PART 4: LITERATURE REVIEW

Authors: Maaike Langelaan (NIVEL), Nanne Bos (NIVEL), Julie Heeren (NIVEL), Janke de Groot (NIVEL)

4 LITERATURE REVIEW ON MTC

4.1 Aim

The most recent systematic reviews on the association of the availability of a system of trauma care with short-term patient outcomes included articles up to 2011.[106, 221] New evidence is available on the topic as the developing of the organisation of trauma care continues.

The aim of this study was to review the recent (from 2012 onwards) level of scientific evidence regarding whether improvement of mortality and length of hospital stay following a major trauma are associated with the existence of major trauma centres and to the characteristics of major trauma centres.

4.2 Research question

The main research question was: what is the level of evidence available on the effect of a major trauma centre (MTC) on mortality (up to 30 days after discharge), length of hospital stay and length of stay at an intensive care unit (ICU)? The sub-questions formulated to answer the main question are:

- Are trauma centres associated with better severely injured patient outcomes compared to non-trauma centres? What is the association between level of trauma centre and patient outcomes?
- What is the association of the severity of the injuries of the patient and the outcomes if treated in a trauma centre?
- Are high patient volume centres associated with better short-term patient outcomes? Is there a volume threshold below which patient outcomes are worse?

4.2.1 Hypothesis

The published literature will demonstrate that mortality (up to 30 days after discharge), length of hospital stay, and length of ICU stay are better for patients treated at a major trauma centre (MTC).

4.3 Methods

4.3.1 Design of the study

We conducted a systematic review, following, as far as possible the PRISMA-statement (Preferred reporting items for systematic review and meta-analysis)[222] and MOOSE (Meta-analysis Of Observational Studies in Epidemiology) guidelines.[223]

4.3.2 Search

4.3.2.1 Search strategy

We searched for primary studies dating from 2012 and younger. Besides, we searched for systematic reviews without date limit to compare our results with evidence from older systematic reviews.

The search strategy is reported in Appendix 1 in the report supplement. The search strategy was developed in consultation with an expert librarian/information specialist at the VU University Medical Centre in Amsterdam, the Netherlands, and in collaboration with KCE. The search strategy included terms identifying patients (major trauma patients / severely injured patients) and the intervention (trauma centres / trauma system).

Appropriate truncation and wildcards were used in the search to account for plurals and/or variations in the spelling of search terms. Language restrictions were not applied. The date of the last search was June 7th, 2016.

Identifying Primary Studies

The search took place in two main steps. To find the most recent primary studies, in the first step we searched for all relevant primary studies according to the search strategy, but with a date limit from 2012 onwards. The search results were deduplicated before screening. All positively screened primary studies were full text searched for inclusion and exclusion criteria.

Identifying Systematic Reviews

We searched for all relevant systematic reviews according to the search strategy with a “systematic review filter”. We used a search filter developed by the librarian experts of VU University Medical Centre to find the reviews. The search filters are shown in the Appendix 1 of the search strategies.

The search results of this second step were deduplicated before screening. All positively screened systematic reviews were full text searched for inclusion and exclusion criteria. The selected systematic reviews were used to compare our findings (with the most recent evidence) with the evidence and conclusions in selected systematic reviews.

4.3.2.2 Search sources

Electronic searches

We searched the following databases:

- Cochrane Database of Systematic Reviews
- Cochrane Central Register of Controlled Trials (CENTRAL)
- Pubmed
- Embase
- CINAHL

The search strategy was modified to the structure of each database, based on the initial PubMed search. In addition we asked the clinical experts of the KCE expert committee from the Belgian field of trauma care about any studies they know of.

4.3.3 Inclusion process

The stepped search process resulted in two sets of studies:

1. Primary studies
2. Systematic reviews

4.3.3.1 Inclusion criteria for primary studies and systematic reviews

Included studies needed to be comparative studies (for example a trial or a study with a before/after study design). The publication addressed the organisation of trauma care within the geographical context of at least one Western European or Anglo-Saxon country. Since the definition of Western Europe is complex and carries economic and cultural connotations, we adopted the definition of the Statistics Norway. They define the "West" as EU28/EEA, USA, Canada, Australia and New Zealand (see the report supplement).[224]

4.3.3.2 Types of participants for primary studies and systematic reviews

The studies to be included had to contain data on patients with major trauma, i.e. severely/critically injured. Several instruments were used for defining severely/critically injured trauma patients. The instruments and thresholds we used are: ISS≥15, International Classification of Diseases (ICD-9) Injury Severity Score (ICISS)<0.85 or AIS≥3.

4.3.3.3 Types of interventions for primary studies and systematic reviews

The studies to be included had to focus on the organization of trauma care, i.e. trauma centres, trauma system, trauma model, trauma network or trauma organizations. Almost all trauma systems follow at least to a certain extent the level criteria for trauma centres outlined by the American College of Surgeons Committee on Trauma (ACS-COT).[225] The different levels, from I to V, refer to the kind of resources available in a trauma centre and the patient volume. If a study did not contain the level of the included trauma centres, we classified the centres according to the ACS-COT criteria, if possible.

4.3.3.4 Types of outcomes for primary studies and systematic reviews

The following primary outcomes were selected to identify the effect of the organization of trauma care: in-hospital mortality OR mortality up to 30 days after discharge OR length of hospital stay OR length of stay at ICU. Secondary short-term outcomes of patients (up to 30 days after discharge) were collected.

4.3.3.5 Types of study design

We included primary studies that were of a comparative design in which there was a comparison between before and after the introduction of a trauma care system or a significant part of it (without changing the level of trauma care), or there was a comparison between different levels of trauma care.

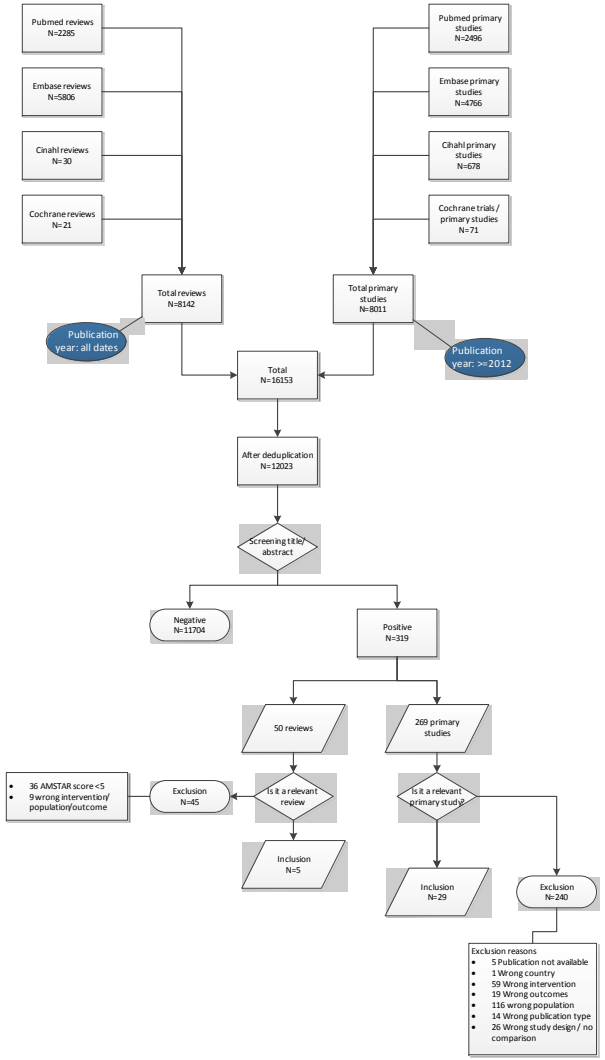
To be included, systematic reviews had to concern specifically the effect of trauma systems for major trauma patients (see paragraph 4.3.3.1). We used the AMSTAR checklist to assess the quality of the systematic reviews. [226] The checklist contains the following points: establishing the research question and inclusion criteria before the conduct of the review, data extraction and inclusion by at least two independent data extractors, comprehensive literature review with searching of at least two databases, key word identification, expert consultation and limits applied, detailed list of included/excluded studies and study characteristics, quality assessment of included studies and consideration of quality assessments in analysis and conclusions, appropriate assessment of homogeneity, assessment of publication bias and a statement of any conflict of interest.

The range of the AMSTAR score is between 0 and 11. The total score was used to classify the overall quality of each review as high (total score 9 to 11), moderate (score 5 to 8), or low (score 0 to 4).[227] Systematic reviews were included for the comparison if AMSTAR score was 5 or higher.

4.3.3.6 *Exclusion criteria for primary studies and systematic reviews*

Studies regarding only trauma patients with burns, disaster trauma patients or terrorism/war trauma patients were excluded.

Figure 20 – Flowchart of stepwise search strategy



4.3.4 Data collection

4.3.4.1 Selection of studies

Bibliographic records were exported to a "Covidence" database for screening and data collection (http://www.covidence.org). Three review authors (ML, JH and NB) screened titles and abstracts for eligibility for all eligibility criteria, so that each title/abstract was screened once. About 10% of all titles were screened twice to obtain an interobserver agreement (kappa, K). The K value is an indication of the strength of the agreement and can be interpreted as follows:[228]

< 0.20 Poor
0.21 - 0.40 Fair
0.41 - 0.60 Moderate
0.61 - 0.80 Good
0.81 - 1.00 Very good

We resolved disagreements through discussion with the third review author.

All full text articles were reviewed independently by different combinations of two authors.

Data extraction and management

One review author (ML, JH or NB) reviewed selected studies and extracted data on the following, using a specifically developed and piloted data extraction file:

1. General information about the study
   a) Aim of the study
   b) Study design
   c) Duration of the study
   d) Inclusion and exclusion criteria
   e) Details of the control and intervention group
   f) Duration of follow-up (if applicable)
   g) Quality of the study
2. Characteristics of trauma patients
   h) Number, age, gender and co-morbidities of participants
   i) Severity of trauma
3. Intervention characteristics
   j) Organisational characteristics of trauma centre, accreditation and designation of the trauma centres, the level of trauma centre (level 1 to 5, or non-trauma centre (NTC) and participation in a trauma network
   k) Country
   l) Patient volume of the trauma centre (per centre)
4. Outcome measures
   m) In-hospital crude mortality, 30-day crude mortality, crude mortality in emergency room
      i) Definition
      ii) Unit of measurement
      iii) How it was measured
      iv) Data
   n) Adjusted mortality, if crude mortality rates were not available
      i) Definition
      ii) Unit of measurement

iii) How it was measured

iv) Data

o) Length of hospital stay and length of ICU stay

i) Definition

ii) Unit of measurement

iii) How it was measured

iv) Data

p) Secondary outcomes

i) Definition

ii) Unit of measurement

iii) How it was measured

iv) Data

5. Authors' conclusions

We used as much as possible the unadjusted crude data to estimate a population average effect. We expected that all included studies used different variables to adjust for confounding, so comparison of the effect estimated would be difficult.

In case, a publication presented only adjusted results, we contacted the study authors to obtain unadjusted data and when not possible we used adjusted data but separately from the unadjusted data.

One other review author (ML, JH, NB, Maria Isabel Farfan (MIF) or Sabine Stordeur (SS)) checked the extracted data. In case of any disagreements, it was resolved through discussion within the team of researchers. Where information was unclear or data were missing, we contacted corresponding authors of the publication. Seven of the fifteen authors provided requested additional information.

For the systematic reviews, two reviewers independently evaluated the quality of included reviews based on the AMSTAR scale, rating each of the 11 items on a binary scale (i.e., 'yes' (score 1), 'no' (score 0), 'not applicable' (score 0) or 'can't answer' (score 0)). Disagreements in the ratings between the two reviewers were discussed and, if a consensus decision was not reached, a third reviewer was called into make a final determination. The range of the overall quality score for each review was between 0 and 11. The total score was used to classify the overall quality of each review as high (total score 9 to 11), moderate (score 5 to 8), or low (score 0 to 4).[227] Systematic reviews were included for the comparison if AMSTAR score was 5 or higher.

4.3.4.2 Assessment of risk of bias in included studies

Cohort studies and uncontrolled before-after studies were included in this review. No randomised controlled trials were included, only a secondary data analysis of two randomised controlled trials. Cohort studies are observational studies in which the starting point is the selection of a study population or cohort. Information is obtained to determine which members of this cohort are exposed to the factor of interest.[229] Most studies in this review are based on registries of routine-data. Data on the patients' characteristics (demographics, admission characteristics and injury characteristics and the outcome(s) of interest are obtained from routine data-collection systems (e.g., hospital registries and national trauma registries).

Uncontrolled before and after studies measure performance before and after the introduction of an intervention in the same study site(s) and observed differences in performance.[230]

Two review authors independently assessed the risks of bias of included studies. Table 49 shows the domains we used for cohort studies and before-after studies according to the Cochrane guidelines and KCE-templates to assess the risk of bias for observational studies.

Table 49 – Domains for assessing risks of bias

Secondary data analysis of two randomised controlled trials [231]	Cohort study, uncontrolled before-after study [232]
Sequence generation	Selection bias
Allocation concealment	Detection bias
Blinding of outcome assessment	Attrition bias
Incomplete outcome data	
Selective outcome reporting	
Other bias	

4.3.5 Analysis

The primary analyses were partly narrative. When possible, studies and outcomes were pooled and further analyses were performed. Studies were included in a meta-analysis if they were: 1) of the same type, and have 2) the same population, 3) the same trauma care system, 4) the same comparison, 5) the same outcomes, and 6) the same statistical methods.

The included studies were explored on methodological and statistical heterogeneity. The latter were quantified by the I^2 statistic. An I^2 value >50% is considered to indicate substantial heterogeneity.[231, 233] It was expected that the data would carry a certain amount of heterogeneity and a random-effects model will be used. If the data turned out to be too heterogeneous for pooling based on methodological heterogeneity and statistical heterogeneity, we would perform a more descriptive review and summarise the available evidence for this intervention.

Evaluation of included studies for meta-analysis were conducted by two review authors (Maaike Langelaan (ML) and Nanne Bos (NB)) and in case of disagreement, the authors consulted a third reviewer (Julie Heeren (JH)). If possible, we conducted sub-analyses for paediatric and elderly trauma patients and for severity of injuries.

To synthesize the evidence, “best-evidence synthesis” was performed. As proposed by the Cochrane Back Review Group, the levels of evidence were ‘strong,’ ‘moderate,’ ‘limited,’ ‘conflicting’, or ‘unknown’.[234] Only RCTs could have the status of an excellent study (low risk of bias). Cohort studies and other observational studies could have the status of fair quality (low to moderate risk of bias) if:

- Use of reliable data in a retrospective study
- Follow up rate of 80%+ and <10% difference in follow-up between groups
- Controlling for possible confounding

The cohort studies and observational studies that did not meet these criteria were qualified as poor quality (high risk of bias).

Table 50 – Levels of Evidence for the Quality of the Measurement Property

Levels	Description
Strong	Consistent findings in multiple studies of good methodological quality OR in one study of excellent methodological quality
Moderate	Consistent findings in multiple studies of fair methodological quality OR in one study of good methodological quality
Limited	One study of fair methodological quality
Conflicting	Conflicting findings
Unknown	Only studies of poor methodological quality

Source: van Tulder et al. (2003) [234]

If appropriate, statistical analyses were carried out using Stata 14.2.[235] For dichotomous outcomes including patient mortality, presence of a complication, and readmission, risk ratios with 95% confidence interval (CI) were used to assess differences in short-term patient outcomes in trauma centres and usual trauma care. For continuous outcomes, including length of hospital stay and length of stay at the ICU, standardized mean differences with 95% CI were calculated with the random effects model.

All outcomes are presented in a “Summary of main findings” table.

4.4 Results

In the search 12,023 references were identified and screened for relevance on title and abstract. 1076 titles were screened twice on title/abstract by the three reviewers. The inter-reviewer agreement was indicated as very good (Kappa 0.82, 95%CI 0.72 - 0.92).

All positive screened primary studies (N=269) and reviews (N=50) were full text searched for inclusion and exclusion criteria). Seven full-texts of primary studies could not be obtained. Finally, this resulted in 29 primary studies and 5 systematic reviews that fulfilled the inclusion criteria. Experts did not suggest any new studies.

4.4.1 Final sample of primary studies

A total of 29 primary studies were selected for data extraction (see section on the included studies in the report supplement).[139, 142, 178, 211, 236-260] Seventeen of the 26 cohort studies were based on registries of routine-collected data. Most studies (N=25) were single country studies and based on data from the USA. Four studies reported on differences between two countries (Table 51). Nine studies [236, 242, 244, 250, 252, 255, 258-260] compared care specific for paediatric patients and six for adults only.[178, 247-249, 254, 259] There were differences in the definitions of severely injured patients between the different studies, but most studies used the ISS as instrument to define the severity. The most frequently used threshold was an ISS score of 16 or higher. Excluded references and reason for the exclusion can be found in the report supplement.

Table 51 – Summary of study characteristics of included primary studies

Characteristic	Number of studies (N)
Type of study	
Cohort study	26
Uncontrolled before-after study	2
Secondary data analysis based on data of two RCTs	1
Country of origin	
Single country	
USA	17
France	1
Germany	1
The United Kingdom	2
Australia	1
Italy	1
The Netherlands	1
Canada	1
Two countries	
Germany and Finland	2
USA and The United Kingdom	1
USA and Canada	1
Specific study population	
Only paediatric patients	9
Only patients with a specific diagnosis	4
Only adults	6
Only geriatric patients	1
No specific study population	9

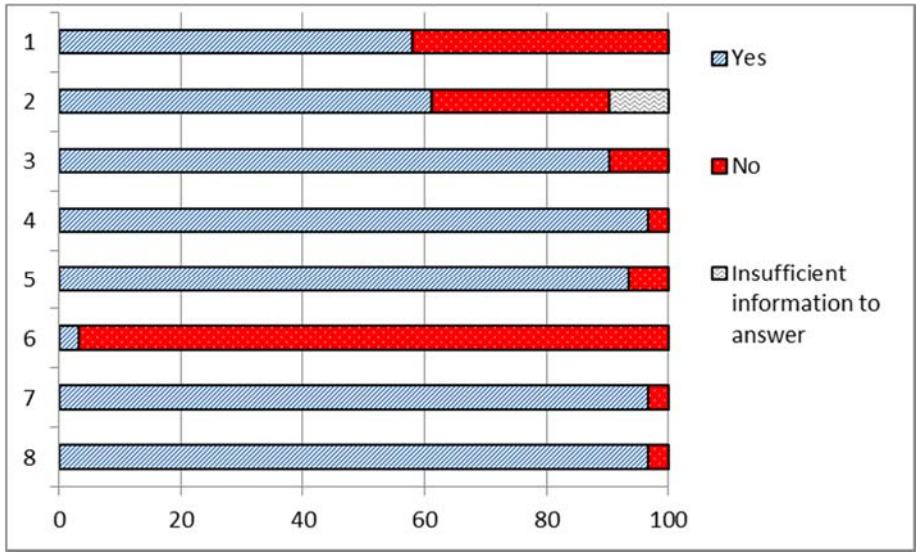
Characteristic	Number of studies (N)
Injury severity	
ISS≥15	2
ISS≥16	14
ISS>16	1
ISS≥25	2
Modified ISS≥25	1
ISS unclear	2
AIS≥3	4
ICISS<0.85	2
Unclear	1
Sample size of included studies (median, IQ-range)	
Median	4540
IQ-range	1054 – 21 360
Min-Max	65 – 414 074
Duration of data collection (years: median, IQ range)	4.1 (2.0 – 5.5)

4.4.2 *Risk of bias in included primary studies*

The most prevalent shortcomings were found in the items relating to selection bias and blinding to the exposure status (Figure 21). The methodological qualities of the individual studies are shown in the report supplement.

In none of the studies, the design could be rated as “high quality of evidence” as we found no randomised controlled trials.

Figure 21 – Proportion of primary studies presenting a risk of bias per item



1. Can selection bias sufficiently be excluded?
2. Are the most important confounding factors identified, are they adequately measured and are they adequately taken into account in the study design and/or analysis?
3. Is the exposure clearly defined and is the method for assessment of exposure adequate and similar in study groups?
4. Are the outcomes clearly defined and is the method for assessment of the outcomes adequate and similar in study groups?
5. Is the likelihood that some eligible subjects might have the outcome at the time of enrolment assessed and taken into account in the analysis?
6. Is the assessment of outcome made blind to exposure status?
7. Is the follow-up sufficiently long to measure all relevant outcomes?
8. Can selective loss-to-follow-up be sufficiently excluded?

4.4.3 Are trauma centres associated with better severely injured patient outcomes compared to non-trauma centres? What is the association between level of trauma centre and patient outcomes?

Twenty-two included studies had extractable data for severely injured patients on unadjusted in-hospital mortality and/or up-to-30 day mortality and/or emergency department mortality.

Five studies contained data on hospital length of stay and 4 on ICU length of stay.

We separated the analyses for three different intervention comparisons:

- High level (level 1 and/or level 2) trauma centres (TC) versus Non-trauma centres (NTC) (4.4.3.1)
- Higher level versus lower level trauma centres (4.4.3.2)
- Special features of a trauma system (3.8.3.3)

4.4.3.1 High level (level 1 and/or level 2) trauma centres (TC) versus Non-trauma centres (NTC)

Mortality

Five studies compared care for severely injured patients between a high level of trauma care (level 1 and 2) and non-trauma centres (Table 52 and Figure 22).[236, 244, 248, 253, 254] The study of Afifi 2015 reported on two comparisons between TCs and NTCs, for a mandated as well as a non-mandated trauma system. Afifi 2015 found a benefit for paediatric patients admitted to a NTCs and compared to TC in a mandated system; (presumably in-hospital) mortality rates were 19% (NTC) versus 30% (TC).[236] They also found a similar result for paediatric patients admitted to NTCs compared to TCs in a non-designated trauma system; mortality rates were 22.5% versus 33.3%.

In the study of Narayan 2015, severely injured trauma patients were more likely to survive in NTCs compared to higher level TCs.[254] This unexpected finding could be explained by a high proportion of transfers of extreme severely injured patients from NTCs and level 2 and 3 centres to level 1 centres. The crude mortality rate was 7.2% in the intervention group (TC) versus 6.1% in the comparison group (NTC). Morrissey 2015 found a survival benefit for severely injured patients admitted to a high level TC. In two studies no difference for in-hospital mortality was found.[244, 248]. Deasy 2012 and Kuimi 2015 found no significant differences for in-hospital mortality rates between level 1 or 2 TC and NTC.[244, 248] Because of clinical heterogeneity, no meta-analysis was performed.

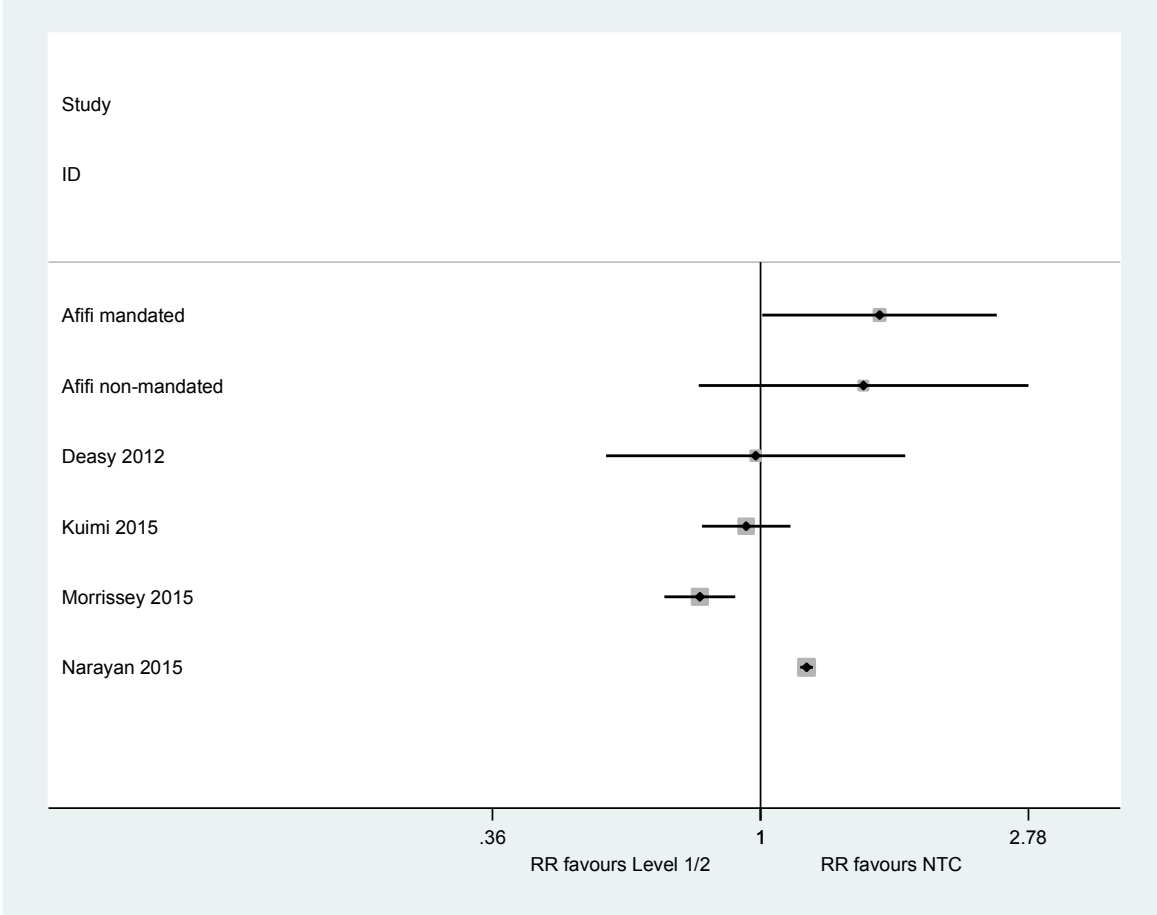
We noticed one article relevant for this comparison, but provided no data to extract [255].

The risk of bias in the five studies was moderate to high. The evidence for a difference between TCs compared to NTCs in unadjusted hospital mortality is conflicting.

Table 52 – Comparison "designated level 1 and/or level 2 TC" vs "NTC", outcome: unadjusted in-hospital mortality for all severely injured patients

Study	Study design	Study population	Country	Level of intervention group	Comparison group	Intervention (n/N)	NTC (n/N)	RR (95% CI)
Afifi 2015	Cohort study	Paediatric	USA, Florida	Level 1+2 in mandated system	NTC in mandated system	103/349	18/96	1.57 (1.01-2.46)
			USA, Indiana	Level 1+2 in non-mandated system	NTC in non-mandated system	40/120	9/40	1.48 (0.79 -2.78)
Deasy 2012	Cohort study	Paediatric	Australia	Level 1 paediatric and adult	NTC	72/1077	13/191	0.98 (0.56 – 1.74)
Kuimi 2015	Cohort study	Only adults, no children	Canada	Level 1+2	NTC	1 454/20 885	137/1 864	0.95 (0.80 – 1.12)
Morrissey 2015	Cohort study	No special group	USA and UK	Level 1	NTC	733/3 588	202/785	0.79 (0.69 – 0.91)
Narayan 2015	Cohort study	Only adults, no children	USA	Level 1+2	NTC	8 301/114 481	21 497/353 443	1.19 (1.16 – 1.22)

Figure 22 – Comparison "designated level 1 and/or level 2 TC" vs "NTC", outcome: unadjusted in-hospital mortality for all severely injured patients



RR=relative risk

One study reported on the comparison between level 1 and NTC for 30 day (presumably after event) mortality (Table 53). The study of Di Bartolomeo 2014 found a significant difference for 30 day mortality rates in patients in favor of patients admitted to a NTC compared with patients admitted to a level 1 TC.[245]

However, in a subgroup patients with particularly severe injuries mortality was significantly lower when they were treated in TCs as compared to NTCs.

Based on one study, there is limited evidence for a negative effect of higher level TCs compared to NTCs on the 30-day in-hospital mortality rate for all severely injured patients combined.

Table 53 – Comparison "designated level 1 and/or level 2 TC" vs "NTC": unadjusted 30-day in-hospital mortality for all severe injured patients

Study	Study design	Study population	Country	Level of intervention group	Level of comparison group	Outcome	Intervention (n/N)	NTC (n/N)	RR (95% CI)
Di Bartelomeo 2014	Cohort study	No special group	Italy	Level 1	NTC	30 day in-hospital mortality	345/2419	183/1640	1.28 (1.08 – 1.51)

Vickers 2015 reported on ER mortality. Mortality in the emergency room was significantly lower for adult patients in level 1 or 2 trauma centres, compared to non-trauma centres (see following table).[259]

Based on one low quality study, there is limited evidence for the effect of higher level TCs compared to NTCs on the emergency room mortality rates.

Table 54 – Comparison "designated level 1 or 2 TC" vs "NTC", outcome: unadjusted mortality at emergency department for all severely injured adult patients

Study	Study design	Study population	Country	Level of intervention group	Level of comparison group	Intervention (n/N)	NTC (n/N)	RR (95% CI)
Vickers 2015	Cohort study	Only adults	USA	Level 1+2	NTC	951/61358	1018/31335	0.48 (0.44 – 0.52)

Ashley 2015 compared 126 NTCs versus a combination of 6 level 1, 10 level 2, 2 level 3 and 1 level 4 trauma centres that were designated (DTC); the unadjusted in-hospital mortality rate at DTCs (15.1%) was higher compared with the rate at NTCs (12.1%). However, after adjusting for injury type and severity, patient demographics, the presence of comorbidities, insurance status and type, and selection bias, a 10% survival advantage on average for severely injured patients treated at a designated trauma centre (DTC) was observed.[237]

Hospital length of stay

Only one study reported the mean hospital length of stay in comparing higher level TCs to NTCs. Afifi 2015 concluded that there is no significant difference in hospital length of stay for severely injured paediatric patients.[236]

Based on one study, there is no evidence of effect with regard to hospital length of stay when level 1 or 2 TCs are compared to NTCs

Table 55 – Comparison Level 1+2 vs NTC, outcome: mean hospital length of stay

Study	Study design	Special group	Country	Level of intervention group	Level of comparison group	Intervention (mean/sd)	Comparison (mean/sd)	SMD (95% CI)
Afifi 2015	Cohort study	Paediatric	USA	Level 1+2	NTC	11.06 (12.7)	9.8 (14.6)	0.10 (-0.13 – 0.32)

Intensive care unit (ICU) length of stay

No studies were found in which ICU length of stay was compared between level 1 or 2 TCs versus NTCs.

4.4.3.2 *Higher level versus lower level trauma centres*

Mortality

For this comparison we found only studies with some type of mortality as outcome and none with regard to hospital or ICU length of stay.

Five studies compared the effect of a higher level TC with a lower level TC on in-hospital mortality, up-to-30 day mortality and ER-mortality.[238, 247, 250-252]

Two studies reported in-hospital mortality (Table 56 and Figure 23). Gomez 2015 states there was no significant difference in crude in-hospital mortality rate in patients admitted to a level 3 TC compared to patients that were transferred to a level 1 or 2 TC; however, Gomez adds that after adjusting for case-mix, patients who were admitted at level 3 centres had a 24% higher likelihood of death (OR1.24, 95% CI 1.08–1.43) when compared to those transferred to level 1–2 centres.[247] In our RR calculation the crude mortality rate appeared to be significant in favour of level 3 TC. Miyata 2015 found that, based on the crude in-hospital mortality rate, severely injured paediatric patients benefited from a level 1 TC compared to a level 2 TC.[252] Mortality rates were 12% versus 15% (Table 56 and Figure 23). However, when adjusted for injury severity, analyses showed no difference in mortality between centre types.

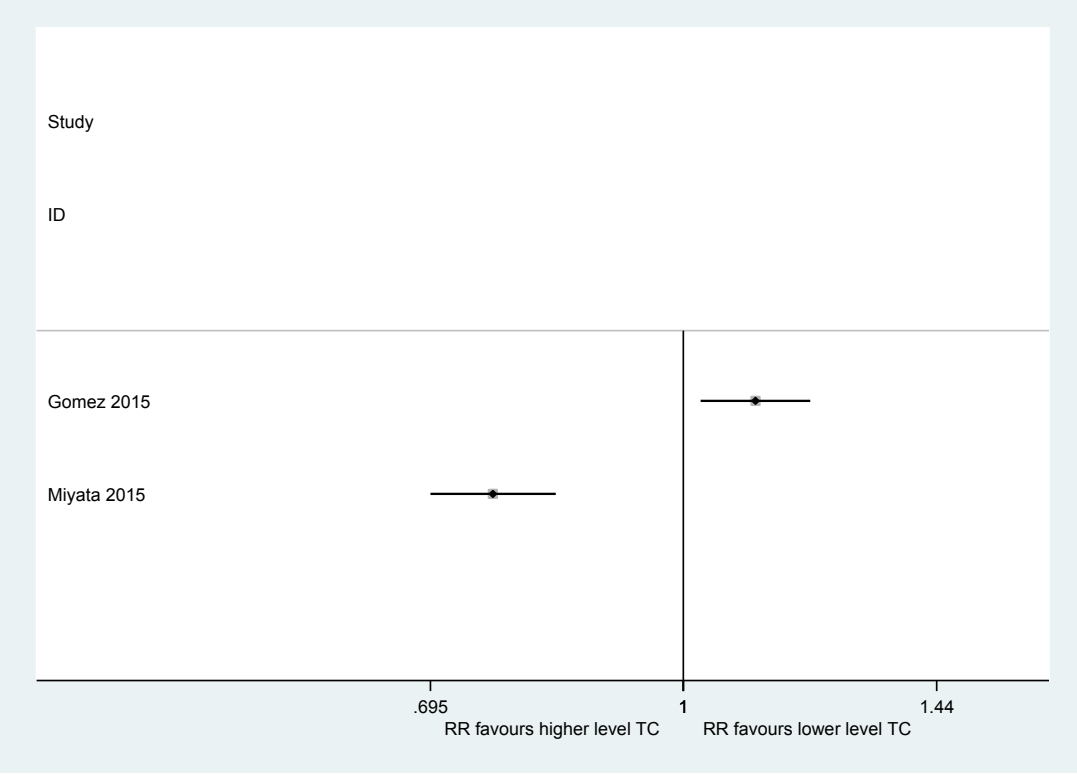
We noticed one article relevant for this comparison, but provided no data to extract [241].

The low quality studies reported conflicting evidence for a difference between higher level TCs compared to lower level TCs in unadjusted hospital mortality rates.

Table 56 – Comparison "higher level TC" vs "lower level TCs", outcome: unadjusted in-hospital mortality for all severely injured patients

Study	Study design	Study population	Country	Level of intervention group	Level of comparison group	Outcome	Intervention (n/N)	NTC (n/N)	RR (95% CI)
Gomez 2015	Cohort study	Only adults	USA	Level 1+2	Level 3	In-hospital mortality	4568/41165	632/6318	1.11 (1.03 – 1.20)
Miyata 2015	Cohort study	Paediatric	USA	Level 1 paediatric	Level 2 paediatric	In-hospital mortality	1132/9690	632/4113	0.76 (0.69 – 0.83)

Figure 23 – Comparison “higher level TC” vs “lower level TCs”, outcome: unadjusted mortality for all severely injured patients



RR=relative risk

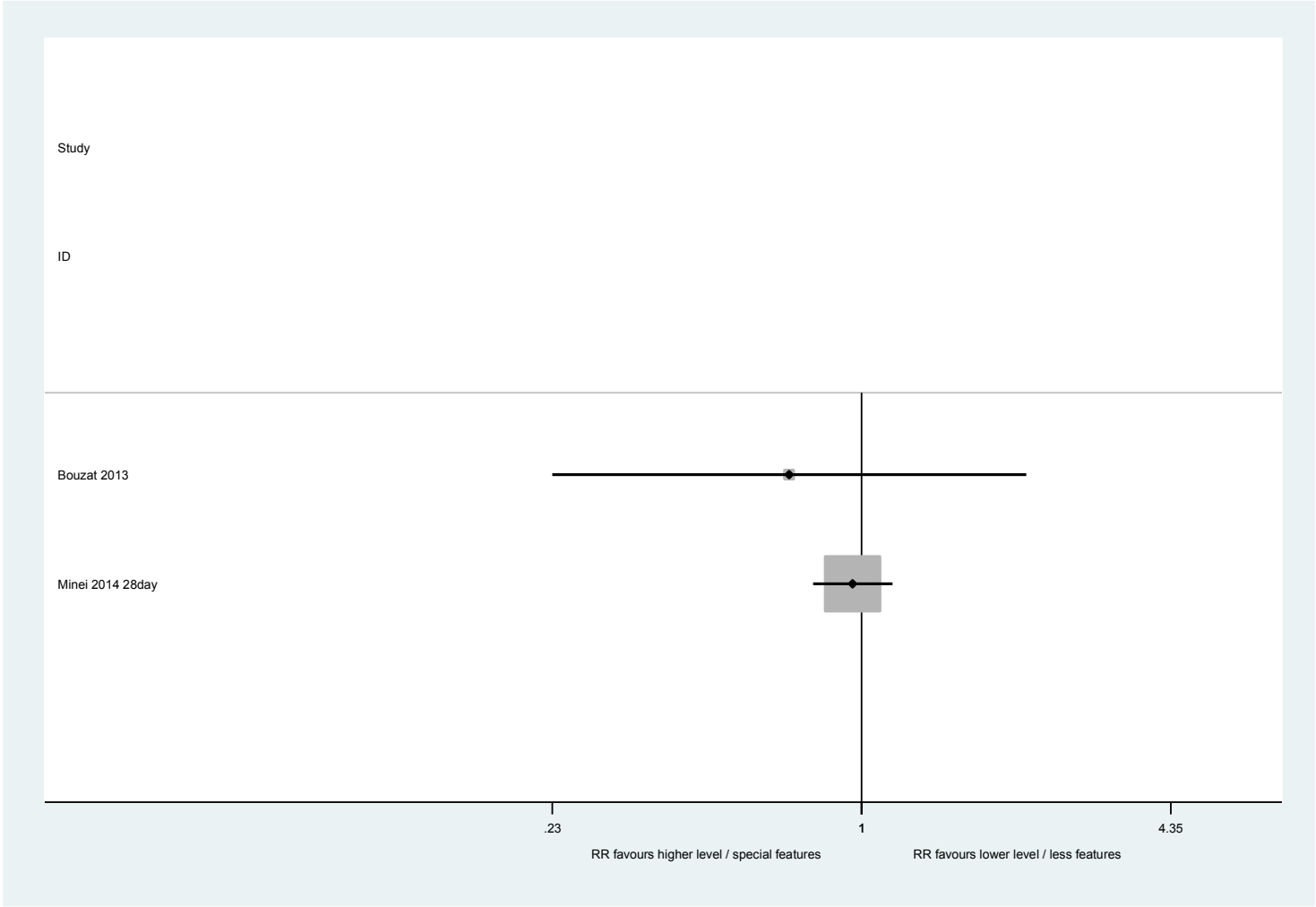
Three studies compared the higher level TCs with lower level TCs or NTCs for up-to-30 day in-hospital mortality (Table 57, Table 58, Figure 24 and Figure 25).[238, 251] The small study of Bouzat 2013 found a non-significant RR in the comparison between level I TC and level 2 TC.[238] Minei 2014 found no significant difference in both 24h mortality and 28 day mortality if level 1 TCs was compared to level 2 TCs.[251] Mills 2015 found no significant association between level of TC (level 1 versus level 2) and adjusted in-hospital 30-day mortality (no exact data was provided).[250]

Based on 3 studies, there is no evidence of effect that admission to a higher level TC is beneficial for severely injured patients on up-to-30 day in-hospital mortality.

Table 57 – Comparison "higher level TC" vs "lower level TCs": unadjusted 30-day in-hospital mortality for all severe injured patients

Study	Study design	Study population	Country	Level of intervention group	Level of comparison group	Outcome	Intervention (n/N)	NTC (n/N)	RR (95% CI)
Bouzat 2013	Cohort study	No special group	France	Level 1	Level 2	mortality at day 28 post trauma	4/29	7/36	0.71 (0.23 – 2.19)
Minei 2014	Secondary data analysis	Only patients with severe TBI or patients in shock	USA and Canada	Level 1	Level 2	28 day mortality	397/1649	102/406	0.96 (0.79 – 1.16)

Figure 24 – Comparison "higher level TC" vs "lower level TCs": unadjusted 30-day in-hospital mortality for all severe injured patients

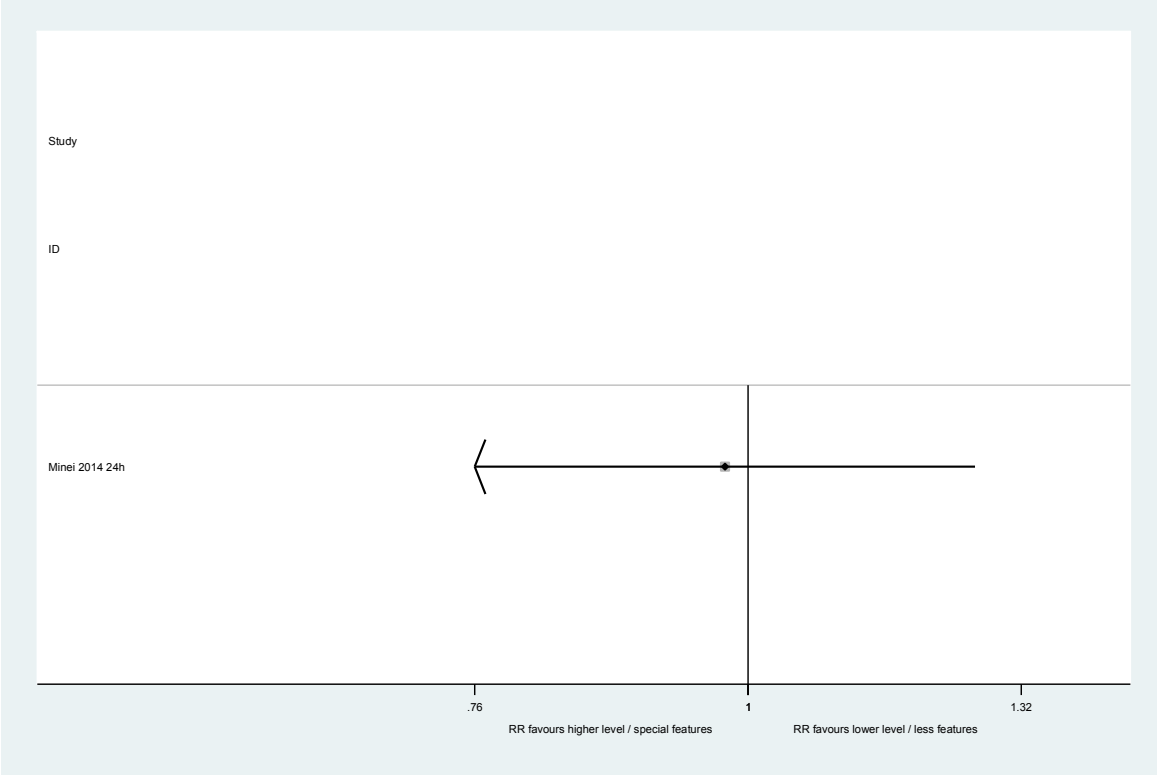


RR=relative risk

Table 58 – Comparison “higher level TC” vs “lower level TCs”: unadjusted 24h mortality for all severe injured patients

Study	Study design	Study population	Country	Level of intervention group	Level of comparison group	Outcome	Intervention (n/N)	NTC (n/N)	RR (95% CI)
Minei 2014	Secondary data analysis	Only patients with severe TBI or patients in shock	USA and Canada	Level 1	Level 2	24h mortality	254/1649	64/406	0.98 (0.76 – 1.26)

Figure 25 – Comparison “higher level TC” vs “lower level TCs”: unadjusted 24h mortality for all severe injured patients



RR=relative risk

Gomez 2015 reported the crude ER mortality in patients admitted to a level 3 TC compared to patients that were transferred to a level 1 or 2 TC as a subanalysis of the total in-hospital mortality rate. Mortality in the emergency room was significantly lower for adult patients in level 1 or 2 trauma centres compared to the level 3 TCs (Table 59).[247]

Based on one low quality study, there is limited evidence for the effect of higher level TCs compared to lower level on the emergency room mortality rates.

Table 59 – Comparison "designated level 1 or 2 TC" vs "lower level", outcome: unadjusted mortality at emergency department for all severely injured adult patients

Study	Study design	Study population	Country	Level of intervention group	Level of comparison group	Intervention (n/N)	NTC (n/N)	RR (95% CI)
Gomez 2015	Cohort study	Only adults	USA	Level 1+2	Level 3	19/41165	23/6318	0.13 (0.07 – 0.23)

4.4.3.3 *Special features of a trauma system*

Mortality

Three articles focused on a change in care within the same TCs (Table 60). Afifi 2015 found no statistical differences in (presumably in-hospital) mortality for paediatric patients admitted to a designated TC in a mandated system versus a designated TC in a non-mandated system.[236] The same applied for the comparisons between admissions in a NTC in a mandated system versus a non-mandated system. Choi 2016 compared in-hospital mortality before and after ACS- of the paediatric TC.[242] According to Choi 2016, severely injured paediatric patients did not have a survival benefit from ACS-verification. Metcalfe 2014 showed that the launch of a trauma network in The United Kingdom resulted in a lower in-hospital mortality rate, but the difference was not significant (10% versus 13%).[139]

Cole 2016 evaluated the impact of the implementation of an inclusive pan-regional trauma system on quality of care (Table 61).[142] They found lower 72h mortality in the inclusive trauma system compared to a non-inclusive trauma system. Mortality rates were 7% versus 15%.

Table 60 – Comparison special features of a trauma centre versus less special features of a trauma centre in designated level 1 and/or level 2 TC", outcome: unadjusted in-hospital mortality for all severely injured patients

Study	Study design	Study population	Country	Level of intervention group	Level of comparison group	Outcome	Intervention (n/N)	comparison (n/N)	RR (95% CI)
Afifi 2015	Cohort study	Paediatric	USA, Florida and Indiana	Level 1+2 in mandated system	Level 1+2 in non-mandated system	In-hospital mortality	103/349	40/120	0.89 (0.66 – 1.21)
				NTC in mandated system	NTC in non-mandated system	In-hospital mortality	18/96	9/40	0.83 (0.41 – 1.70)
Choi 2016	Before-after study	Paediatric	USA	Level 1 paediatric with ACS verification	Level 1 paediatric no ACS verification	In-hospital mortality	32/208	30/208	1.07 (0.67 – 1.69)
Metcalfe 2014	Before-after study	No special group	UK	Hospitals after launch of trauma network and designation to MTC	NTC (hospitals before designation as MTC)	In-hospital mortality	65/639	29/230	0.81 (0.53 – 1.22)

Table 61 – Different comparisons for outcome: unadjusted up to 72-hours mortality for all severe injured patients

Study	Study design	Study population	Country	Level of intervention group	Level of comparison group	Outcome	Intervention (n/N)	comparison(n/N)	RR (95% CI)
Cole 2016	Cohort study	No special group	UK	Inclusive trauma system	Non inclusive trauma system	72h mortality	22/321	119/795	0.46 (0.30 – 0.71)

In this analysis three studies were included reporting the up-to-30 day mortality on meaningful changes in the organisation of trauma systems, without changing the level of trauma centre (Table 62). [178, 239, 240] Brinck 2015 and Brinck 2016 focused on the 30 day mortality in two different countries/trauma systems.[239 , 240] Severely injured patients in the German trauma system had higher risk to die within 30 days than severely injured patients in Finland. Joosse 2012 performed a small study on patients with severe traumatic brain injury.[178] They found no significant difference for unadjusted 30 day mortality between patients directly or indirectly transferred to a level 1 TC.

The variety of the interventions is too large to draw an overall conclusion about the effect of special features of TCs on mortality (all definitions confounded).

Table 62 – Special features in level 1 centres: unadjusted up-to-30-day in-hospital mortality for all severe injured patients

Study	Study design	Study population	Country	Level of intervention group	Level of comparison group	Outcome	Intervention (n/N)	NTC (n/N)	RR (95% CI)
Brinck 2015	Cohort study	No special group	Germany and Finland	German level 1 TCs	Helsinki Trauma Unit	30 day mortality	2847/19398	197/1624	1.21 (1.06 – 1.39)
Brinck 2016	Cohort study	Only unconscious patients	Germany and Finland	German level 1 TCs	Helsinki trauma unit	30 day mortality	2123/5243	139/398	1.16 (1.01 -1.33)
Joosse 2012	Cohort study	Only patients with severe TBI	The Netherlands	Direct transfer to level 1 TC	Indirect transfer to Level 1 TC	30 day mortality	15/56	8/24	0.80 (0.39 – 1.64)

Hospital length of stay

Metcalfe 2014 evaluated the effect of the establishment of the launch of a trauma network.139 Patients had a longer hospital stay after the launch of the trauma network. Brinck 2015 found that severely injured patients stayed longer in German hospitals than in the higher volume Helsinki trauma unit. Length of stay was significantly shorter for a TC with ACS than without this verification according to the study of Choi 2016. Ovalle 2014 found a significant difference in hospital length of stay in favour of adult trauma centre with a paediatric qualification (see table 63).

The variety of the interventions is too large to draw an overall conclusion about the effect of special features of TCs on hospital length of stay.

Table 63 – Comparison special features of a trauma centre versus less special features of a trauma centre in designated level 1 and/or level 2 TC", outcome: (median/mean) hospital length of stay for all severely injured patients

Study	Study design	Special group	Country	Level of intervention group	Level of comparison group	Intervention (mean/sd)	Comparison (mean/sd)	SMD (95% CI)
Brinck 2015	Cohort study	No special group	Germany and Finland	Level 1 TCs in Germany	Helsinki trauma unit in Finland	25 (22)	12 (12)	0.61 (0.56 – 0.66)
Choi 2016	Before-after study	Paediatric	USA	Level 1 with ACS verification	Level 1 no ACS verification	10.1 (1.2)	11.2 (1.4)	-0.84 (-1.04 – -0.64)
Ovalle 2014	Cohort study	Paediatric	USA	Adult TC with paediatric qualification	Adult TC no paediatric qualification	4.84 (0.16)	5.01 (0.17)	-1.03 (-1.09 – -0.97)

Study	Study design	Special group	Country	Level of intervention group	Level of comparison group	Intervention median	Comparison median	Mann–Whitney U test,
Metcalfe 2014	before- after study	No special group	United Kingdom	After launch of trauma network	Before launch of trauma network	14	12	0.599

Intensive care unit (ICU) length of stay

Four studies measured ICU length of stay to compare different aspects of the trauma system. Brinck 2015 found that severely injured patients in Germany had a higher mean ICU length of stay than the severely injured patients in the higher volume Helsinki trauma unit (respectively 12 versus 8 days). Zacher 2015 found the opposite; the severely injured patients in higher volume trauma centres had a longer mean length of stay at the ICU (respectively 10.7 versus 7.3 days). Choi 2016 concluded that ACS-verification of a level 1 TC significantly lowered the mean ICU length of stay. Metcalfe 2014 found no difference on ICU length of stay (median of 6 days) after the launch of a trauma network for severely injured patients (see following table).

The variety of the interventions is too large to draw an overall conclusion about the effect of special features of TCs on ICU length of stay.

Table 64 – Comparison special features of a trauma centre versus less special features of a trauma centre", outcome: (median/mean) ICU length of stay for all severely injured patients

Study	Study design	Special group	Country	Level of intervention group	Level of comparison group	Intervention (mean/sd)	Comparison (mean/sd)	SMD (95% CI)
Brinck 2015	Cohort study	No special group	Germany and Finland	Level 1 TCs in Germany	Helsinki trauma unit in Finland	12 (14)	8 (8)	0.29 (0.24 – 0.34)
Choi 2016	Before-after study	Paediatric	USA	Paediatric level 1 with ACS verification	Paediatric level 1 no ACS verification	4.1 (0.4)	4.8 (0.7)	-1.23 (-1.44 - -1.02)
Zacher 2015	Cohort study	No special group	Germany	High volume TC	Low volume TC	10.7 (14.4)	7.3 (9.4)	0.29 (0.25 – 0.32)

Study	Study design	Special group	Country	Level of intervention group	Level of comparison group	Intervention median	Comparison median	Mann–Whitney U test,
Metcalfe 2014	before- after study	No special group	United Kingdom	After launch of trauma network	Before launch of trauma network	6.0	6.0	0.181

4.4.3.4 *Secondary outcomes*

Metcalfe 2014 evaluated the patients with a good recovery according to the Glasgow outcome scale [261] at discharge. They found no significant difference for good recovery for severely injured patients after the launch of a trauma network.

Afifi 2015 found that significantly more severely injured paediatric patients were discharged home in TCs compared to NTCs. The difference between the patients discharged home from mandated versus non-mandated system was not significant.

Ovalle 2014 found significantly less hospital complications for severely injured paediatric patients admitted to a TC with a paediatric qualification compared to patients admitted to a TC without this qualification (Table 65).

Brinck 2015 compared the number of ventilation days between patients in a German trauma system compared to those in Finland; German patients were ventilated longer.

All evidence on the secondary outcomes is based on just one, low quality study per outcome. Therefore the evidence is limited.

Table 65 – Secondary outcomes for severely injured patients

Study	Secondary outcome	Special group	Country	Intervention group	Comparison group	Intervention (n/N)	Comparison (n/N)	Effect size
Metcalfe 2014	Glasgow outcome scale "good recovery" at discharge	No special group	UK	After launch of trauma network	Before launch of trauma network	254/639	90/230	1.02 (0.84 – 1.23)
Afifi 2015	Discharge home	Only paediatric patients	USA, Florida and Indiana	level 1+2 Mandated system	NTC Non-mandated system	138/349 55/120	58/96 20/40	0.65 (0.53 – 0.81) 0.92 (0.64 – 1.32)
Ovalle 2014	Hospital complications			adult trauma centres with paediatric qualification	adult trauma centres without paediatric qualification	333/2049	423/1871	0.72 (0.63 – 0.82)
Study	**Study design**	**Special group**	**Country**	**Intervention group**	**Comparison group**	**Intervention (median/IQ range)**	**Comparison (median/IQ range)**	
Brinck 2015	Ventilation days		Germany and Finland	Trauma system in Germany	Trauma system in Finland	10 (5-13) days	6 (5-7) days	

4.4.3.5 *Paediatric patients*

Five studies reported on unadjusted in-hospital mortality in severely injured paediatric patients (Table 66).[236, 242, 244, 252, 257] The studies report on trauma systems of different countries and compared different types of TCs. Therefore they are not comparable and an overall estimate could not be calculated. Afifi 2015 found that paediatric patients admitted to a NTC have lower in-hospital mortality rates compared to patients admitted to a higher level TC (mortality rates 19-22% versus 30-33%). Deasy 2012 found no differences in crude in-hospital mortality rate, but in adjusted analyses they found that being treated at a Level 1 trauma centre was associated with lower adjusted odds of in-hospital mortality [adjusted OR 95% CI: 0.27 (0.11, 0.68)] for Australian paediatric patients. Severely injured paediatric patients did not have a survival benefit from ACS-verification concluded Choi 2016. Ovalle 2014 evaluated the addition of a paediatric qualification to an adult TC. Ovalle 2014 reported that paediatric patients benefit from adults centres with a paediatric qualification compared to the usual adult TCs. Mortality rates were 13% versus 15%. Miyata 2015 showed that severely injured paediatric patients have better in-hospital mortality outcomes in a level 1 TC compared to a level 2 TC (mortality rate 12% versus 15%). However after using a matched –control cohort in level1 and level 2, benefits of being treated in a level 1 centre are no longer no statistically significant.

Sathya 2015, Mills 2015, Odetola 2016 and Wang 2013 also analysed in-hospital mortality rates in children treated in TC (compared to other settings) but data could not be extracted for the analysis included in Table 66.

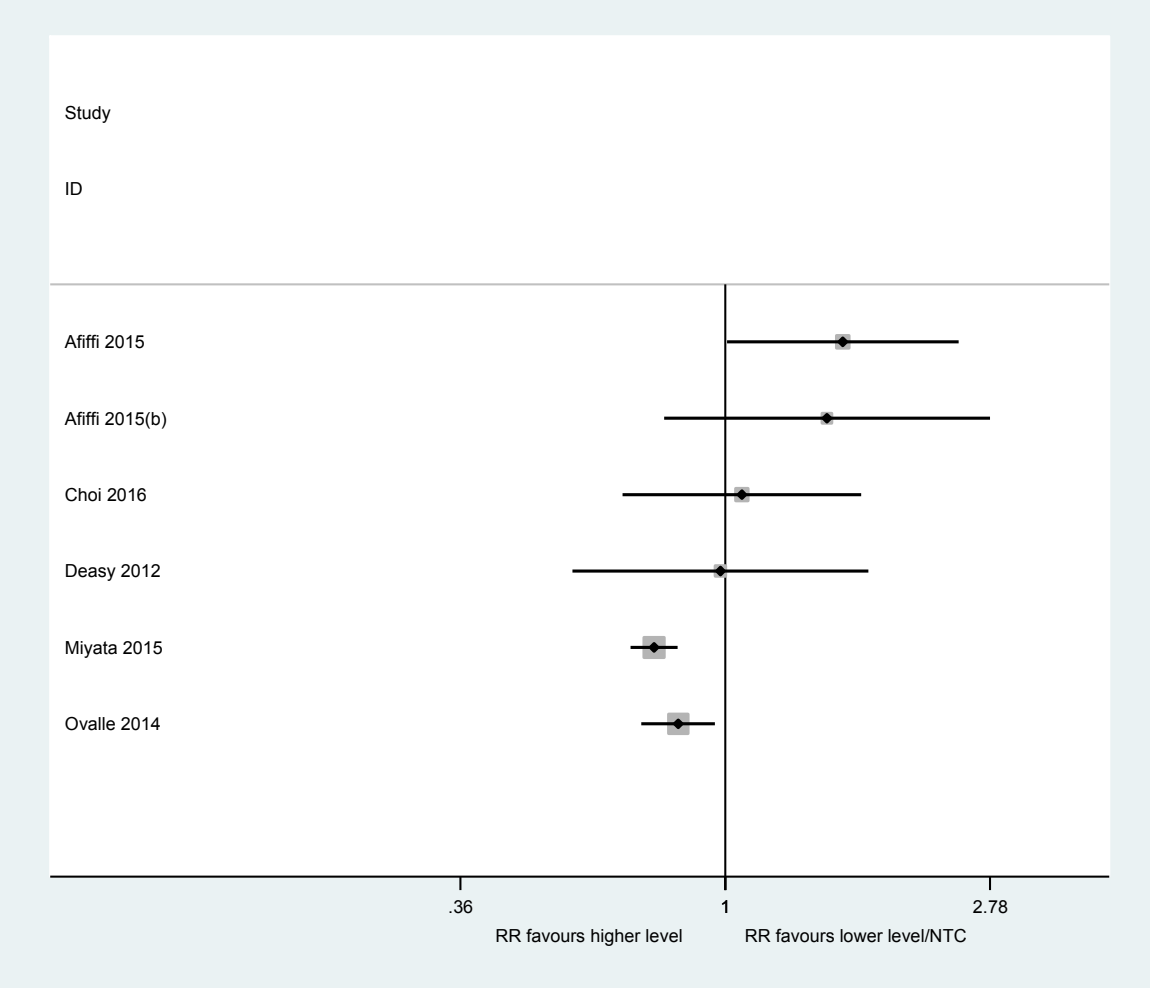
The low to moderate quality studies reported conflicting evidence for the effect of trauma care for paediatric patients.

Table 66 – Comparison "higher level" vs "lower level/NTC" or "special features" vs "less special features", outcome: unadjusted in-hospital mortality for all severely injured paediatric patients

Study	Study design	Study population	Country	Level of intervention group	Level of comparison group	Intervention (n/N)	comparison (n/N)	RR (95% CI)
Afifi 2015	Cohort study	Paediatric	USA, Florida	Level 1+2 in mandated system	NTC in mandated system	103/349	18/96	1.57 (1.01-2.46)
			USA, Indiana	Level 1+2 in non-mandated system	NTC in non-mandated system	40/120	9/40	1.48 (0.79 -2.78)
Choi 2016	Before-after study	Paediatric	USA	Level 1 paediatric with ACS verification	Level 1 paediatric no ACS verification	32/208	30/208	1.07 (0.67 – 1.69)
Deasy 2012	Cohort study	Paediatric	Australia	Level 1 paediatric and adult	NTC	72/1077	13/191	0.98 (0.56 – 1.74)
Miyata 2015	Cohort study	Paediatric	USA	Level 1 paediatric	Level 2 paediatric	1132/9690	632/4113	0.76 (0.69 – 0.83)
Ovalle 2014	Cohort study	Paediatric	USA	Adult TC with paediatric qualification	Adult TC no paediatric qualification	299/2329	366/2378	0.83 (0.72 – 0.96)

RR=relative risk

Figure 26 – Comparison "higher level" vs "lower level/NTC" or "special features" vs "less special features", outcome: unadjusted in hospital mortality for all severely injured paediatric patients



RR=relative risk

Odetola 2016 compared outcomes for children with spinal cord injury treated in TC and non-TC. Odetola 2016 reported that despite the more severely injured receiving care at trauma centres, unadjusted mortality was not different in hospitalised children treated in TC vs. NTC (6.1 vs. 6.6%, p = 0.86).

Sathya compared in-hospital mortality for paediatric patients treated in adult TCs versus mixed TCs (adult and children), and paediatric TCs. Sathya 2015 found that severely injured children (ISS ≥25) treated at paediatric trauma centres (PTC) had lower odds of death compared to those treated at adult TCs and mixed TCs. These results hold for adjusted and unadjusted mortality rates.

Additionally, Wang 2013 demonstrated that, in California, seriously injured children cared for in TCs have decreased adjusted mortality compared to children cared for in non-trauma hospital settings.[260]

Mills 2015 compared 30-day in-hospital mortality after a severe traumatic brain injury in patients treated in Level I and II paediatric and adult TC. Mills 2015 found no significant association between level of TC (level 1 paediatric versus other TC) in adjusted in-hospital 30-day mortality (risk ratios presented in a figure).[250]

Table 67 – Comparison "higher level/ paediatric TCs" vs "NTC" or "lower level/paediatric TCs", outcome: overview of adjusted outcomes for mortality for all severely injured paediatric patients

Study	Special group	Country	Outcome description	Intervention group	Comparison group	Description effect size	Effect size
Sathya 2015	Only paediatric patients	USA	In-hospital mortality	Paediatric TC	Mixed TC	regression estimates (adjusted odds ratios)	1.62 (1.15-2.29)
				Paediatric TC	Adult TC	regression estimates (adjusted odds ratios)	1.75 (1.25-2.44)
Wang 2013	Only paediatric patients	USA	In-hospital mortality	TC	NTC	regression estimates (in percentage points)	-0.79 (-0.80 - -0.30)
				Paediatric TC	Adult TC	regression estimates (in percentage points)	0.64 (−0.26 - 1.54)

4.4.3.6 Geriatric patients

Olufajo 2016 concluded that major trauma geriatric patients mortality rate is significantly lower in level 2 versus level 1 trauma centres, and level 3/4 is not significantly better compared to level 1 trauma centres. [256]

Based on one low quality study, there is limited evidence for the effect of higher level TCs compared to lower level TCs on the in-hospital mortality rate for geriatric patients.

Table 68 – Comparison "higher level TCs" vs "NTC" or "lower level TCs", outcome: overview of adjusted outcomes for mortality for all severely injured geriatric patients

Study	Special group	Country	Outcome description	Intervention group	Comparison group	Description effect size	Effect size
Olufajo 2016	Only geriatric patients	USA	In-hospital mortality	Level 1 TC	Level 2 TC	Adjusted OR	0.73 (0.57-0.93)
				Level 1 TC	Level 3-4 TC	Adjusted OR	0.75 (0.43 –1.33)

4.4.4 What is the association of the severity of the injuries of the patient and the outcomes if treated in a trauma centre?

Six studies explored the relationship between severity of the injuries and mortality if treated in a trauma centre.[237, 245, 246, 248, 249, 259] Vickers 2015 compared patients with ISS 16-24 to ISS 25-75 and found that patients with ISS 25-75 have better outcomes (lower mortality) at the emergency department in level 1+2 TCs compared to treatment at the emergency departments of NTCs (see Table 69).

Ashley 2015 looked at differences in survival between MTC and NTC for severe injury patients in total and per severity category. They found a 9.6 % improvement in survival probability for all severe injury patients in favour of a MTC, but in this was 8.3% in the least critical, 22% in the intermediate critical and 16.5% in the most critical patients; they concluded that patients with more severe injuries have better outcomes (higher probability of survival) at DTC compared to NTCs (Table 70). Di Bartolomeo 2014, Glance 2012, Kuimi 2015 found that a benefit appeared in terms of lower mortality as the severity of injury increased (Table 70). Di Bartolomeo 2014 found that MTC care, compared to NTC provided no survival benefit when analyzed for all severe injury patients together. However, in subgroup analysis a significantly decreased mortality by 30% was found in the most injured patients (TMPM-ICD9 > 0.12). Glance 2012 found that patient with an ISS between 9 and 15 and with ISS between 15 and 25 had similar risks of adjusted mortality in Level I and Level II trauma centres, but very severely injured patients (ISS >25) admitted to Level I trauma centres had a significant 22% lower odds) of mortality.

Matsushima 2016 found that level 1 centres had lower odds compared to level 2 centres of in-hospital mortality for patients with a higher ISS but not for patients that were less severely injured (no exact data was provided).

The six studies were of low to moderate quality and all pointed out in the same direction. There is moderate evidence that patients with more severe injuries have better outcomes in higher level TCs compared to lower level TCs or NTCs.

Table 69 – Comparison of higher level TCs versus lower level TCs or NTCs for different categories of severity of injury for outcome: unadjusted mortality for all severe injured patients in emergency department

Study	Study design	Study population	Country	Level of intervention group	Level of comparison group	Outcome	Injury severity	Intervention (n/N)	NTC (n/N)	RR (95% CI)
Vickers 2015	Cohort study	Only adults, no children	USA	Level 1+2	NTC	mortality in emergency department	ISS 16-24	314/44817	258/26021	0.71 (0.60 – 0.83)
							ISS 25-75	637/16541	760/5314	0.27 (0.24 – 0.30)

Table 70 – Comparison "higher level" vs "lower level/NTC" or "special features" vs "less special features", outcome: overview of other outcomes for mortality for different categories of severely injured patients

Study	Type of study	Special group	Country	Outcome description	Intervention group	Comparison group	Description effect size	Injury severity	Effect size
Ashley 2015	Cohort study	No special group	USA	Improvement in probability of survival when treated at a DTC versus NTC	DTC	NTC	probability	Most critical trauma (ICISS<0.25)	16.5% (p<0.01)
								Intermediate critical (0.25=<ICISS<0.5)	22.0% (p<0.01)
								Least critical (0.5=<ICISS<0.85)	22.0% (p<0.01)
Di Bartolomeo 2014	Cohort study	No special group	Italy	Effect estimate of trauma-centre care on mortality	Level 1 TCs	NTCs	OR	TMPM-ICD9 >0.12	0.71 (0.52 – 0.97)
								TMPM-ICD9 >0.10 & <0.12	0.75 (0.56 – 1.01)
								TMPM-ICD9 >0.08 & <0.10	0.77 (0.58 – 1.02)
								TMPM-ICD9 >0.06 & <0.08	0.89 (0.69 – 1.18)
								TMPM-ICD9 >0.04 & <0.06	0.91 (0.70 – 1.18)
								TMPM-ICD9 >0.02 & <0.04	0.98 (0.77 – 1.25)
								TMPM-ICD9 >0.00 & <0.02	1.51 (0.68 – 3.33)
Glance 2012	Cohort study	No special group	USA	Adjusted odds ratio of in-hospital mortality for level I versus level II trauma centres	Level 1 TC	Level 2 TC	OR	ISS>=15 & ISS<25	0.84 (0.64 – 1.03)
								ISS>=25	0.78 (0.64 – 0.95)
Kuimi 2015	Cohort study	Only adults, no children	Canada	in-hospital mortality associate with access to trauma care	Access to trauma care	No access to trauma care	OR	ICISS<0.85	0.99 (0.81 – 1.22)
								ICISS<0.75	0.91 (0.73-1.15)
Matsushima 2016	Cohort study	Only adults, no children	USA	in-hospital mortality for patients without DNR-order	Level 1	Level 2	OR	ISS 20	1.03 (0.77 – 1.38)
								ISS 60	0.55 (0.33 – 0.92)

4.4.5 *Are high patient volume centres associated with better short-term patient outcomes? Is there a volume threshold below which patient outcomes are worse?*

Three studies reported on the association of annual patient volume and short-term patient outcomes (Table 71 and Table 72).[211, 243, 251] Minei 2014 found no significant difference of unadjusted 28-day or 24-hours mortality for patients admitted to lower volume TCs compared to high volume TCs; however, in adjusted multivariate analyses it was found that as trauma centre admission volume increased there were reduced odds in both all-patient 24-hour and 28-day mortality of 7% for every 500 trauma patient admission increase to a trauma centre.[251]

Zacher 2015 concluded that the hospital volume of severely injured patients was identified as an independent predictor of survival. A clear cut-off value for volume could not be established, but at least 40 patients per year per hospital appeared beneficial for survival (Table 71).[211] Clement 2013 included patients with subdural, subarachnoid, and extradural haemorrhage following injury.[243] For patients admitted to higher volume TCs (≥6 admissions per year) there was a significantly reduced risk of in-hospital mortality as compared with the group with fewer than 6 annual patients (Table 72). However this conclusion must be interpreted with care as lower volume hospitals are more often lower level TCs that treat not only less patients but also less severe injured patients. These patients have obviously more chances to survive the injuries.

- There is limited evidence that patients admitted to higher volume TCs have a reduced risk of in-hospital mortality.
- Two thresholds were found: 6 and 40 patients per year per TC. For both thresholds the evidence for the effect of hospital volume on in-hospital mortality is limited as both thresholds are based on one lower quality study.

Table 71 – Comparison high volume TCs" vs "low volume TCs", outcome: unadjusted mortality for all severely injured patients

Study	Study type	Special group	Country	Outcome	Level of intervention group	Level of comparison group	Intervention (n/N)	Comparison (n/N)	RR (95% CI)
Minei 2014				28-day mortality	>= 3000	<= 1000	149/635	69/284	0.97 (0.75 – 1.24)
					>= 3000	1001 – 1999	149/635	116/504	1.02 (0.82 – 1.26)
					>= 3000	2000 – 2999	149/635	105/438	0.98 (0.79 – 1.22)
				24-hours mortality	>= 3000	<= 1000	96/635	41/284	1.05 (0.75 – 1.47)
					>= 3000	1001 – 1999	96/635	74/504	1.03 (0.78 – 1.36)
					>= 3000	2000 – 2999	96/635	71/438	0.93 (0.70 – 1.24)
Zacher 2015	Cohort study	No special group	Germany	In-hospital mortality	>=100 admissions per year	1-19 admissions per year	1195/5955	1235/7654	1.24 (1.16 – 1.34)
					>=100 admissions per year	20-39 admissions per year	1195/5955	1544/8264	1.07 (1.00 – 1.15)
					>=100 admissions per year	40-59 admissions per year	1195/5955	1361/6961	1.03 (0.96 – 1.10)
					>=100 admissions per year	60-79 admissions per year	1195/5955	1159/5761	1.00 (0.93 - 1.07)
					>=100 admissions per year	80-99 admissions per year	1195/5955	951/4694	0.99 (0.92 – 1.07)

Table 72 – Comparison "lower volume level TCs" vs "higher volume TCs", outcome: adjusted odds ratios for in-hospital mortality for severely injured neuro trauma patients

Study	Special group	Country	Outcome description	Intervention group	Comparison group	Description effect size	Effect size
Clement 2013	severely neuro trauma patients	USA	adjusted odds ratio for in-hospital mortality	6-11 admissions per year	<6 admissions per year	adjusted OR	0.45 (0.29 – 0.68)
				12-23 admissions per year	<6 admissions per year		0.56 (0.38 – 0.81)
				24-59 admissions per year	<6 admissions per year		0.63 (0.44 – 0.90)
				>= 60 admissions per year	<6 admissions per year		0.59 (0.41 – 0.87)

4.4.6 Systematic reviews

The report supplement includes details on the systematic reviews that were included (N=5) [106, 221, 262-264] or excluded (N=45) [108, 124, 265-307] for comparison with our final results. Four of these systematic reviews report on the effect on mortality or length of stay related to different levels of trauma care or specialized trauma care versus non-specialized trauma care.[221, 262-264]

Mann 1999 based on 42 (USA & Canada) studies concluded that the evidence is 'suggestive' that hospital mortality is reduced in severely injured trauma patients with the implementation of trauma care system, but also that compelling evidence is lacking.[264] Biewener 2005 performed a review that focused on pre-hospital airway transport and to a smaller extent on the comparison of mortality between level 1 and lower levels of trauma centres. For this comparison they could include 6 studies, originating from USA (2), Canada (2), Australia (1) and Germany (1). In 5 of the 6 studies a significant lower mortality rate was found for level 1 trauma centres. However, the author warns that weak study designs and high heterogeneity prohibits definitive conclusions.[262] Celso 2006 found an improved odds of survival in 8 of the 14 included (13 USA & 1 Canada) studies after the implementation of a trauma system; they also performed a meta-analysis based on 6 studies that showed a 15% reduction in mortality in favour of the presence of a trauma system.[263] The most recent systematic review on this topic of Kim 2014; they included 50 studies (of which 47 originated from USA & Canada): 10 of 17 articles showed that level I trauma centres had better patient outcomes (mainly mortality) than level II centres; the achievement of trauma centre verification by American College of Surgeons or State was beneficial to decreasing mortality and length of stay in 9 of 11 studies; the relationship between volume of annual trauma patients and in-hospital mortality and hospital length of stay was not clear but high trauma admission volume was beneficial in 8 of 16 studies.[221]

Along with Kim (2014)[221], Caputo et al. (2014)[106] focused on the relationship between patient volume and mortality. Of the 16 articles on this topic included in each review, 10 are common to both them.

Caputo 2014 focused on the relationship between patient volume and mortality in level I trauma centres; they included 19 USA studies: Sixteen studies examined the relationship between institutional trauma centre volume and mortality. Of the 16 studies, 12 examined the volume of severely injured patients and 8 examined overall trauma patient volume. High institutional volume was associated with at least somewhat improved mortality in 10 of 16 studies (63%); however, nearly half of these studies found only some subpopulations experienced benefits. In the remaining six studies, volume was not associated with any benefits. Four studies (25%) analysed the impact of surgeon volume on mortality. High volume per surgeon was associated with improved mortality in only one of four studies (25%).

In line with Mann 1999 and Kim 2013 we found conflicting evidence about reduced mortality rates in higher level trauma centres based on 29 primary studies.

With regard to volume, the reviews of Kim 2014 and Caputo_2014 warn that the evidence base is not firm, due to weak (mainly retrospective) study designs and large heterogeneity (e.g. severity of injury, definitions used) between studies. Both reviews state that definitive conclusions cannot be drawn about the impact of higher level of trauma centres or higher volume of patients on mortality. We conclude that there is limited evidence that patients admitted to higher volume TCs have a reduced risk of in-hospital mortality. In accordance to both systematic reviews we found the quality of studies low.

Most reviews discussed the problem of the diversity among the included studies. Unclear and variations of definitions (trauma centres/levels, patients, injury severity scores) and incompleteness of data registries made it difficult for authors to formulate generalizable recommendations. Also the heterogeneity of data-analyses was discussed and made it difficult to perform meta-analyses. Mann 1999 addresses this issue by criticizing the study designs of the included studies resulting in a lack of evidence. Therefore most reviewers recommend further research on this topic, which takes into account the above mentioned limitations before sound conclusions and recommendations can be formulated. We agree to this conclusion.

4.5 Discussion

Our systematic review revealed 29 studies of variable methodological quality examining short term outcomes for the organisation of trauma care for severely injured patients. Short-term outcomes included in-hospital mortality (up to 30-day mortality after discharge), length of stay in hospital and in the ICU. Studies including mortality, however, only had information on in-hospital mortality. The studies were clinically and statistically heterogeneous and as a consequence we could not perform a meta-analysis.

4.5.1 Summary of main results

Table 73 shows a summary of the main findings. The effect of higher level TCs (for example level 1 or level 2 TCs) compared to lower level (e.g. level 3 TCs or NTCs) or TCs with more special features compared to TCs with less special features was analysed. We found conflicting evidence for the effect of higher level trauma centres compared to lower level trauma centres or non-trauma centres for all severely injured patients and for severely injured paediatric patients. There is limited evidence that patients benefit from admission to an emergency room in a higher level trauma centre compared to lower level care. We found some evidence that admission to a higher level trauma centre reduces the hospital length of stay compared to admissions at a non-trauma centre, but this evidence was not found for ICU length of stay. Some improvements in trauma care to achieve more special features, i.e. ACS verification, setting up an inclusive trauma system or having a paediatric qualification in an adult trauma centre, seem to be effective, but the evidence is limited.

Patients with the most severe injuries seems to benefit from admissions to higher level trauma centres compared to patients with less severe injuries. One explanation might be that patients with the most severe injuries admitted to a high level TC are younger than patients admitted to a lower level TC or NTC. Elderly patients with trauma are at high risk for complications and death from injuries that would not necessarily prove fatal to their younger counterparts.[26]

We could not find evidence that there is a positive relation between hospital volume and patient outcomes and no optimal threshold for hospital volume was found.

Table 73 – Summary of main findings

Research question	Sub analysis	Studies (N)	Best evidence synthesis	Comparing best evidence synthesis with systematic reviews
Are trauma centres associated with better severely injured patient outcomes compared to non-trauma centres? What is the association between level of trauma centre and patient outcomes?	unadjusted mortality for “designated level 1 and/or level 2 TC” vs “NTC”	5	The risk of bias in the five studies was moderate to high. The evidence for a difference between TCs compared to NTCs in unadjusted hospital mortality is conflicting.	Mortality rates can be lowered significantly through primary treatment at a level 1 TC
		1	Based on one study, there is limited evidence for a negative effect of higher level TCs compared to NTCs on the 30-day in-hospital mortality (presumably after event) mortality rate for all severely injured patients combined.	Reduction in mortality in favour of the presence of a trauma system Achieving ACS trauma centre verification is beneficial to patient outcomes.

Research question	Sub analysis	Studies (N)	Best evidence synthesis	Comparing best evidence synthesis with systematic reviews
		1	Based on one low quality study, there is limited evidence for the effect of higher level TCs compared to NTCs on the emergency room mortality rates.	The benefit of level 1 centres compared to level 2 centres is not clear
		1	Based on one study, there is no evidence of effect with regard to hospital length of stay when level 1 or 2 TCs are compared to NTCs	Weak evidence that organised systems of trauma care are an effective health care policy.
	unadjusted mortality for "higher level TC" vs "lower level TC"	2	The low quality studies reported conflicting evidence for a difference between higher level TCs compared to lower level TCs in unadjusted hospital mortality rates.	
		3	Based on 3 studies, there is no evidence of effect that admission to a higher level TC is beneficial for severely injured patients on up-to-30 day in hospital mortality.	
		1	Based on one low quality study, there is limited evidence for the effect of higher level TCs compared to lower level on the emergency room mortality rates.	
	special features of a trauma centre versus less special features	7	The variety of the interventions is too large to draw an overall conclusion about the effect of special features of TCs on mortality (all definitions confounded).	
		4	The variety of the interventions is too large to draw an overall conclusion about the effect of special features of TCs on hospital length of stay.	
		4	The variety of the interventions is too large to draw an overall conclusion about the effect	

Research question	Sub analysis	Studies (N)	Best evidence synthesis	Comparing best evidence synthesis with systematic reviews
			of special features of TCs on ICU length of stay.	
		4	All evidence on the secondary outcomes is based on just one, low quality study per outcome. Therefore the evidence is limited. Secondary outcomes • Glasgow outcome scale "good recovery" at discharge • Discharge home • Hospital complications • Ventilation days	
	unadjusted in-hospital mortality rates for trauma care for children	5	The low to moderate quality studies reported conflicting evidence for the effect of trauma care for paediatric patients.	
	unadjusted in-hospital mortality rates for trauma care for geriatric patients	1	Based on one low quality study, there is limited evidence for the effect of higher level TCs compared to lower level TCs on the in-hospital mortality rate for geriatric patients.	
What is the association of the severity of the injuries of the patient and the outcomes if treated in a trauma centre?	Hospital mortality for higher trauma care versus lower trauma care for different categories of injury severity	6	The six studies were of low to moderate quality and all pointed out in the same direction. There is moderate evidence that patients with more severe injuries have better outcomes in higher level TCs compared to lower level TCs or NTCs.	Not reported
Are high patient volume centres associated with better short-term patient outcomes? Is there a volume threshold below which patient outcomes are worse?	Unadjusted mortality for "higher volume TC" vs "lower volume TC"	3	There is limited evidence that patients admitted to higher volume TCs have a reduced risk of in-hospital mortality.	The relationship between volume of annual trauma patients and outcomes is not clear. It is unclear whether an optimal volume exists It has not been demonstrated that the ACS criteria improves survival
	Volume threshold below which patient outcomes are worse	2	Two thresholds were found: 6 and 40 patients per year per TC. For both thresholds the evidence for the effect of hospital volume on in-hospital mortality is limited as both thresholds are based on one lower quality study.	

4.5.2 Potential biases in the review process

The large number of studies not fulfilling our inclusion criteria demonstrates the degree of difficulty in constructing a concise search in this area. This is mainly caused by a huge variability in the definitions used for trauma centres and severely injured patients. For example, studies from Canada mainly use another threshold for severely injured trauma patients.[308, 309] Other studies reported on the longitudinal outcomes of trauma systems without or with a minor change in aspects of the trauma system.[14, 80, 310, 311,181] Surprisingly, the number of studies reporting on volume and effect of trauma systems on patient outcomes was low. As a result of our focus on comparison between different levels of TCs in trauma systems, articles about the relationship between volume and patient outcomes may have been excluded from the selection.

Some studies were excluded because they failed to provide enough information on the patient or hospital characteristics or on the outcome measures. It is possible that the studies which analysed data from the same registry resulted in patients being counted twice. There is time overlap between these studies and inclusion criteria are not equal. Furthermore, registry data may have been limited by incomplete registration of interventions and outcomes. Some studies did not provide data for calculation of unadjusted mortality, and this may have influenced the possibility of calculating an overall relative risk of unadjusted mortality.

On the other hand, reporting the unadjusted outcomes did not reflect on the differences between study populations and hospital characteristics, limiting the evidence for our findings. It was interesting to see that some conclusions were reversed depending of adjusted or non-adjusted outcomes were used; however, different authors used different variables to adjust their analyses, making it impossible to compare adjusted outcomes across studies.

Besides the analyses were limited by under powering of studies due to small sample sizes or mortality rates, and the lack of adjustment for possible confounders.

The risk of publication bias is a well-recognized limitation of systematic reviews.[312] This was minimized by including studies in all languages in order to avoid bias introduced by the tendency to publish very unique results in an English journal and otherwise in a journal of native language. However, the number of non-English articles published in electronic indexed journals is limited.

4.5.3 Quality of the evidence

We found no randomised controlled studies. Because this was suspected, we had chosen to include cohort studies, before-after-studies and routine-data-based studies a priori. This was done in order to pursue the best available evidence.[313]

The overall quality of the studies in this review was low as assessed by the risk of bias tools. All cohort studies had a high risk of bias across all domains. The low quality of the studies is supposed to lead to biased findings. Strong evidence can only be found in studies of high methodological quality. As our systematic review only retrieved studies of lower quality, the best evidence could not exceed a moderate level of evidence. Although the levels of evidence in this review were arbitrary, it seems unlikely that a different rating system would have resulted in different conclusions. A common study method was to use existing trauma registry data, but the registries use different definitions for inclusion. This makes comparison between the studies difficult. Generally, our conclusions are more conservative and therefore less convincing than the conclusions of the authors of the individual studies.

4.5.4 Implications for practice and research

Due to the weakness of the evidence and the clinical and statistical heterogeneity we were unable to determine an overall estimate for the benefit of trauma care for severely injured patients. Based on moderate or limited evidence the benefits of trauma care seems to be greatest for the most severely injured patients.

Further research is needed to evaluate the effect of the organisation of trauma care on short term patient outcomes like mortality and length of stay. In line with this, two systematic reviews are in progress and are expected to be published in 2017.[314, 315] At this moment, however, there is a lack of information and present studies lack quality. Ideally, a RCT would be used to test our hypothesis that mortality (up to 30 days after discharge), length

of hospital stay, and length of ICU stay are better for patients treated at a major trauma centre (MTC). However, it will be very difficult to perform because isolation of the interested trauma care component is difficult to realize in daily practice due to the complex organisation of hospitals.

Some studies report on the patient outcomes shortly after introduction of the trauma system or aspects of it. It is advisable to study the effect of the intervention both on short term (for example, 1 year after the introduction) as on long term (for example 3 years after the introduction). Also, not only in-hospital mortality rates provide information, but also 30-day mortality rates after discharge is relevant in the context of studying this topic. Including mortality after discharge could remove the bias introduced by in-hospital mortality in admissions with a shorter length of stay.[316]

Use of comprehensive nationwide trauma registries will be the most promising method to answer the research questions. The registries should include all data from prehospital care to hospital discharge and beyond. The registries should use the same definitions for all variables to make comparisons possible.

Key points

- **Based on moderate or limited evidence the benefits of trauma care seems to be greatest for the most severely injured patients presented to a higher level trauma centre.**
- **Establishing comprehensive National Trauma Registries can provide more solid answers the research questions.**
- **Further research is needed to evaluate the effect of the organisation of trauma care on short term patient outcomes like mortality and length of stay. At this moment there is a lack of information and present studies lack quality.**

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