The volume-outcome relationship in severely injured patients: a systematic review and meta-analysis

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Abstract

Background: The volume-outcome relationship in severely injured patients remains under debate and this has consequences for the designation of trauma centers.

Objectives: The aim of this study was to evaluate the relationship between hospital or surgeon volume and health outcomes in severely injured patients.

Methods: Six electronic databases were searched from 1980 up to January 30th 2018 to identify studies that describe the relationship between hospital or surgeon volume and health outcomes in severely injured patients (preferably Injury Severity Score (ISS) above 15). Selection of relevant studies, data extraction and critical appraisal of the methodological quality were performed by two independent reviewers. Pooled adjusted and unadjusted estimates of the effect of volume on in-hospital mortality, only in study populations with ISS > 15, were calculated with a random-effects meta-analysis. A mixed effects linear regression model was used to assess hospital volume as continuous parameter.

Results: Eighteen observational cohort studies were included. The majority (13/18, 72%) reported an association between higher hospital or surgeon volume and lower mortality rate. Overall, the quality of the included studies was reasonable, with insufficient adjustment as one of the most common limitations. Eight studies were included in the meta-analysis with a total of 222,418 patients. High hospital volume (>240 admitted severely injured patients per year) was associated with a lower risk of mortality (adjusted odds ratio 0.85, 95% confidence interval (CI) 0.76-0.94). Four studies were included in the regression model, providing a beta of -0.17 per 10 patients (95% CI -0.27 to -0.07). There was no clear association between surgeon volume and mortality rates based on three available studies.

Conclusion: Our systematic overview of the literature reveals a modest association between high volume centers and lower mortality in severely injured patients, suggesting that designation of high volume centers might improve outcomes among severely injured patients.

Level of evidence: level III, Systematic review and meta-analysis

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Keywords: Trauma, Severely Injured, Hospital volume, Volume-outcome Relationship

Background

Each year, about 4.8 million people die worldwide as a result of injuries (1). In adults younger than 45 years, injury is even the major cause of death (2). Therefore, trauma imposes a substantial burden on society: In the Netherlands, the annual total costs of injuries are €3.5 billion (3). The implementation of trauma systems and dedicated level I trauma centers has reduced mortality of severely injured patients and improved functional outcome at discharge (4).

The American College of Surgeons Committee on Trauma (ACS-COT) requires a minimum of 240 admission of severely injured patients (Injury Severity Score (ISS) >15) per year for all level 1 trauma centers. Alternatively, individual trauma surgeons should admit at least 35 severely injured patients per year (5, 6). These volume requirements are originally based on the volume-outcome relationship in other surgical specialties such as cardiothoracic surgery (7-9). Two previously published systematic reviews on the impact of volume on outcome concluded that the benefit of high volume of annually admitted trauma patients in terms of health outcomes remains unclear (10, 11) .

However, these systematic reviews did not perform a meta-analysis. It is likely that a potential positive effect of volume on outcome is more visible in a meta-analysis, because it increases power. The aim of this systematic review and meta-analysis is to evaluate the volume-outcome relationship in severely injured patients.

Methods

Literature search

The search engines Embase.com (Medline and Embase), Pubmed, Web of Science, Cochrane Central and Google Scholar were searched until January 30th 2018 (date last searched) to identify published studies that examined the association between the volume of severely injured patients and different health outcomes. There were time restrictions; only articles published after 1980 were taken into account. The search was designed by an experienced biomedical information specialist. The search algorithm included subject heading (MeSH) terms and text words for injured patients, hospital volume, trauma center and different health outcomes (see appendix). In order to identify potential additional studies, we checked the reference lists of studies included and contacted experts in the field of trauma.

Study selection and inclusion criteria

Observational cohort studies that examined the association between hospital or surgeon volume of severely injured patients and different health outcomes were included. Studies were included when a severely injured population was defined as patients with ISS >15 or, when ISS was not used, with clinical and anatomical patient characteristics comparable to to the severity of ISS >15 confirmed by an experienced trauma surgeon. Studies that focused on patients with specific anatomical injuries or studies that only used pediatric cohorts were excluded. Studies not written in English were excluded.

Two reviewers (CS and EW) independently screened titles and abstracts to identify potentially eligible articles. Full-text reports of the potentially eligible articles were retrieved and these two reviewers independently screened these full-text articles to identify eligible studies. Any disagreement was resolved through discussion or, if necessary, a third review author (HL) was consulted to reach consensus. The PRISMA flowchart was used to provide an overview of the data screening process (12).

Data extraction and quality assessment

Data extraction was performed by two independent reviewers (CS and EW). Extracted information included study characteristics (publication year, study design, study period, setting, sample size), patient characteristics (inclusion and exclusion criteria), type of volume (hospital or surgeon), definition of volume (unit of measurement, continuous or categorical variable with corresponding thresholds), health outcomes, and key figures (adjusted and unadjusted estimates of the effect of volume and outcome).

Based on previous literature on quality of observational studies, a quality assessment form was made to assess quality, generalizability and risk of bias of the included studies (13). The quality assessment form was applied to each study by two independent reviewers (CS and EW). Also, the risk for publication bias was assessed using funnel plots.

Data analysis

A meta-analysis was performed to determine the relationship between hospital volume and outcome in severely injured patients. Hospital volume was defined as the mean annual number of admitted severely injured patients. Studies were included in meta-analyses when severely injured was defined as ISS>15 to reduce heterogeneity. The outcome of the meta-analysis was mortality, defined as either in-hospital mortality or death within 30 days following trauma.

The association between patient volume per hospital and mortality was assessed in two ways: using a threshold of 240 patients to separate high volume centers from low volume centers (5, 6) and using volume as a continuous parameter.

For the meta-analysis, only studies with cut-offs close to 240 were included. Both adjusted and unadjusted outcomes were used to calculate pooled effect estimates. For the adjusted estimates, the adjusted odds ratio (OR) was used when reported. To calculate unadjusted ORs, mortality rates per study and volume group were used. The lowest volume group was used as a reference, results were transformed (1/effect size) if necessary. Studies that did not report either mortality rates or ORs were excluded from the meta-analysis. The pooled unadjusted OR was calculated with the Mantel-Haenszel method, the pooled adjusted OR was calculated with the inverse variance method. A random effects model was used to pool the estimates and to account for expected heterogeneity since studies had different study populations, were from different regions and time frames. Heterogeneity was assessed using the Q-test quantified by the I^2 statistic.

To assess hospital volume in a continuous way, data from studies reporting volumes and in-hospital mortality from at least two volume groups were used. Only studies using the definition for severely injured as ISS > 15 were included. Volume was calculated as the mean number of severely injured patients per hospitals per year in a specific volume group and outcome was the reported mortality rate. A random effects linear regression model, with in-hospital mortality as outcome, a random effect for study to adjust for study differences, adjustments for mean age and mean ISS and weighted for the number of patients in each volume group was used. A random effects model was used to account for heterogeneity of studies and inter-study variance (14). By weighting the number of patients in each volume group, larger studies were had more influence in the regression model compared to smaller studies.This resulted in a beta regression coefficient for the effect of 10 additional patients per year on mortality. The effect of hospital volume was tested for non-linearity using the likelihood ratio test with natural cubic splines.

Analyses were performed with the R software environment (version 3.2.2 or higher, the R Foundation for Statistical Computing, Vienna, Austria) and Review Manager (RevMan, version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014).

Results

In the initial search, 9,181 records were identified (Figure 1). After removing the duplicates, 5,364 records were screened on title and abstract. The remaining 202 potentially eligible articles were selected for full-text assessment and eighteen of these studies were included in the systematic review (Table 1).

Study characteristics

Fifteen (83%) were retrospective cohort studies (15-29), one study (6%) was a secondary analysis of two randomized controlled trials (30) and two studies (11%) were prospective cohort studies (31, 32) (Table 1). Fifteen studies (83%) were conducted in the United States (15-17, 19-27, 30, 32, 33), one study (6%) was conducted in Germany (28), one study was conducted in Japan (29), and one study was conducted in the United Kingdom (31). The National Trauma Databank (NTDB) from the United States was used in three studies (18%) (15, 19, 33). Other studies selected their sample from nation, state or hospital registries. Seventeen studies (94%) evaluated the hospital volume-outcome relationship (14-16, 18-25, 27-32) and three studies (18%) examined the surgeon volume-outcome relationship (20, 23, 27).

Mortality was defined as in-hospital mortality in sixteen studies (89%) (15-17, 19-29, 32, 33), in one study (6%) as 24-hour mortality (30) and in one study as 6-months mortality (31) (Table 1). Other outcomes reported were hospital length of stay (21, 25), discharge locations (17), intensive care length of stay (18), severe disability at discharge (18), total costs per admission (29) and complication rates (30). Thirteen studies (72%) used the ISS to define the severity of injuries. In ten studies (59%) the population examined had an ISS of at least 16 (17, 21-24, 26-28, 31, 33), three studies (18%) examined patients with an ISS of 15 or more

(15, 16, 19) and one study (6%) used a threshold of 13 (20). In three studies (17%) ISS was not used to define injury severity (25, 30, 32). As an alternative, a combination of clinical and anatomical characteristics like the Abbreviated Injury Scale (AIS), Glasgow Coma Score (GCS), Systolic Blood Pressure, Trauma Score (TS) or admission to the intensive care unit were used in these three studies (25, 30, 32). These characteristics were confirmed as comparable to ISS > 15 by an experienced trauma surgeon.

Seven studies (39%) (19, 20, 23, 25, 28, 29, 31) analyzed hospital volume as a continuous parameter and used the annual volume of severely injured patients (Table 1). Three studies (17%) (15, 24, 33) used a cut-off of 240 severely injured trauma patients per year. Three studies (17%) (21, 26, 32) quantified hospital volume based on the total volume of trauma patients categorized in two groups, all defined 'high volume' as above 1200 annual patients. For surgeon volume, two studies examined the volume-outcome relationship with volume as a continuous parameter (20, 23), while in one study a total of 35 or more severely injured patients admitted per surgeon per year was defined as 'high surgeon volume'(27).

Quality assessment

All studies reported the total number of severely injured patients and had a limited impact of loss of follow-up (Figure 2). Most studies (72%) were considered to have a representative study population and the number of patients per volume group was frequently reported (89%). In 72% of the studies the reported mortality was clearly defined as in-hospital mortality and crude ORs were reported in 94% of the studies. Shortcomings mostly concerned the adjusted analyses; only ten (56%) studies reported adjusted ORs, and when adjustments were made the type of adjustments were not always mentioned.

Effect of hospital volume

Eleven of the seventeen (65%) studies on hospital volume reported lower mortality rates in high volume centers compared to low volume centers (15, 17, 23-26, 28-32). Five studies (28%) did not find a positive nor a negative association between hospital volume and mortality (16, 19-21, 33). One study (6%) looked at specific subgroups of ISS (16-24 and >25) and did not find any evidence that high volume hospitals perform better than low volume hospitals in terms of mortality in extremely severe injured patients (ISS>25) (34). Another study that divided its population into blunt and penetrating injury found that the relationship between volume and mortality was stronger in penetrating injuries (14). Other outcomes were reported too infrequently.

Meta-analysis

Eight studies evaluating the relationship between trauma center volume and in-hospital mortality in severely injured patients could be included in the meta-analysis with a total of 222,418 patients (15-17, 19, 23, 24, 33). All of these studies presented crude mortality rates, and adjusted ORs were reported in four out of eight studies (50%). The pooled effect estimate showed no association between volume and mortality when using the unadjusted ORs (OR 1.00, 95% confidence interval (CI): 0.92-1.10, $p = 0.93$, Figure 3A), with large heterogeneity ($I^2 = 84\%$, $p < 0.001$). When including adjusted estimates only, high volume was associated with lower mortality (OR 0.85, 95% CI: 0.76-0.94, $p = 0.003$, Figure 3B), with moderate heterogeneity ($I^2 = 44\%$, $p = 0.13$). There was no suggestion for publication bias (Figure 5). Four studies could be used for the analysis of the effect of continuous hospital volume on mortality and showed a similar association (Beta: -0.17 per 10 patients, 95% CI -0.27 to -0.07, $p < 0.01$, Figure 4). The effect of hospital volume was considered to be linear (p=0.998).

Surgeon volume

Three of the eighteen studies (17%) examined the relationship between surgeon volume and in-hospital mortality in severely injured patients (20, 23, 27). One study reported that increased per-surgeon volume in the treatment of seriously injured patients is associated with lower mortality (20). The authors suggest that a surgeon should treat at least 35 severely injured patients per surgeon per year. The other two studies found no relationship (23, 27).

Discussion

This study aimed to evaluate the relationship between hospital or surgeon volume and health outcomes after severe trauma. The systematic review included eighteen studies, of which eight studies were included in the meta-analysis and four studies were included in the regression analysis. Our results indicate that a significant association between hospital volume and mortality exists, although the effect is modest. Overall, the quality of the included articles was reasonable, with insufficient adjustment as one of the most common limitations. No clear conclusions can be drawn with respect to surgeon volume due to an insufficient number of studies.

There might be several reasons explaining the fact that high volume hospitals perform better. The most obvious declaration is the 'practice makes perfect' hypothesis, which suggests that physicians and nurses can develop higher proficiency in the care of severely injured patients in case of high exposure (35). Although trauma patients all present in different ways, trauma care is a highly standardized in terms of initial approach in the Emergency Department (36), where lifesaving interventions are performed even before the precise injuries are known. Personalized care is needed once the full extent of injury, and the patient's pre-existing health status is known - but this requires competence in complex operations and procedures and high fidelity team work. More exposure to this process may result in more efficiency, which is of extreme importance in the care for severely injured patients.

Another possible explanation might be the infrastructure of high volume trauma centers. The development of designated trauma services or trauma teams for the management of severely injured patients in high volume centers decreases mortality (37, 38). Also, the presence of in-house coverage by trauma surgeons at high volume centers is believed to improve outcomes, although there is no empirical evidence showing an actual decrease in mortality (39, 40).

Another possibility is the ability of each center to treat the range of injuries presenting, high volume centers could have more skills on site compared to small volume centers. There is also a possibility that high volume centers implement significant changes in trauma care like new technological improvements earlier. High volume centers have the commitment and resources to implement advances in trauma care which could lead to a decrease in mortality.

Some hospitals are more likely to receive more severely injured patients (i.e. with higher ISS) than other hospitals due to trauma center designation or hospital location. Furthermore, it is evident that the risk of mortality increases with higher ISS (41). When examining the relationship between volume of severely injured patients and mortality it is of high importance to adjust for this case-mix differences. Nevertheless, in the studies included in this systematic review, the severity of injury is not always taken into account. Due to the lack of these adjustments, it is hard to correctly interpret the results of these studies.

Most studies used of a cut-off value of 240 severely injured patients per year. This cut-off value has been arbitrarily chosen by the ACS-COT and was originally based on studies from other surgical specialties like cardiothoracic surgery (7-9). Although several studies with a continuous analysis of the volume-outcome relationship have been published, the ideal cut-off value remains unclear. As suggested in Figure 4, the optimal cut-off may be higher than 240, but more extensive continuous analysis of the volume-outcome relationship is needed. Also, it might be possible that there is an infliction point where mortality begins to increase, but extreme high volume centers are needed to examine this association and these were not included in our meta-analysis. Furthermore, using a higher cut-off value will lead to more centralization of trauma care. This may increase transport times of severely injured patients, which is associated with increased mortality rates in trauma patients (42-44). However, this might be less important in small countries like the Netherlands and other European countries.

Two previously published systematic reviews on the impact of volume on outcome did not find a clear benefit for severely injured patients in high volume centers (10, 11). However, both studies did not perform a meta-analysis and looked at a smaller amount of studies. Our meta-analysis and regression analysis revealed new insights and showed more consistent results that severely injured patients benefit from treatment in high volume centers.

A limitation of our study is that only few studies could be included for the meta-analysis. As a result, pooled findings might be largely influenced by the results of one study. There was no indication of publication bias. Furthermore, we only assessed the relationship of volume with mortality. Other outcomes like hospital length of stay and quality of life after trauma are also important indicators of quality of care and might as well be influenced by hospital or surgeon volume. Another limitation is that a majority of our included studies, almost 90%, were conducted in the United States. Variations in the structure of trauma centers might make our results less generalizable to trauma centers in Europe. The high amount of studies conducted in the United States was also the cause for including studies with the same data source in the meta-analysis. This makes it possible that patients are included in the meta-analysis more than once. In addition, a clear definition of severely injured patients was lacking. Most studies included in our systematic review used ISS to define injury severity, since it is the universal injury severity measure in trauma registries and research. But we also had to include three studies with other definitions of injury severity, like clinical and anatomical characteristics. Although an experienced trauma surgeon confirmed these studies as comparable to ISS > 15, it still increases heterogeneity of the study population. In addition, the ISS has been regarded as the golden standard to define injury severity over the last decades (45-47). However, questions about the accuracy of the ISS have been raised. First, it does not account for multiple injuries in the same body region (48, 49). This could cause underscoring of the overall injury severity in patients with severe injury in one body region. Second, an equal AIS score in different body regions is assumed to be equal in injury severity (48, 50).

To the best of our knowledge, our search identified all studies that examined the relationship between volume of severely injured patients and mortality. Although most articles reported a positive relationship between volume and outcome, the cut-off of high volume and low volume hospitals was inconsistent across different studies. Some studies adopted the ACS-COT volume requirements of 240 or more severely injured patients per year, while other studies appeared to arbitrarily defined the volume cut-offs. This variance in cut-offs might be a good explanation for the difference in results. Although we tried to make equal volume groups, inconsistency in volume groups remained due to the limited available data. However, excluding even more studies in our meta-analysis would make our findings less generalizable.

Conclusion

In conclusion, this systematic review and meta-analysis revealed an association between larger hospital volume and lower mortality in severely injured patients. Our findings suggest that designation of high volume centers can improve outcomes among severely injured patients. Future studies with more rigorous methodological case mix adjustment, additional outcome measures and standardized cut-off values for high volume in combination with continuous analyses are needed to further define the effect of hospital volume on mortality and outcome of severely injured patients.

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Author Contributions

CS: literature search, study selection, data extraction, data-analysis, drafting the manuscript

EW: literature search, study selection, data extraction, data-analysis, drafting the manuscript

EV: study selection, data-analysis, critical revision of the manuscript

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Author, year	Unit	Study design	Country	Period	Data Source	Patients	Volume definition	Outcomes	Key findings (unadjusted and adjusted estimates)

Bennett, 2011	Hospital	RCS	USA	2001- 2006	NTDB	115,538	Categorical, 3 groups <240 240-480 >480	In-hospital mortality	There is a complex volume-outcome relationship for level I trauma centers in the United States. +
Cooper, 2000	Hospital	RCS	USA	1994- 1995	NYTR	26,793	Categorical, 3 groups <151 151-250 >250	In-hospital mortality	No association between hospital volume and health outcomes for trauma centers in New York State could be made. -
Cudnik, 2009	Hospital	RCS	USA	2003- 2006	OHTR	18,103	Level I vs Level II Level I: average of 110 patients per year Level II: average of 36 patients per year	In-hospital mortality, discharge locations	Severely injured patients have improved survival when taken to a Level I trauma center compared to those taken to level II trauma centers, which have a lower annual volume of trauma patients. +
Demetriades, 2005	Hospital	RCS	USA	1996- 2003	NTDB	12,254	Categorical, 2 groups <240 ≥240	In-hospital mortality, intensive care unit stay, severe	Health outcomes are not influenced by the volume of major trauma admissions. -

							Level I vs Level II	disability at discharge	
Endo, 2017	Hospital	RCS	Japan	2010 - 2015	DPC	116,329	Continuous + categorical, 5 groups 1-50 51-100 101-150 151-200 >200	Survival to hospital discharge, total health care cost per admission	Higher hospital volume was significantly associated with a survival benefit and lower total costs per admission in severe trauma patients. +
Freeman, 2006	Hospital	PCS	United Kingdom	1990-1993	RHD	2,190	Continuous	Mortality at 6 months	Severely injured patients had better health outcomes in higher volume departments. +
Glance, 2002	Hospital	RCS	USA	1999	NTDB	7,371	Continuous and categorical, 4 groups <140 140-261 262-462	In-hospital mortality	Higher trauma center volumes are not associated with improved patients outcomes. -

							>462		
Konvolinka, 1995	Hospital + Surgeon	RCS	USA	1988 - 1989	PTOS	13,002	Continuous	In-hospital mortality	Higher hospital volume does not contribute to better survival rates. - To achieve reasonable survival rates, surgeons need to treat at least approximately 35 seriously injured patients. +
London, 2003	Hospital	RCS	USA	1998 - 1999	RHD	98,245	Categorical and dichotomous (total trauma) <1200 ≥1200	In-hospital mortality, hospital length of stay	Health outcomes in low-volume centers were comparable to higher-volume centers. -
Lucas,	Hospital	RCS	USA	Feb 1997-	TCSR	25,020	Continuous	In-hospital mortality	Mortality decreased when centers admitted more severely injured

2001				June 2000					patients. +
Marx, 2001	Hospital	RCS	USA	2003-2006	NYTR	52,838	Categorical <180 vs ≥180 <240 vs ≥240	In-hospital mortality	An higher volume of severely injured patients contributes to lower in-hospital mortality. +
Margulies, 2000	Hospital + surgeon	RCS	USA	1998-1999	DHS-EMS TR	1,754	Continuous	In-hospital mortality	The volume of trauma institutions is associated with better survival in severely injured patients. + Surgeon volume, however does not contribute to better survival. -
Minei, 2014	Hospital	ARCT	USA & Canada	2006 - 2009	ROC	2222	Continuous and categorical (total trauma), 4 groups ≤1000 1001-1999 2000-2999	24 hour mortality, 28 day mortality, complications	Mortality decreased with increased total trauma center volume. +

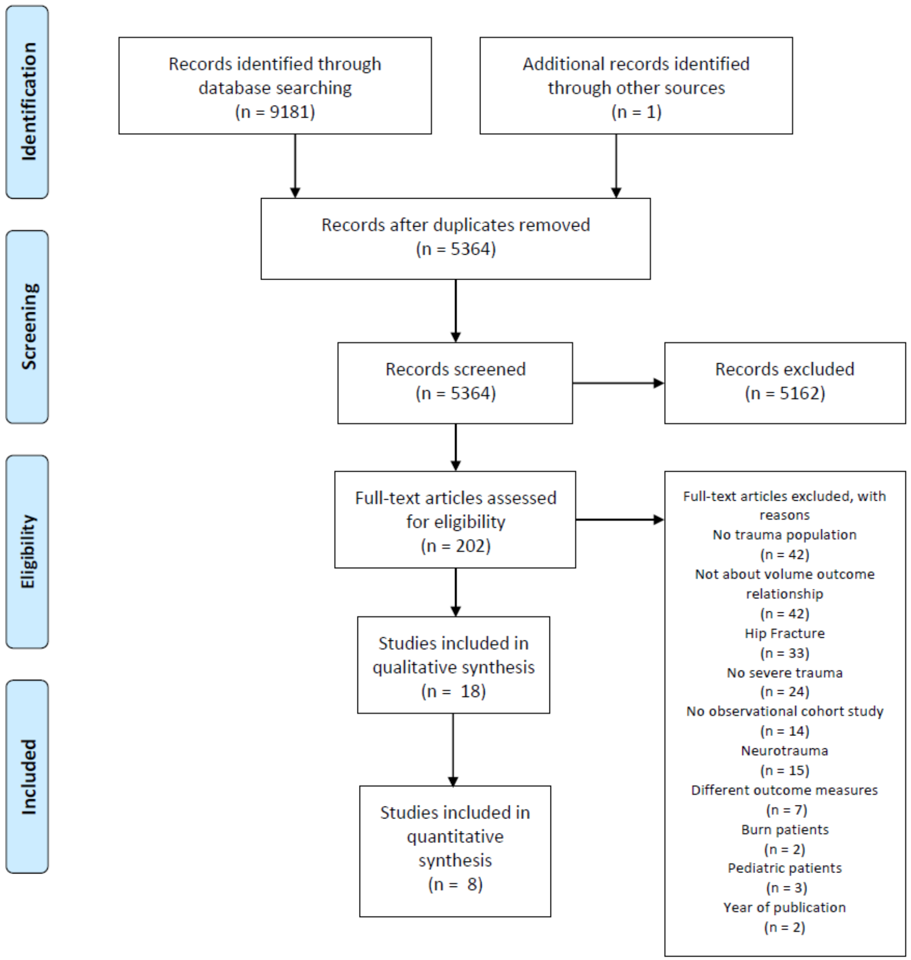
							≥3000		
Nathens, 2001	Hospital	RCS	USA	Nov 1997-Jul 1998	UHC	1019	Continuous	In-hospital mortality and hospital length of stay (LOS)	Patients outcomes strongly improve with higher trauma center volume. +
Olufajo, 2015	Hospital	RCS	USA	2007-2011	CSID	61,915	Categorical (total trauma), 2 groups <1200 ≥1200 Geriatric trauma volume per 100 increase	In-hospital mortality, Failure to rescue rate (FTR)	Higher geriatric trauma volume is associated with lower hospital mortality among geriatric patients. +
Pasquale, 2001	Hospital	PCS	USA	1992-1996	PTR	13,942	Categorical (total trauma), 2 groups <1200 ≥1200	In-hospital mortality	There exists an association between volume and in-hospital mortality. +
Sava, 2003	Surgeon	RCS	USA	1990-2001	RHD	20,695	Categorical, 2 groups ≤35	In-hospital mortality	Surgeon volume appeared to not influence outcome in severely injured patients.

							>35		-
Zacher, 2015	Hospital	RCS	Germany	2009-2013	DGU	39,289	Continuous + categorical, 5 groups 1-19 20-39 40-59 60-79 80-99 ≥100	In-hospital mortality	Hospital volume of severely injured patients was identified as a predictor of survival. +

Table 1 Overview of included articles

Abbreviations:
RCS = Retrospective Cohort Study
PCS = Prospective Cohort Study
USA = United States
ARCT = Analysis of Randomized Controlled Trials
NTDB = National Trauma Data Bank
NYTR = New York's Trauma Registry
OHTR = State of Ohio Trauma Registry
RHD = Regional Hospital Discharge
PTOS = Pennsylvania Trauma Outcome Study
TCSR = Trauma Center Survey Reports
ROC = multicenter trials network Resuscitation Outcomes Consortium?
DHS-EMS TR = Department of Health Services-Emergency Medical Services trauma registry
PTR = Pennsylvania Trauma Registry
UHC = University Healthsystem Consortium
CSID = California Sate Inpatient Database
DGU = Deutsche Geschellschaft für Unfallchirurgie
DPC = Japanese Diagnosis Procedure Combination

PRISMA 2009 Flow Diagram



From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). *P*referred *R*eporting *I*tems for *S*ystematic Reviews and *M*eta-*A*nalyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

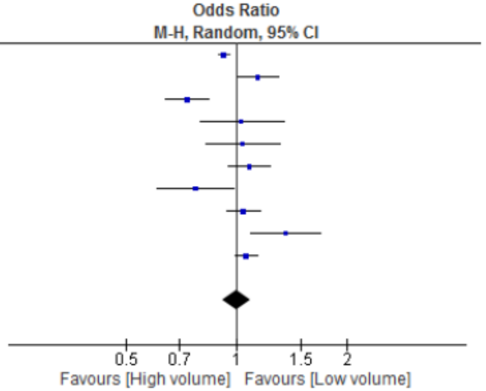
Figure 2: quality assessment

Study	Population-based	Nationwide	In- and exclusion criteria clearly described	Representative study population	Total number of severely injured patients reported	Number of patients per volume group reported	Cut-off volume groups clearly reported	OR/HR hospital-volume reported	OR/HR reported + 95% CI	Limited impact of loss of follow-up	Cleary stated in-hospital mortality	Crude ORs reported/ % mortality reported	Adjusted ORs reported	All confounders mentioned for adjusted OR	Adjusted for patients demographic characteristics	Adjusted for severity	Adjusted for trauma center level	Adjusted for mechanism of injury	None declared conflict of interests	Funding sources identified
Bennett et al.	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	-
Cooper et al.	+	-	+	+	+	+	+	-	-	+	+	+	-	-	-	-	-	-	-	-
Cudnik et al.	+	-	+	+	+	+	-	+	+	+	+	+	+	+	-	-	+	-	-	-
Demetriades et al.	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+	-	-
Endo et al.	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	+	+	-	+	+
Freeman et al.	+	-	+	+	+	+	+	-	-	+	-	+	-	-	-	-	-	-	-	-
Glance et al.	+	+	+	+	+	+	+	-	-	+	+	+	-	-	-	-	-	-	-	+
Konvolinka et al.	+	-	-	-	+	-	-	-	-	+	+	+	-	-	-	-	-	-	-	-
London et al.	+	-	+	+	+	-	+	+	-	+	+	-	+	+	+	+	+	-	-	-
Lucas et al.	+	-	-	+	+	+	-	-	-	+	+	+	-	-	-	-	-	-	-	-
Marx et al.	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-	-	-	-
Margulies et al.	+	-	+	+	+	+	+	-	-	+	-	+	-	-	-	-	-	-	-	+
Minei et al.	-	-	+	-	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	-
Nathens et al.	+	+	+	-	+	+	+	-	-	+	+	+	-	-	-	-	-	-	-	+
Olufajo et al.	+	-	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	+	-
Pasquale et al.	+	-	+	-	+	+	+	+	+	+	-	+	+	+	+	+	-	-	-	-
Sava et al.	+	-	-	+	+	+	+	-	-	+	-	+	-	-	-	-	-	-	-	-
Zacher et al.	+	+	+	+	+	+	+	-	+	+	+	+	+	-	+	+	-	-	+	-

Figure 3: In-hospital mortality unadjusted (A) and adjusted (B)

Study or Subgroup	High volume Events	High volume Total	Low volume Events	Low volume Total	Weight	Odds Ratio M-H, Random, 95% CI
Bennett, 2011	10837	74316	6398	41014	14.0%	0.92 [0.89, 0.96]
Cooper, 2000	494	3215	704	5135	11.1%	1.14 [1.01, 1.29]
Cudnik, 2008	687	3624	432	1790	10.6%	0.74 [0.64, 0.84]
Demetriades - Level I Trauma Centers, 2005	1173	4625	80	323	6.3%	1.03 [0.79, 1.34]
Demetriades - Level II Trauma Centers, 2005	215	725	193	668	7.2%	1.04 [0.82, 1.31]
Glance - Blunt Trauma, 2004	561	3055	553	3219	10.9%	1.08 [0.95, 1.23]
Glance - Penetrating Trauma, 2004	220	580	228	517	6.9%	0.77 [0.61, 0.99]
Lucas, 2001	915	13813	713	11207	12.0%	1.04 [0.94, 1.16]
Margulies, 2001	358	1112	166	642	7.6%	1.36 [1.10, 1.69]
Marx, 2011	1800	24876	1913	27962	13.2%	1.06 [0.99, 1.14]
Total (95% CI)		**129941**		**92477**	**100.0%**	**1.00 [0.92, 1.10]**
Total events	17260		11380			

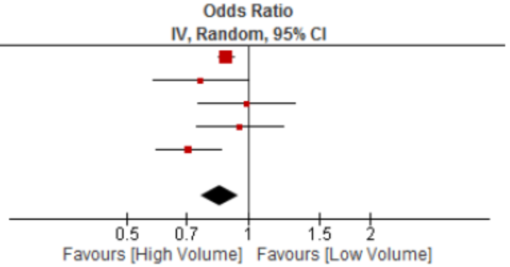
Heterogeneity: Tau² = 0.01; Chi² = 55.73, df = 9 (P < 0.00001); I² = 84%
Test for overall effect: Z = 0.08 (P = 0.93)



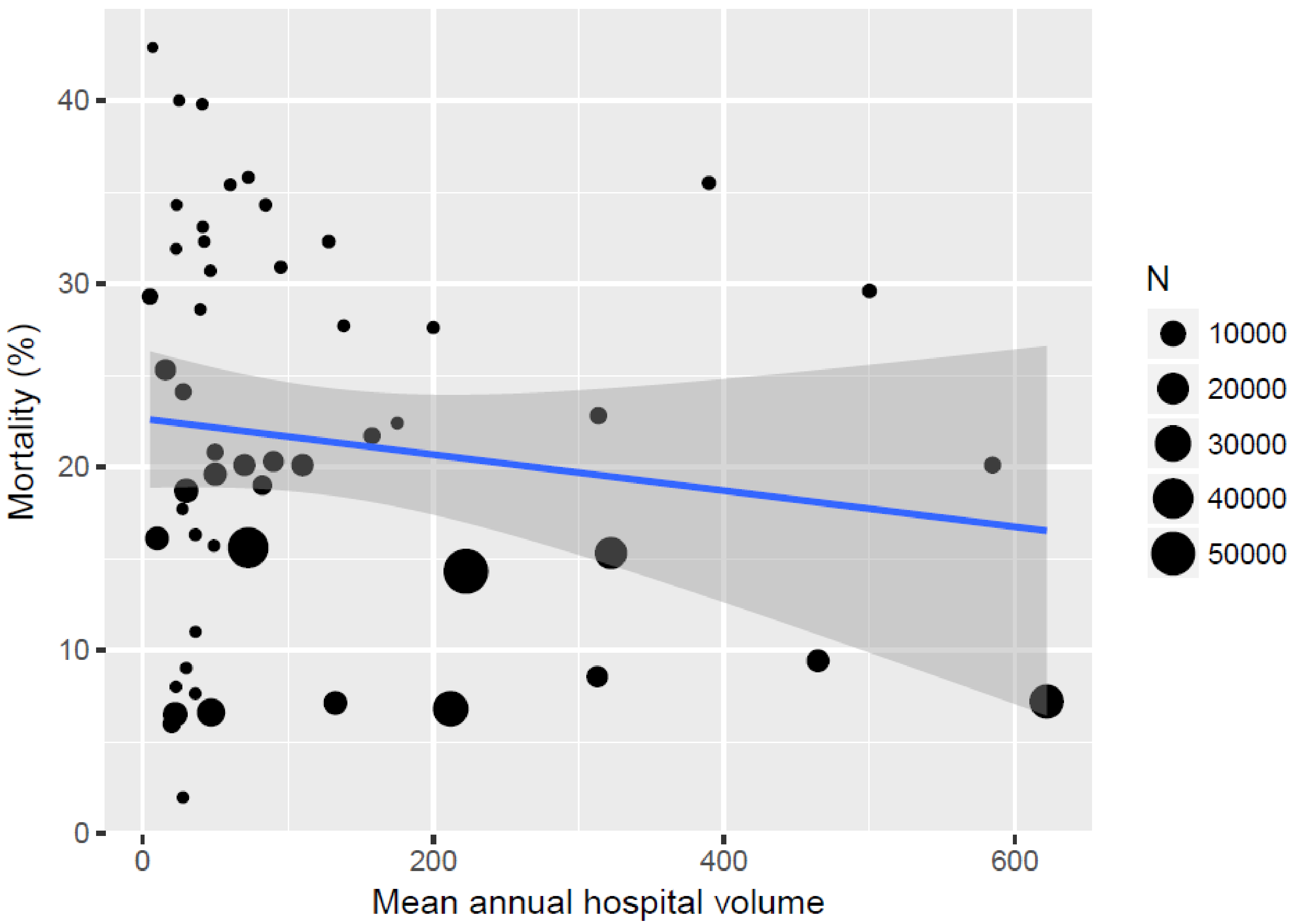
A: In-hospital mortality unadjusted

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Bennett, 2011	-0.1278	0.0237	44.0%	0.88 [0.84, 0.92]
Cudnik, 2008	-0.2744	0.1379	11.8%	0.76 [0.58, 1.00]
Demetriades - Level I Trauma Centers, 2005	-0.0101	0.1417	11.3%	0.99 [0.75, 1.31]
Demetriades - Level II Trauma Centers, 2005	-0.0513	0.1275	13.3%	0.95 [0.74, 1.22]
Marx, 2011	-0.3439	0.0952	19.5%	0.71 [0.59, 0.85]
Total (95% CI)			**100.0%**	**0.85 [0.76, 0.94]**

Heterogeneity: Tau² = 0.01; Chi² = 7.12, df = 4 (P = 0.13); I² = 44%
Test for overall effect: Z = 3.00 (P = 0.003)

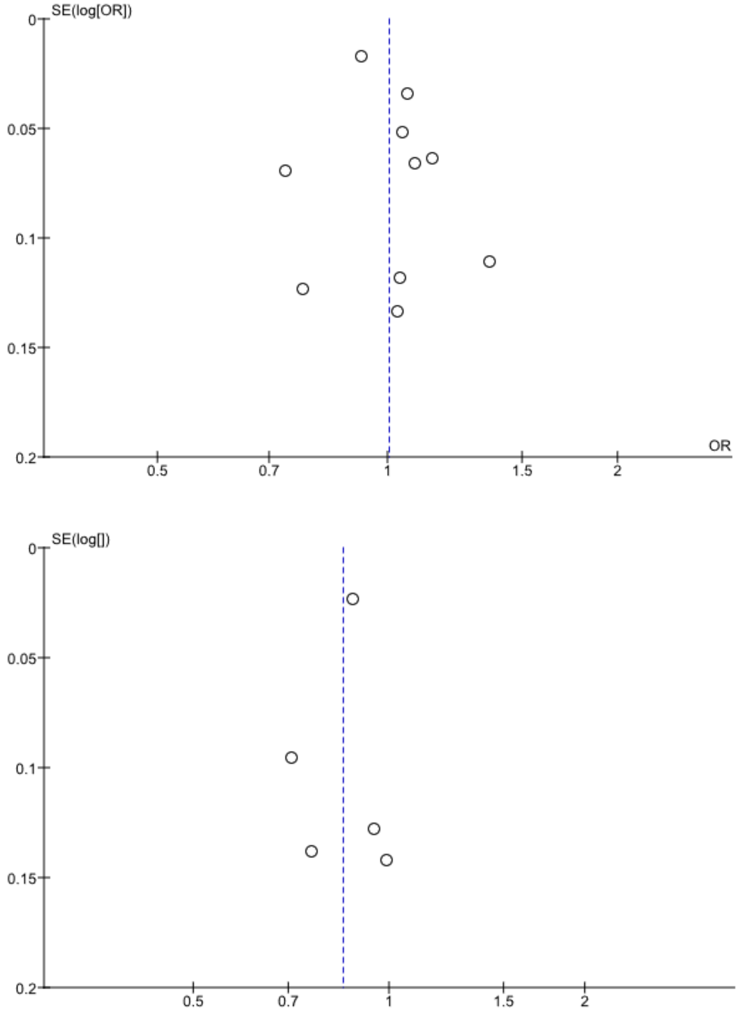


B: In-hospital mortality adjusted



Mortality (%)
40
30
20
10
0
0
200
400
600
Mean annual hospital volume
N
10000
20000
30000
40000
50000

Figure 5


SE(log[OR])
0
0.05
0.1
0.15
0.2
0.5
0.7
1
1.5
2
OR
SE(log[])
0
0.05
0.1
0.15
0.2
0.5
0.7
1
1.5
2