

A standardised radiologic template improves classification of traumatic brain injury. (this thesis)

Level I trauma centres produce improved survival in major trauma populations. (this thesis)

Improved quality of life may facilitate return to work after major trauma. (this thesis)

When analyzing health status of major trauma patients across different levels of trauma care, an ISS > 15 at cut-off point is questionable. (this thesis)

The distinction must be drawn between databases and registries; a database is merely an electronic set of data that is neither systematised nor organised for the explicit use for answering health-related questions. (Rubinger et al., Injury 2021)

As volume alone is an imperfect correlate of quality, policy-makers need to know what volume is a proxy for in order to devise volume-based policies. (Huguet et al., BMC Health Services Research 2022)

Post-intensive care syndrome is not a medical diagnosis, but a concept for improving education and awareness of post-ICU impairments. (Hiser, Journal of Intensive Care 2023)

The Transmural Trauma Care Model may be cost-effective compared with regular care, depending on the decision-makers willingness to pay and the probability of cost-effectiveness that they perceive as acceptable. (Wiertsema, Int J Technol Assess Health Care 2019)

The challenge to the core belief system or assumptive world can be a new way to define trauma, rather than making reference to certain types of events. (Tedeschi, World Psychiatry 2023)

The very foundations of truth are inherently subjective. (Bernardo Kastrup)

CHAPTER 17

Publications

In this thesis

van Ditshuizen JC, Niemeyer MJS, Van Lieshout EMM, Den Hartog D, Visser JJ, van Wessem KJP, et al. Coding traumatic brain injury with the abbreviated injury scale following a standardised radiologic template will improve classification of trauma populations. Eur Radiol 2025. https://doi.org/10.1007/s00330-025-11384-9

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Not in this thesis

Sewalt CA, Venema E, van Zwet E, van Ditshuizen JC, Schuit SCE, Polinder S, et al. The Relationship between Hospital Volume and In-Hospital Mortality of Severely Injured Patients in Dutch Level-1 Trauma Centers. J Clin Med. 2021;10(8). https://doi.org/10.3390/jcm10081700

Driessen MLS, van Ditshuizen JC, Waalwijk JF, van den Bunt G, FFA IJ, Reininga IHF, et al. Impact of the SARS-CoV-2 pandemic on trauma care: a nationwide observational study. Eur J Trauma Emerg Surg. 2022;48(4):2999-3009. https://doi.org/10.1007/s00068-022-01891-5

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Vianen NJ, Campfens JR, Brouwer-Bergsma M, van Ditshuizen JC, Giannakopoulos GF, Hoogerwerf N, et al. Establishing Outcome Parameters for Helicopter Emergency Medical Services Research in the Netherlands: Results of a Mixed-Methods Delphi Consensus Study. Prehosp Emerg Care. 2024:1-18. https://doi.org/10.1080/10903127.2024.2413038

Collaboratives

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CHAPTER 18

Portfolio

PhD Portfolio

Summary of PhD training and teaching

Name PhD candidate: J.C. van Ditshuizen Erasmus MC Department: Department of Surgery	PhD trajectory period: 2019-2024 Promotor(s): Prof. dr. M.H.J. Verhofstad Copromotor(s): Dr. D. den Hartog Dr. E.M.M. van Lieshout

1. PhD training

	Year	Workload (Hours/ECTS)
General courses		
Scientific Writing	2016-2018	2.0
Research Integrity	2016-2018	0.3
English Language	2016-2018	1.4
Regelgeving en Organisatie Klinisch Onderzoek (BROK)	2023	1.5
NIHES research master epidemiology public health – Common core		
Study Design	2016-2018	4.3
Biostatistical Methods 1: Basic Principles	2016-2018	5.7
Biostatistical Methods 2: Classical Regression Models	2016-2018	4.3
Master Research	2016-2018	32.6
Required		
Principles of Research in Medicine and Epidemiology	2016-2018	0.7
Methods of Public Health Research	2016-2018	0.7
Introduction to Public Health	2016-2018	0.7
Methods of Health Services Research	2016-2018	0.7
Primary and Secondary Prevention Research	2016-2018	0.7
Social Epidemiology	2016-2018	0.7
Public Health Research Methods	2016-2018	5.7
Site Visit to the Municipal Health Service Rotterdam	2016-2018	0.3
Integration Module	2016-2018	0.3
International Comparison of Health care Systems	2016-2018	1.4

Specific courses		
NIHES research master epidemiology public health - electives		
Repeated Measurements in Clinical Studies	2016-2018	1.4
Missing Values in Clinical Research	2016-2018	0.7
Markers and Prognostic Research	2016-2018	0.7
Logistic Regression	2016-2018	1.4
Fundamentals of Medical Decision Making	2016-2018	0.7
Advanced Analysis of Prognosis Studies	2016-2018	0.9
Oral and Poster Presentations		
International Orthopaedic Trauma Association	2022	1.0
Chirurgendagen	2023	1.0
Trauma Symposium Landelijk Netwerk Acute Zorg	2025	1.0
European Congress of Trauma and Emergency Surgery	2025	2.0
(Inter)national conferences		
Dutch P-HEMS congress: 'Alle HEMS aan dek'	2023	0.6
Traumadagen	2024	0.3
2. Teaching		
	Year	**Workload (Hours/ECTS)**
Supervising Master's theses		
Claire van der Driessche	2019	2.0
Leonne Rojer	2022	2.0
3. Summary of broader personal, professional, and scientific development		
Introduction Data Science and Machine Learning		
Member National Board Dutch Nationwide Trauma Registry		
Member Regional Board Trauma Network		
Member National Board Dutch P-HEMS Network		

A

CHAPTER 19

About the author

About the author

Jan van Ditshuizen was born 1980 in Nieuwegein. After finishing pre-university education (VWO) at Emmauscollege Rotterdam, he studied Civil Engineering for a short period at TU Delft, followed by Physiotherapy at Hogeschool Rotterdam, from which he graduated in 2004. He continued his studies at the Free University Amsterdam with Human Movement Sciences. His master research was done at The Perception & Motor Systems Laboratory in Brisbane, Australia. During his studies he lived in Amsterdam and worked in restaurants. After moving back to Rotterdam, he was able to get a job as a physiotherapist in combination with location manager of a practice. In 2013 he started working as a datamanager trauma registry for Traumacentrum Zuidwest Nederland. He finished a master epidemiology public health at NIHES Erasmus MC Graduate School in 2018. When covid became pandemic, he helped with data and coordination of spreading covid patients over the acute health care region Southwest. After the pandemic Jan started working for Helicopter Emergency Medical Services Netherlands part-time in combination with his regular work. Besides work, Jan is a music lover and does a lot of sports. Jan lives with his wife Anja and their kids Hugo and Tilda in Rotterdam.