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Title Page

Impact of pre-hospital transfer strategies in major trauma and head injury: Systematic review, meta-analysis and recommendations for study design

Authors: Pickering A, Cooper K, Harnan S, Sutton A, Mason S, Nicholl J.

Corresponding author:

Alastair Pickering, Consultant in Emergency Medicine, MD

Emergency Department,

Hull Royal Infirmary

Hull & East Yorkshire Hospitals NHS Trust,

Anlaby Road, Hull, HU3 2JZ

Alastair.Pickering@hey.nhs.uk

Tel: 01482 602865, Fax: 01482 674058

Authors: (address below)

K. Cooper, Senior Research Fellow, PhD, k.l.cooper@sheffield.ac.uk

S. Harnan, Research Fellow, MSc, s.harnan@sheffield.ac.uk

A. Sutton, Information Specialist, MSc, a.sutton@sheffield.ac.uk

S. Mason, Professor of Emergency Medicine, MD, s.mason@sheffield.ac.uk

J. Nicholl, Dean, FMedSci, j.nicholl@sheffield.ac.uk

School of Health and Related Research,

University of Sheffield,

Regent Court,

30 Regent Street,

Sheffield, S1 4DA

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Abstract

Background: It is unclear whether trauma patients should be transferred initially to a trauma centre or local hospital.

Methods: A systematic review and meta-analysis assessed evidence for direct transport to specialist centres (SC) versus initial stabilisation at non-specialist centres (NSC) for major trauma or moderate-to-severe head injury. Nine databases were searched from 1988 to 2012. Limitations in study design informed recommendations for future studies.

Results: Of 19 major trauma studies, five (N=19,910) included patients not transferred to SC and adjusted for casemix. Meta-analysis showed no difference in mortality for initial triage to NSC vs. SC (odds ratio [OR] 1.03, 95% CI 0.85-1.23). Within studies excluding patients not transferred to SC, unadjusted analyses of mortality non-significantly favoured transfer via NSC (16 studies; N=37,079; OR 0.83, 95% CI 0.68 to 1.01) while adjusted analysis non-significantly favoured direct triage to SC (9 studies; N=34,266; OR 1.18, 95% CI 0.96 to 1.44). Of 11 head injury studies, all excluded patients not transferred to SC and half were in remote locations. There was no significant mortality difference between initial triage to NSC vs. SC within adjusted analyses (3 studies; N=1,507; OR 0.74, 95% CI=0.31-1.79) or unadjusted analyses (10 studies; N=3,671; OR 0.87, 95% CI=0.62-1.23).

Conclusions: This systematic review demonstrated no difference in outcomes for direct transport to a trauma centre versus initial triage to local hospital. Many studies had significant limitations in design and heterogeneity was high. Recommendations for future studies include: i) inclusion of patients not transferred to specialist centre and those dying during transport; ii) clear description of centres plus transport distances/times; iii) adjustments for casemix; and iv) assessment of morbidity as well as mortality.

Level of evidence: Systematic review and meta-analysis of predominantly Level IV studies (non-RCT, more than one negative criterion).

Keywords: trauma, head injury, transfer, systematic review, meta-analysis

Background

The development of regional major trauma centres as the hub of a network of hospitals for severely injured patients is a widely recognized model of care. Evidence from international studies demonstrates improved clinical outcomes in areas with regional trauma networks compared to models of care where severely injured patients are transferred to the nearest local hospital.[1;2] For example previous studies have shown the odds of death for major trauma patients with severe head injury in the UK based on Trauma Audit and Research Network (TARN) data was three times that in a mature regionalized trauma network in Australia (OR 3.22, 95% CI 2.84-3.65).[3]

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However, the decision to bypass the nearest hospital to transfer a patient directly to a regional major trauma centre is difficult and dependent on pre-hospital clinical assessment and prioritisation. From the trauma and head injury literature, trauma centres have reported improved clinical outcomes when compared with care in a non-specialist centre.[4] However, the benefits of early correction of hypoxia and hypotension are also recognised for improving outcomes,[5-8] and this would more likely be achieved quickly by delivery of patients to the nearest hospital. Current opinion supports the direct transfer of major trauma and head injured patients to the major trauma centre from the point of injury, but the evidence for this strategy remains unclear.

Working from an underlying assumption that the best outcomes for patients are achieved through management in a specialist centre, the aim of this study was to review the current evidence for a policy of triage and direct transfer to the specialist (major trauma) centre (SC) compared with initial transfer to the local hospital, with secondary transfer to the SC if appropriate, for patients experiencing severe multi-system trauma or moderate-to-severe head injury. The methodological limitations of included studies are also reviewed, and used to generate recommendations for future studies in this area.

Methods

A systematic review was undertaken according to the general principles recommended in the PRISMA statement.[9]

Search strategy

The following databases were searched: MEDLINE; MEDLINE In-Process; EMBASE; CINAHL; Cochrane Library including Cochrane Database of Systematic Reviews, Cochrane CENTRAL Controlled Trials Register, DARE, NHS EED and HTA databases, with relevant bibliographies, from 1988 to December 2012. The search was limited to articles published from 1988 onwards, as the organisation of emergency care has changed significantly since studies published before that date. A full search strategy is available from the authors on request.

Screening of retrieved articles

A title and initial abstract sift were undertaken by two reviewers, with involvement of a third reviewer where necessary. Potentially relevant articles were then fully screened by two reviewers and any uncertainties resolved through discussion with a third reviewer. Data were extracted by one reviewer and checked by a second.

Included populations and outcomes

Studies of major trauma (defined as an Injury Severity Score of >15 or other clear definition) or moderate-to-severe head injury (defined as Glasgow Coma Scale <13 or other clear definition) were included. The review was restricted to more severe cases since these patients were considered more likely than less severe cases to benefit from treatment in a specialist centre.(11-13)[10-12] Relevant outcomes included mortality, morbidity, length of stay, time and distance data.

Included study design

Studies were included if they compared patients directly triaged to a specialist centre (SC) versus those initially triaged to a non-specialist centre (NSC) with some or all later transferred to a SC. Studies were excluded if they compared patients ever treated in a SC versus those never treated in a SC, since the aim was to assess the optimum initial triage route rather than the optimum location for overall management.

Risk of bias assessment

A bespoke tool for assessing risk of bias in included studies was developed for this review, based on relevance to the research question and robustness of analysis methods. This included four criteria:

1. Whether NSC group included (or adjusted for exclusion of) patients not transferred to SC
2. Whether analyses were adjusted for differences in age and severity between groups
3. Whether sample included all relevant patients (rather than restricting to specific clinical subtypes or those receiving specific intervention)
4. Whether no more than 5% patients were excluded from analyses due to missing data.

Data synthesis

Study data were meta-analysed using Review Manager version 5.0.12. Random effects models were used where clinical or statistical heterogeneity existed between studies. Data were converted so all odds ratios (ORs) compared initial triage to NSC versus direct triage to

SC; similarly, ORs for survival were converted to mortality. Hence for the presented mortality data an OR greater than 1 favours the direct to SC cohort, whilst for morbidity data (reporting on favourable outcomes) an OR greater than 1 favours the initial triage to NSC group.

Results

Number of retrieved studies

The literature search for this review (and for a wider review of emergency triage) identified 7767 references, of which 193 were examined as full texts. In total, 19 studies of trauma (within 20 references) and 11 studies of head injury (within 11 references) were included in this review. One reference covered both trauma and head injury. The PRISMA diagram is included as Appendix 1 and the PRISMA checklist as Appendix 2.

Major trauma: included studies

The study characteristics for the trauma studies are shown in Table 1. All nineteen studies of trauma (within 20 references)[13-32] were controlled cohort studies; no randomised studies were identified. Eight studies were conducted in the USA,[15;18-20;24;25;30;31] four in Canada,[13;21;23;25] two in Australia,[26;27] one in Hong Kong,[22] one in Taiwan[28] and three in Europe.[14;16;17] Study size ranged from 222 to 11,398 patients. Thirteen studies identified major trauma patients based on ISS>15,[13;14;16;17;19;20;22;24-28] two Canadian studies based on ISS>12 (included since this appeared to be the standard definition of major trauma in this setting),[21;23] one based on ISS>24,[31] one based on ≥1 injury with Abbreviated Injury Scale (AIS) ≥ 3,[15] and two based on other parameters.[18;30]

The SC was described in thirteen studies as a Level I trauma centre or equivalent,[14-16;18;20-25;28;30;31] with the other six studies using different criteria (Table 1).[13;17;19;25-27] NSCs were described in four studies as Level II-IV trauma centres[16;21;23;30] and in the remainder as non-trauma centres or other hospitals (Table 1). The majority of trauma studies excluded deaths before arrival at the SC; two excluded deaths before arrival at either the SC or NSC;[13;16] one included pre-hospital deaths,[14] two presented data including and excluding these deaths,[17;22] and for three this was not reported or was unclear.[26;27;31]

Head injury: included studies

The study characteristics for the head injury studies are shown in Table 1.

All eleven studies of head injury were controlled cohort studies;[23;33-42] no randomised studies were identified. Study size varied from 60 to 1,118 patients. Two studies were conducted in the USA,[37;38] two in Canada,[23;33] three in Norway,[35;36;39] one in New Zealand,[34] one in Taiwan,[40] one in the Netherlands[41] and one in Israel.[42] Study size varied from 60 to 1,118 patients. Five studies included patients with severe head injury (GCS≤8);[33;35;36;38;40] one with moderate-to-severe head injury (GCS≤12);[37] two with AIS≥3 for head injury;[23;34] and three with brain injury requiring neurosurgery.[39;41;42]

All studies described the specialist centre as having neurosurgical care available (or as a Level I trauma centre). NSCs were described as local hospitals, non-trauma centres or (in one study) Level II-III trauma centres.[23] All studies excluded deaths before SC arrival, except one which excluded deaths before transfer to SC;[37] one study excluded deaths before neurosurgery.[39]

Risk of bias in included studies

Four criteria assessing risk of bias and relevance to the research question were assessed (Box 1). Only one-third of trauma studies and none of the head injury studies included or adjusted for patients not transferred to SC. Around half of the trauma studies and a quarter of head injury studies adjusted for differences in age and severity between groups. The majority of trauma and head injury studies included all relevant patients (rather than restricting to specific clinical subtypes or those receiving specific interventions). Finally, around a quarter of trauma studies and half of the head injury studies excluded no more than 5% of patients from the analyses due to missing data (the majority of the remainder did not report sufficient data to assess this). These findings partially inform the recommendations below.

Box 1: Risk of bias due to study designs

Risk of bias criteria	**n/N (%) studies with low risk of bias**
1) NSC group includes or adjusts for patients not transferred to SC	Trauma: 7/19 (37%) Head injury: 0/11 (0%)
2) Analyses adjusted for differences in age and severity between groups	Trauma: 11/19 (58%) Head injury: 3/11 (27%)
3) Sample includes all relevant patients (not just specific clinical subtypes/interventions)	Trauma: 17/19 (89%) Head injury: 8/11 (73%)
4) No more than 5% patients excluded from analyses due to missing data	Trauma: 5/19 (26%) (additional 13/19 (68%) unclear risk) Head injury: 5/11 (45%) (additional 5/11 (45%) unclear risk)

Mortality data

Trauma

All nineteen trauma studies reported mortality; this was measured at one year in one study[15] and one month in five studies;[13;14;16;18;30] the remainder reported in-hospital mortality (this was assumed where unclear). Follow-up durations are shown on the meta-analysis figures.

Only seven studies accounted for all patients initially triaged to NSC (whether or not they were later transferred to SC), either by including these patients directly or by adjusting for their exclusion.[13-17;26;27] Of these seven studies, five adjusted for age and severity in the analyses of mortality.[13-15;26;27] These five studies were considered the highest quality, although their design was heterogeneous (factors contributing to this heterogeneity are discussed below). One Canadian study significantly favoured direct transfer to SC,[13] one study in the Netherlands non-significantly favoured initial transfer to NSC,[14] and three studies in the USA and Australia showed no difference between groups.[15;26;27] A meta-analysis of these five studies (total N=19,910) showed no difference in mortality between groups (OR for NSC vs. SC = 1.03, 95% CI 0.85 to 1.23) with a moderate level of heterogeneity (I^2=47%); see Table 2 and Figure 1. Meta-analysis of the unadjusted data for six studies which included all patients initially triaged to NSC (total N=17,523) also showed no statistically significant difference in mortality between groups (OR 1.04, 95% CI 0.72 to 1.50) with a high level of heterogeneity (I^2=94%).

The remaining studies only compared patients transferred from NSC to SC versus those directly triaged to SC, generally because the data was obtained from SC databases. Unadjusted analysis of mortality for sixteen studies (N=37,079) showed a non-significant trend favouring initial triage to the NSC (OR 0.83, 95% CI 0.68 to 1.01, I^2=86%). Conversely, adjusted analysis of 9 studies (N=34,266) non-significantly favoured direct triage to SC (OR 1.18, 95% CI 0.96 to 1.44, I^2=77%). (Table 2; Figure 2). This demonstrates the potential effect of adjusting for casemix and the importance of caution when interpreting results.

Head injury

All eleven head injury studies reported mortality. This was reported in-hospital for six studies,[23;33;34;37;40;42] at 2 weeks in one study,[38] 1 month in one study,[41] 6 months in two studies,[35;36] and ranged from 2-76 months in one study;[39] follow-up durations are shown on the meta-analysis figures following the author and date. All eleven studies of head injury compared transfers from NSC to SC versus direct triage to SC; no studies included or accounted for NSC patients who were not transferred to SC. Most studies were conducted in remote areas and involved long transport distances.

Only three studies adjusted for age and severity in the analyses of mortality. Two non-significantly favoured transfer: a study in Norway involving long transfer times (times to SC arrival were 5.5h for transfer group and 1.8h for direct group)[36] and a study in Taiwan where most traumas occurred within 30 mins of a hospital.[40] The other study significantly favoured direct triage to SC; this study in New York state covered urban and rural areas (times to SC arrival were 4.5h for transfer group and 1.1h for direct group).[38] Meta-analysis of these three studies (total N=1,507) showed no significant difference in mortality between groups (OR for transfers vs. direct = 0.74, 95% CI 0.31 to 1.79); heterogeneity was high (I^2=80%) and the meta-analysis should be interpreted with caution as the included studies showed different directions of effect (Table 2; Figure 3).

Ten studies reported unadjusted mortality data. A meta-analysis (total N=3,671) again showed no significant difference between groups (OR for transfers vs. direct = 0.87 95% CI 0.62 to 1.23, I^2=66%); see Table 2 and Figure 4. The meta-analysis is sub-grouped by country/continent and urban or rural area: one urban study significantly favoured direct triage to SC, four studies in urban/rural areas or with short transport distances showed no significant difference, while four of five studies in rural areas involving long transfer distances favoured transfer (two statistically significant). While this pattern makes intuitive sense, further studies in urban areas would be required to confirm this finding. In addition, exclusion of transport deaths may skew results within studies involving long transport distances.

Morbidity data

No trauma studies reported morbidity outcomes. Limited morbidity data were reported for head injury studies. Four studies reported median Glasgow Outcome Scale (GOS) at follow-up,[35;36;39;41] with one study also reporting the number of patients with a favourable GOS score of 4-5;[39] two studies reported the number discharged home.[37;42] There was no clear difference between groups on these outcomes (Table 3).

Length of stay

Seven studies of trauma and three of head injury reported length of stay in hospital and/or intensive care unit (ICU). Hospital/ICU stays were longer for patients initially triaged to NSC than for those directly triaged to SC in all trauma studies and two of three head injury studies, though differences were not statistically significant (Table 4).

Time and distance data

For trauma, little data were reported in terms of urban or rural setting and distances between centres. Six studies reported longer times from injury to SC arrival for patients initially triaged to NSC than for those directly triaged to SC;[17;24;26-28;30] this information was not reported for other studies. These data were somewhat better reported for head injury studies. Times from injury to SC arrival were longer for transferred patients than for direct triage to SC in all seven studies reporting this;[34-39;41] times from injury to neurosurgery were also longer for transfers in the five studies reporting this.[34;36;39;41;42]

Discussion

Principal findings

Overall, thirty relevant articles were included, investigating over 50,000 patients, but there was significant heterogeneity between studies and limitations in study methodology affecting the ability to draw any definitive conclusions. Within the remit of the search strategy nineteen relevant studies of major trauma were included, of which only five accounted for all patients initially triaged to NSC and adjusted for age and severity. Meta-analysis of these five studies showed no difference in mortality between those directly transferred to the SC and those initially triaged to the NSC.

Eleven studies of head injury were included, half of which were conducted in rural or remote geographical locations. All were restricted to comparing transfer from NSC to SC with direct triage to SC; none included patients remaining at the NSC. Meta-analyses showed no significant difference between initial triage to NSC and direct transfer to SC in either adjusted or unadjusted analyses. Studies in rural areas with long transport distances appeared more likely to favour initial triage to NSC than studies in mixed urban/rural areas (which showed little difference between groups), though the exclusion of patients dying before SC arrival may have skewed results.

Strengths and limitations of this review

This study has systematically reviewed the published evidence around triage strategies, following major trauma and significant head injury (moderate to severe), for delivery to a specialist centre. Within this a structured assessment of the risk of bias has been performed, with a bespoke tool designed for this review, which has identified a number of deficiencies in methodology across the included studies. These have impacted on the ability to perform robust meta-analyses and limited the generalisability of study findings. One example is shown in our analysis of major trauma studies that only compare transfers from NSC to SC versus direct triage to SC. Analysis of unadjusted mortality data favoured transfer via NSC while using adjusted data favoured direct triage to SC, demonstrating the importance of appropriate adjustment for confounders.

Previous reviews

A previous review by Hill et al. (2011)[43] also assessed the effects of direct transport versus inter-hospital transfer for trauma patients. Their inclusion criteria differed somewhat from ours, mainly in that inclusion was not restricted by trauma severity. Thirteen studies were included in both reviews. The review by Hill et al. included 22 studies which did not meet our inclusion criteria (12 not restricted to severe trauma; 2 very specific trauma types; 3 for paediatric injuries; 3 with data collected pre-1988; 1 with no relevant data and 1 without appropriate study design). We included ten studies not in the Hill et al. review.

The authors present meta-analyses for mortality, in which most studies excluded patients not transferred from the NSC. The OR for mortality for initial triage to NSC vs. direct to SC was 1.04 (95% CI=0.88-1.22) with significant heterogeneity (I^2=82%). These findings concur with ours in that there is no clear evidence for a difference in mortality between these transfer pathways for major trauma patients. One major difference from our review is their inclusion of all severities of trauma, which may not reflect the population most likely to benefit from direct transfer to a specialist centre and could lead to undue influence of studies demonstrating no significant difference between strategies as a result of the lesser severity of injuries being investigated.

Implications of the review findings

The findings of this review led to the conclusion that there is no significant difference in mortality rates between the two triage strategies compared. The methodological frailties and heterogeneity identified mean that this cannot be considered a definitive conclusion. For policymakers and clinicians this means that the findings of this review do not contradict the current national recommendations around triage and transfer decisions following significant injury in the UK. Future recommendations should be based on better quality evidence than is currently available and robust evaluations of the current systems.

Review of study designs and recommendations for future research

Based on our review of study designs and the limitations of existing studies, we recommend the following for future studies aiming to compare triage strategies (Box 2).

Box 2: Limitations in study design to be addressed in future studies

Recommendations	Rationale
Selection of study cohorts	
5) Inclusion of all major trauma patients triaged to local hospital, whether or not later transferred to specialist centre	Assessment of system effectiveness should include all severely injured patients within the system measured from the point of injury
6) Exclusion of patients for whom the specialist centre is the nearest hospital	This subgroup of patients will not be affected by triage decisions and contaminate any analysis of outcomes based on this pre-hospital decision-making
7) Inclusion of patients dying during transport/transfer (both to the initial hospital and from NSC to SC)	To robustly compare two different strategies of delivery, from the point of injury, it is important to include all patients prospectively. Failure to do this may mean that the effects of transporting injured patients long distances are not taken into account
Data collection and analysis	
8) Adjustment for clinical factors such as age and injury severity	Adjusting for clinical factors such as age and severity which are known to affect outcomes is vital for providing a fair comparison between systems
9) Reporting of outcomes at different time points (including in-hospital) and reporting of morbidity as well as mortality outcomes	Mortality outcomes, when assessing bypass or triage decisions, should be reported early (e.g. in-hospital) to avoid confounding by other factors in the patient pathway. Reporting key morbidity outcomes in addition to mortality is important when assessing the effect of triage decisions
Description of centres and settings	

10) Clear description of specialist and non-specialist hospitals being compared	Specific facilities available at each SC and NSC are not always consistently described within existing studies and so sub-grouping the level of care to perform a meaningful analysis was not possible
11) Clear reporting of geographical setting and distances and times for each group to arrive at the initial hospital and the specialist centre	Descriptions of setting, level of rurality, distances and transfer times (both to initial hospital and to specialist centre) should all be reported in order to improve generalisability of study findings

Conclusion

A comprehensive systematic review of the current literature for major trauma and moderate-to-severe head injury does not demonstrate evidence of any difference in clinical outcomes for initial triage to local hospital (with potential for later transfer) versus direct transport to a specialist centre.

Many studies had significant limitations in design and there was marked heterogeneity between studies. There is a need for high quality research in a UK setting. Future research should concentrate on prospective, comprehensive data collection from the point of injury, include appropriate adjustments for confounders, and consider reporting on a wider range of relevant outcomes.

Author contributions

JN conceived the idea for the study and oversaw its running; SM assisted AP in the clinical aspects of the study and overall coordination; KC, AS & SH performed the literature searches, systematic review and meta-analysis; all authors listed made significant contributions to the final report and drafting of the article.

References

(1) Celso B, Tepas J, Langland-Orban B, Pracht E, Papa L, Lottenberg L et al. A systematic review and meta-analysis comparing outcome of severely injured patients treated in trauma centers following the establishment of trauma systems. Journal of Trauma-Injury Infection & Critical Care 2006; 60(2):371-378.

(2) Mann CN, Mullins RJ, Mackenzie EJ, Jurkovich GJ, Mock CN. Systematic Review of Published evidence regarding trauma system effectiveness. Journal of Trauma-Injury Infection & Critical Care 1999; 47(3 Suppl).

(3) Gabbe BJ, Lecky FE, Bouamra O, Woodford M, Jenks T, Coats TJ et al. The Effect of an Organized Trauma System on Mortality in Major Trauma Involving Serious Head Injury: A Comparison of the United Kingdom and Victoria, Australia. Annals of Surgery 2011; 253(1):138-143.

(4) Patel HC, Bouamra O, Woodford M, King AT, Yates DW, Lecky FE et al. Trends in head injury outcome from 1989 to 2003 and the effect of neurosurgical care: an observational study. Lancet 2005; 366(9496):1538-1544.

(5) Chesnut RM, Marshall LF, Klauber MR, Blunt BA, Baldwin N, Eisenberg HM et al. The role of secondary brain injury in determining outcome from severe head injury. Journal of Trauma-Injury Infection & Critical Care 1993; 34(2):216-222.

(6) Jeremitsky E, Omert L, Dunham CM, Protetch J, Rodriguez A. Harbingers of poor outcome the day after severe brain injury: hypothermia, hypoxia, and hypoperfusion. Journal of Trauma-Injury Infection & Critical Care 2003; 54(2):312-319.

(7) Manley G, Knudson MM, Morabito D, Damron S, Erickson V, Pitts L. Hypotension, Hypoxia, and Head Injury: Frequency, Duration, and Consequences. Arch Surg 2001; 136:1118-1123.

(8) Moppett IK. Traumatic brain injury: assessment, resuscitation and early management. British Journal of Anaesthesia 2007; 99(1):18-31.

(9) Moher D, Liberati A, Tetzlaff J, Altman DG. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. Ann Intern Med 2009; 151(4):264-9, W64.

(10) Nathens AB, Jurkovich GJ, Maier RV, Grossman DC, MacKenzie EJ, Moore M et al. Relationship between trauma center volume and outcomes. JAMA: Journal of the American Medical Association 2001; 285(9):1164-1171.

(11) Demetriades D, Martin M, Salim A, Rhee P, Brown C, Doucet J et al. Relationship between American College of Surgeons trauma center designation and mortality in patients with severe trauma (injury severity score > 15). Journal of the American College of Surgeons 2006; 202(2):212-215.

(12) Demetriades D, Martin M, Salim A, Rhee P, Brown C, Chan L. The effect of trauma center designation and trauma volume on outcome in specific severe injuries. Annals of Surgery 2005; 242(4):512-517.

(13) Haas B, Gomez D, Zagorski B, Stukel TA, Rubenfeld GD, Nathens AB. Survival of the fittest: the hidden cost of undertriage of major trauma. Journal of the American College of Surgeons 2010; 211(6):804-811.

(14) de Jongh MA, Meeuwis JD, van Baar ME, van Stel HF, Schrijvers AJ. Evaluation of trauma care by comparing mortality risks and admission policy in a Dutch trauma region. Injury 2008; 39(9):1007-1012.

(15) Rivara FP, Koepsell TD, Wang J, Nathens A, Jurkovich GA, MacKenzie EJ. Outcomes of trauma patients after transfer to a level I trauma center. Journal of Trauma-Injury Infection & Critical Care 2008; 64(6):1594-1599.

(16) Biewener A, Aschenbrenner U, Rammelt S, Grass R, Zwipp H. Impact of helicopter transport and hospital level on mortality of polytrauma patients. Journal of Trauma-Injury Infection & Critical Care 2004; 56(1):94-98.

(17) Nardi G, Massarutti D, Muzzi R, Kette F, de Monte A, Carnelos GA et al. Impact of emergency medical helicopter service on mortality for trauma in north-east Italy. A regional prospective audit. European Journal of Emergency Medicine 1994; 1(2):69-77.

(18) Nirula R, Maier R, Moore E, Sperry J, Gentilello L. Scoop and run to the trauma center or stay and play at the local hospital: hospital transfer's effect on mortality. Journal of Trauma-Injury Infection & Critical Care 2010; 69(3):595.

(19) Clancy TV, Maxwell JG, Covington DL, Brinker CC, Blackman D. A statewide analysis of level I and II trauma centers for patients with major injuries. Journal of Trauma-Injury Infection & Critical Care 2001; 51(2):346-351.

(20) O'Keefe GE, Jurkovich GJ, Copass M, Maier RV. Ten-year trend in survival and resource utilization at a level I trauma center. Annals of Surgery 1999; 229(3):409-415.

(21) Sampalis JS, Denis R, Lavoie A, Frechette P, Boukas S, Nikolis A et al. Trauma care regionalization: a process-outcome evaluation. Journal of Trauma-Injury Infection & Critical Care 1999; 46(4):565-579.

(22) Kam CW, Kitchell AK, Yau HH, Kan CH. Outcome of major trauma patients in a Hong Kong general hospital. European Journal of Emergency Medicine 1998; 5(3):297-306.

(23) Sampalis JS, Denis R, Frechette P, Brown R, Fleiszer D, Mulder D. Direct transport to tertiary trauma centers versus transfer from lower level facilities: impact on mortality and morbidity among patients with major trauma. Journal of Trauma-Injury Infection & Critical Care 1997; 43(2):288-295.

(24) Young JS, Bassam D, Cephas GA, Brady WJ, Butler K, Pomphrey M. Interhospital versus direct scene transfer of major trauma patients in a rural trauma system. American Surgeon 1998; 64(1):88-91.

(25) Boulanger BR, McLellan BA, Sharkey PW, Rizoli S, Mitchell K, Rodriguez A. A comparison between a Canadian regional trauma unit and an American level I trauma center. Journal of Trauma-Injury Infection & Critical Care 1993; 35(2):261-266.

(26) Fatovich DM, Phillips M, Jacobs IG. A comparison of major trauma patients transported to trauma centres vs. non-trauma centres in metropolitan Perth. Resuscitation 2011; 82(5):560-563.

(27) Fatovich DM, Phillips M, Langford SA, Jacobs IG. A comparison of metropolitan vs rural major trauma in Western Australia. Resuscitation 2011; 82(7):886-890.

(28) Hsiao KY, Lin LC, Chou MH, Chen CC, Lee HC, Foo NP et al. Outcomes of trauma patients: direct transport versus transfer after stabilisation at another hospital. Injury 2012; 43(9):1575-1579.

(29) Garwe T, Cowan LD, Neas BR, Sacra JC, Albrecht RM, Rich KM. A propensity score analysis of prehospital factors and directness of transport of major trauma patients to a level I trauma center. Journal of Trauma-Injury Infection & Critical Care 2011; 70(1):120-129.

(30) Garwe T, Cowan LD, Neas BR, Sacra JC, Albrecht RM. Directness of transport of major trauma patients to a level I trauma center: a propensity-adjusted survival analysis of the impact on short-term mortality. Journal of Trauma-Injury Infection & Critical Care 2011; 70(5):1118-1127.

(31) Koczirka S, Tinkoff G, Jones M, Marco DR, Reed JF, Megargel RE. Trends in the overall mortality rate in severely injured trauma patients transported from scene to a level i trauma center from 1998-2007. Annals of Emergency Medicine Conference: American College of Emergency Physicians, ACEP 2011 Research Forum San Francisco, CA United States Conference Start: 20111015 Conference End: 20111016 Conference Publication: (var pagings) 2011; 58(4 SUPPL.#1):October.

(32) Haas B, Stukel TA, Gomez D, Zagorski B, de MC, Sharma SV et al. The mortality benefit of direct trauma center transport in a regional trauma system: A population-based analysis. Journal of Trauma and Acute Care Surgery 2012; 72(6):June.

(33) Simons R, Brasher P, Taulu T, Lakha N, Molnar N, Caron N et al. A population-based analysis of injury-related deaths and access to trauma care in rural-remote Northwest British Columbia. Journal of Trauma-Injury Infection & Critical Care 2010; 69(1):11-19.

(34) Kejriwal R, Civil I. Time to definitive care for patients with moderate and severe traumatic brain injury--does a trauma system matter? New Zealand Medical Journal 2009; 122(1302):40-46.

(35) Moen KG, Skandsen T, Karlsen BH, Hara S, Solheim O, Strand IH et al. Patients with severe head injury in Norway - transfer and outcome. Journal of Neurotrauma 2009; 26(8):A35 Abstract P132.

(36) Moen KG, Klepstad P, Skandsen T, Fredriksli OA, Vik A. Direct transport versus interhospital transfer of patients with severe head injury in Norway. European Journal of Emergency Medicine 2008; 15(5):249-255.

(37) Tiesman H, Young T, Torner JC, McMahon M, Peek-Asa C, Fiedler J. Effects of a rural trauma system on traumatic brain injuries. Journal of Neurotrauma 2007; 24(7):1189-1197.

(38) Hartl R, Gerber LM, Iacono L, Ni Q, Lyons K, Ghajar J. Direct transport within an organized state trauma system reduces mortality in patients with severe traumatic brain injury. Journal of Trauma-Injury Infection & Critical Care 2006; 60(6):1250-1256.

(39) Sollid S, Munch-Ellingsen J, Gilbert M, Ingebrigtsen T. Pre- and inter-hospital transport of severely head-injured patients in rural Northern Norway. Journal of Neurotrauma 2003; 20(3):309-314.

(40) Hsiao KY, Chen IC, Yang CJ, Hsiao CT, Chen KH. Is direct transport to a trauma centre best for patients with severe traumatic brain injury? A study in south-central Taiwan. EMERG MED J 2012; 29(2):156-159.

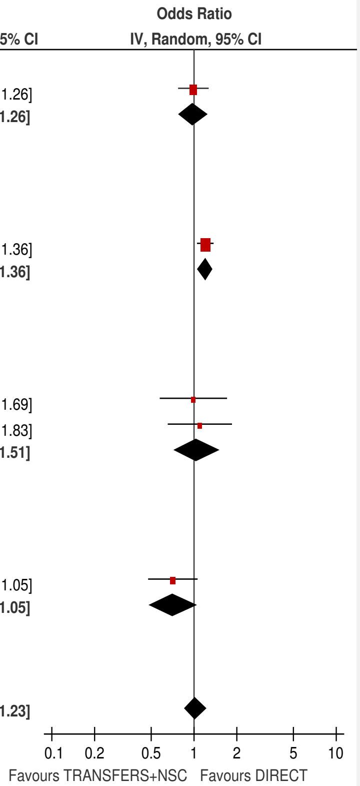
(41) Joosse P, Saltzherr TP, van Lieshout WA, van EP, Ponsen KJ, Vandertop WP et al. Impact of secondary transfer on patients with severe traumatic brain injury. The Journal of Trauma and Acute Care Surgery 2012; 72(2):487-490.

(42) Lin G, Teplitsky A, Hymas G, Bahouth H. Evacuation of wounded with intracranial injury to a hospital without neurosurgical service versus primary evacuation to a level I trauma centre. Injury 2012; 43(12):2136-2140.

(43) Hill AD, Fowler RA, Nathens AB. Impact of interhospital transfer on outcomes for trauma patients: a systematic review. J TRAUMA 2011; 71(6):1885.

Figure 1: Trauma: Adjusted mortality for initial triage to NSC vs. direct triage to SC (includes or adjusts for patients not transferred from NSC)

Study or Subgroup	log[Odds Ratio]	SE	TRANSFERS+NSC Total	DIRECT Total	Weight	Odds Ratio IV, Random, 95% CI
3.1.1 USA: transfers adjusted for NSC deaths vs. direct to SC (excluded transport deaths)						
Rivara 2008 (1y)	-0.01005	0.1216	863	2150	26.4%	0.99 [0.78, 1.26]
Subtotal (95% CI)			**863**	**2150**	**26.4%**	**0.99 [0.78, 1.26]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 0.08 (P = 0.93)						
3.1.2 Canada: transfers + NSC deaths vs. direct to SC (excluded transport deaths)						
Haas 2010 (1m)	0.1823	0.0633	3917	7481	38.6%	1.20 [1.06, 1.36]
Subtotal (95% CI)			**3917**	**7481**	**38.6%**	**1.20 [1.06, 1.36]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 2.88 (P = 0.004)						
3.1.3 Australia: transfers + NSC deaths vs. direct to SC (unclear if included transport deaths)						
Fatovich 2011a (in-hosp)	-0.01	0.2728	1152	2005	9.6%	0.99 [0.58, 1.69]
Fatovich 2011b (in-hosp)	0.095	0.2606	1443	2005	10.3%	1.10 [0.66, 1.83]
Subtotal (95% CI)			**2595**	**4010**	**19.8%**	**1.05 [0.72, 1.51]**
Heterogeneity: Tau² = 0.00; Chi² = 0.08, df = 1 (P = 0.78); I² = 0%						
Test for overall effect: Z = 0.24 (P = 0.81)						
3.1.6 Europe: transfers + NSC vs. direct to SC (included transport deaths)						
de Jongh 2008 (1m)	-0.3425	0.1997	517	382	15.2%	0.71 [0.48, 1.05]
Subtotal (95% CI)			**517**	**382**	**15.2%**	**0.71 [0.48, 1.05]**
Heterogeneity: Not applicable						
Test for overall effect: Z = 1.72 (P = 0.09)						
Total (95% CI)			**7892**	**14023**	**100.0%**	**1.03 [0.85, 1.23]**
Heterogeneity: Tau² = 0.02; Chi² = 7.58, df = 4 (P = 0.11); I² = 47%						
Test for overall effect: Z = 0.26 (P = 0.79)						
Test for subgroup differences: Chi² = 7.50, df = 3 (P = 0.06), I² = 60.0%						

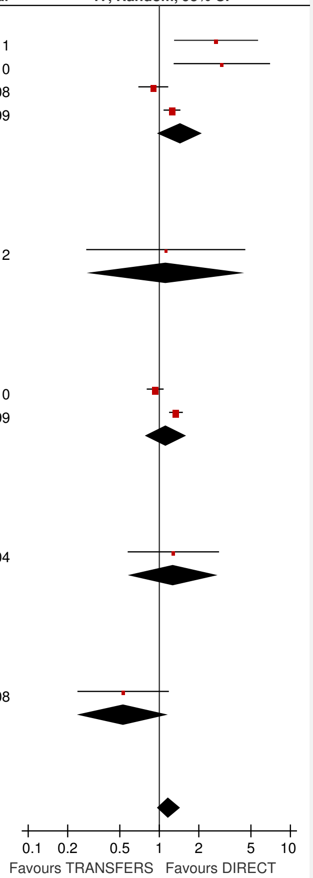


Time of outcome measurement is shown for each study following author/date. Rivara et al. (2008) data is a hazard ratio but has been included as an approximation for the OR since it is a large and important study. Fatovich et al. (2011a and 2011b) use the same patient data for their direct-to-SC groups. The meta-analysed OR excluding Rivara 2008 and Fatovich 2011b does not change substantially (OR 0.98; 95% CI 0.69 to 1.39). Studies are sub-grouped by location, definition of groups, and whether transport deaths were included.

Figure 2: Trauma: Adjusted mortality for transfers NSC to SC vs. direct triage to SC (excludes patients not transferred from NSC)

Study or Subgroup	log[Odds Ratio]	SE	TRANSFERS Total	DIRECT Total	Weight	Odds Ratio IV, Random, 95% CI	Year
6.1.1 USA (excluding transport deaths)							
Garwe 2011 (2 wk)	0.997	0.3709	600	1398	5.7%	2.71 [1.31, 5.61]	2011
Nirula 2010 (1m)	1.0986	0.4267	318	787	4.6%	3.00 [1.30, 6.92]	2010
Rivara 2008 (1y)	-0.1054	0.1282	863	2150	16.5%	0.90 [0.70, 1.16]	2008
O'Keefe 1999 (in-hosp)	0.2231	0.0699	3840	3840	20.2%	1.25 [1.09, 1.43]	1999
Subtotal (95% CI)			**5621**	**8175**	**47.0%**	**1.44 [0.97, 2.12]**	
Heterogeneity: Tau² = 0.10; Chi² = 14.80, df = 3 (P = 0.002); I² = 80%							
Test for overall effect: Z = 1.82 (P = 0.07)							
6.1.2 Taiwan (excluding transport deaths)							
Hsiao 2012a (in-hosp)	0.113	0.7073	75	156	1.9%	1.12 [0.28, 4.48]	2012
Subtotal (95% CI)			**75**	**156**	**1.9%**	**1.12 [0.28, 4.48]**	
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.16 (P = 0.87)							
6.1.3 Canada (excluding transport deaths)							
Haas 2010 (1m)	-0.0726	0.0705	3469	7481	20.2%	0.93 [0.81, 1.07]	2010
Sampalis 1999 (in-hosp)	0.2927	0.0563	3856	4680	20.9%	1.34 [1.20, 1.50]	1999
Subtotal (95% CI)			**7325**	**12161**	**41.1%**	**1.12 [0.78, 1.60]**	
Heterogeneity: Tau² = 0.06; Chi² = 16.39, df = 1 (P < 0.0001); I² = 94%							
Test for overall effect: Z = 0.62 (P = 0.54)							
6.1.7 Europe (excluding transport deaths)							
Biewener 2004 heli (1m)	0.2469	0.4039	92	210	5.0%	1.28 [0.58, 2.83]	2004
Subtotal (95% CI)			**92**	**210**	**5.0%**	**1.28 [0.58, 2.83]**	
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.61 (P = 0.54)							
6.1.8 Europe (including transport deaths)							
de Jongh 2008 (1m)	-0.6349	0.4042	69	382	5.0%	0.53 [0.24, 1.17]	2008
Subtotal (95% CI)			**69**	**382**	**5.0%**	**0.53 [0.24, 1.17]**	
Heterogeneity: Not applicable							
Test for overall effect: Z = 1.57 (P = 0.12)							
Total (95% CI)			**13182**	**21084**	**100.0%**	**1.18 [0.96, 1.44]**	
Heterogeneity: Tau² = 0.05; Chi² = 35.39, df = 8 (P < 0.0001); I² = 77%							
Test for overall effect: Z = 1.60 (P = 0.11)							
Test for subgroup differences: Chi² = 5.02, df = 4 (P = 0.29), I² = 20.3%							

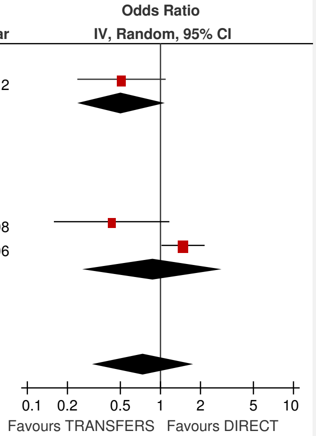
Odds Ratio
IV, Random, 95% CI



Time of outcome measurement is shown for each study following author/date. Rivara et al. (2008) and Garwe et al. (2011) data are hazard ratios but have been included as approximations for the ORs since they are large and important studies; the meta-analysed OR excluding these data does not change substantially (OR 1.17; 95% CI 0.95 to 1.45). Studies are sub-grouped by location and whether transport deaths were included.

Figure 3: Head injury: Adjusted mortality for transfers NSC to SC vs. direct triage to SC

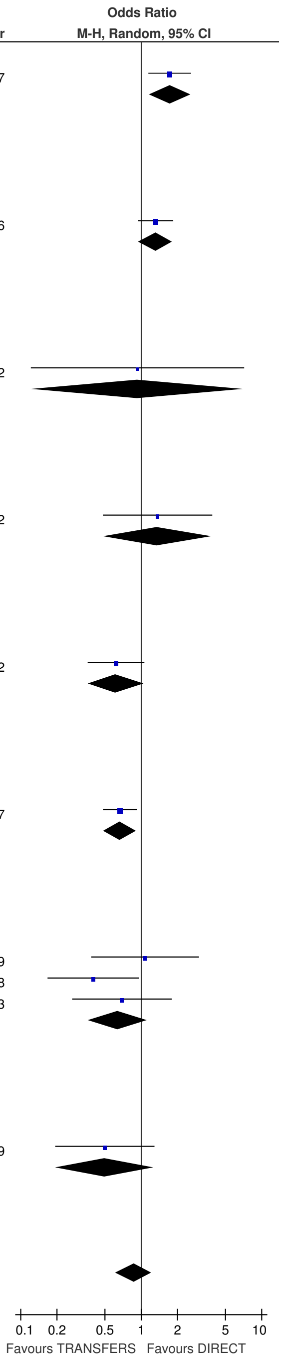
Study or Subgroup	log[Odds Ratio]	SE	TRANSFERS Total	DIRECT Total	Weight	Odds Ratio IV, Random, 95% CI	Year
2.1.1 Time to SC for transfers: not reported							
Hsiao 2012b (in-hosp)	-0.673	0.3846	167	87	32.5%	0.51 [0.24, 1.08]	2012
Subtotal (95% CI)			**167**	**87**	**32.5%**	**0.51 [0.24, 1.08]**	
Heterogeneity: Not applicable							
Test for overall effect: Z = 1.75 (P = 0.08)							
2.1.2 Time to SC for transfers: 4.1-6h							
Moen 2008 (6m)	-0.844	0.5044	60	75	27.7%	0.43 [0.16, 1.16]	2008
Hartl 2006 (2-week)	0.392	0.1849	254	864	39.8%	1.48 [1.03, 2.13]	2006
Subtotal (95% CI)			**314**	**939**	**67.5%**	**0.87 [0.26, 2.89]**	
Heterogeneity: Tau² = 0.62; Chi² = 5.29, df = 1 (P = 0.02); I² = 81%							
Test for overall effect: Z = 0.22 (P = 0.82)							
Total (95% CI)			**481**	**1026**	**100.0%**	**0.74 [0.31, 1.79]**	
Heterogeneity: Tau² = 0.47; Chi² = 10.03, df = 2 (P = 0.007); I² = 80%							
Test for overall effect: Z = 0.66 (P = 0.51)							
Test for subgroup differences: Chi² = 0.55, df = 1 (P = 0.46), I² = 0%							



Time of outcome measurement is shown for each study following author/date. Studies are subgrouped by time to SC for transfer group.

Figure 4: Head injury: Unadjusted mortality for transfers NSC to SC vs. direct triage to SC

Study or Subgroup	TRANSFERS Events	TRANSFERS Total	DIRECT Events	DIRECT Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
2.2.1 Canada: urban							
Sampalis 1997 (in-hosp)	74	486	44	466	14.9%	1.72 [1.16, 2.56]	1997
Subtotal (95% CI)		**486**		**466**	**14.9%**	**1.72 [1.16, 2.56]**	
Total events	74		44				
Heterogeneity: Not applicable							
Test for overall effect: Z = 2.68 (P = 0.007)							
2.2.2 USA: urban and rural							
Hartl 2006 (2-week)	65	254	179	864	15.9%	1.32 [0.95, 1.82]	2006
Subtotal (95% CI)		**254**		**864**	**15.9%**	**1.32 [0.95, 1.82]**	
Total events	65		179				
Heterogeneity: Not applicable							
Test for overall effect: Z = 1.65 (P = 0.10)							
2.2.3 Israel: urban and rural							
Lin 2012 (in-hosp)	2	31	2	29	2.5%	0.93 [0.12, 7.08]	2012
Subtotal (95% CI)		**31**		**29**	**2.5%**	**0.93 [0.12, 7.08]**	
Total events	2		2				
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.07 (P = 0.94)							
2.2.4 Netherlands: urban and rural							
Joosse 2012 (1m)	8	24	15	56	6.9%	1.37 [0.49, 3.85]	2012
Subtotal (95% CI)		**24**		**56**	**6.9%**	**1.37 [0.49, 3.85]**	
Total events	8		15				
Heterogeneity: Not applicable							
Test for overall effect: Z = 0.59 (P = 0.55)							
2.2.5 Taiwan: rural, fairly short distances							
Hsiao 2012b (in-hosp)	86	167	55	87	12.8%	0.62 [0.36, 1.05]	2012
Subtotal (95% CI)		**167**		**87**	**12.8%**	**0.62 [0.36, 1.05]**	
Total events	86		55				
Heterogeneity: Not applicable							
Test for overall effect: Z = 1.78 (P = 0.08)							
2.2.6 USA: mostly rural, long distances							
Tiesman 2007 (in-hosp)	105	379	128	350	16.1%	0.66 [0.49, 0.91]	2007
Subtotal (95% CI)		**379**		**350**	**16.1%**	**0.66 [0.49, 0.91]**	
Total events	105		128				
Heterogeneity: Not applicable							
Test for overall effect: Z = 2.56 (P = 0.01)							
2.2.7 Norway: mostly rural, long distances							
Moen 2009 (6m)	8	34	12	54	7.0%	1.08 [0.39, 2.99]	2009
Moen 2008 (6m)	9	60	23	75	8.5%	0.40 [0.17, 0.94]	2008
Sollid 2003 (2-76m)	10	38	16	47	7.7%	0.69 [0.27, 1.77]	2003
Subtotal (95% CI)		**132**		**176**	**23.2%**	**0.63 [0.36, 1.11]**	
Total events	27		51				
Heterogeneity: Tau² = 0.02; Chi² = 2.18, df = 2 (P = 0.34); I² = 8%							
Test for overall effect: Z = 1.58 (P = 0.11)							
2.2.8 New Zealand: mostly rural, long distances							
Kejriwal 2009 (in-hosp)	7	73	17	97	7.7%	0.50 [0.20, 1.28]	2009
Subtotal (95% CI)		**73**		**97**	**7.7%**	**0.50 [0.20, 1.28]**	
Total events	7		17				
Heterogeneity: Not applicable							
Test for overall effect: Z = 1.45 (P = 0.15)							
Total (95% CI)		**1546**		**2125**	**100.0%**	**0.87 [0.62, 1.23]**	
Total events	374		491				
Heterogeneity: Tau² = 0.16; Chi² = 26.66, df = 9 (P = 0.002); I² = 66%							
Test for overall effect: Z = 0.79 (P = 0.43)							
Test for subgroup differences: Chi² = 24.25, df = 7 (P = 0.001), I² = 71.1%							



Time of outcome measurement is shown for each study following author/date.

Table 1: Study characteristics: Trauma and head injury

Study	Dates, country (area), N centres	N patients	Inclusion/exclusion; definitions of groups	Severity (inclusion)	Severity (baseline): ISS and GCS	Age	Data source	System co-ordination	Description of centres	Adjustments
Trauma studies										
Initial triage to NSC vs. direct triage to SC (either including patients not transferred from NSC or adjusting for their exclusion)										
Fatovich 2011a[26]	1997-2006 Australia (Perth) 4 SCs, 6 NSCs	Total: 3083 A: 2005 B2:1078 B1 (deaths): 74	Analysis of non-transferred patients only included deaths at NSC, not those who survived but were not transferred. Included deaths in ED or within 24h of admission. Excluded those presenting >7 days after injury admitted for <24h.	ISS > 15	ISS (Median, IQR): A: 24 (17-29) B2: 24 (17-29)	Mean (SD): A: 43.9 (24.3) B2: 39.1 (24.3)	SC registry, Death Registry. Retrospective	Inclusive trauma system	SC: Trauma centres NSC: Non-trauma centres Investigator based at SC	Age, ISS, RTS, N regions injured, time to ambulance arrival and SC arrival, and corrected for selection bias of deaths in NSC
Fatovich 2011b[27]	1997-2006 Australia (Perth) 4 SC, NSCs	Total: 3333 A: 2005 B2: 1328 B1 (deaths): 185	Analysis of non-transferred patients only included deaths at NSC, not those who survived but were not transferred. Included deaths in ED or within 24h of admission. Excluded those presenting >7 days after injury admitted for <24h.	ISS > 15	ISS (Median, IQR): A: 24 (17-29) B2: 25 (18-29)	Mean (SD): A: 43.9 years (24.3) B2: 34.2 years (18.3)	SC registry, Death Registry, Royal Flying Doctor database. Retrospective	Inclusive trauma system	SC: Trauma centres NSC: Non-trauma centres Investigator based at SC	Age, ISS, RTS, N regions injured, time to ambulance arrival and SC arrival, and corrected for selection bias of deaths in NSC
Haas 2010[13]	2002-2007 Canada (Ontario) 9 SCs, NSCs	Total: 11,398 A: 7,481 B1+B2: 3,917	Excluded deaths before or within 30 mins of SC/NSC arrival. Other exclusions: discharged home from ED (SC or NSC) or admitted to NSC Group definitions: B1: only patients dying in NSC ED (not those who survived but were not transferred to SC). B2: only transfers from NSC ED. Included only B1+B2 patients surviving at least 1 hour in NSC (for whom direct transfer to SC may have been feasible)	ISS > 15 or death within 24h	% ISS 16-24, 25-47, 48-75: A: 46%, 48%, 4% B1+B2: 39%, 49%, 3% B2: 43%, 53%, 3%	Mean (SD): A: 49 (22) B1: 59 (23) B2: 48 (20) B1+B2: 48 (21)	Databases of trauma deaths, ED visits, hospitalisations Retrospective	NR	SC: Level I and II trauma centres NSC: Non-trauma centres Unclear whether investigator based at SC or NSC	Age, gender, ISS, comorbidities (Charlson score), mechanism of injury, whether AIS>3 in head/chest/abdomen

Study	Dates, country (area), N centres	N patients	Inclusion/exclusion; definitions of groups	Severity (inclusion)	Severity (baseline): ISS and GCS	Age	Data source	System co-ordination	Description of centres	Adjustments
de Jongh 2008[14]	2000-2006 Netherlands (Noord-Brabant) 1 SC, 11 NSCs	Total: 899 A: 382 B1: 448 B2: 69	Included patients admitted to SC or NSC, or dead on arrival, or who died in ED	ISS > 15	ISS (median, IQR): A: 25 (17-30) B1: 19 (16-25) B2: 25 (17-26)	Mean (SD): A: 40 (21) B1: 45 (22) B2: 36 (22)	Regional trauma registry (prospective); NSC registries (prospective & retrospective)	Regional trauma network for data collection; no centralisation of care. Policy of transport to nearest hospital for stabilisation then transfer to SC if necessary	SC: Level 1 trauma centre with large neurosurgical unit NSC: Other hospitals Investigator based at SC	Age, ISS, GCS, severe brain injury (AIS ≥ 4)
Rivara 2008[15]	2001-2002 USA (14 states) 18 SCs, 51 NSCs	Weighted: Total: 10,349 A: 7,570 B2: 2,779 Unweighted: Total: 3,013 A: 2,150 B2: 863	Excluded deaths before or within 30 mins of SC arrival. Other exclusions: arrival at SC/NSC >24h after injury; patients admitted to NSC. Analyses: included all deaths in SC and sample living to discharge; analyses weighted to account for sampling. See Adjustments for accounting for deaths before transfer	At least one injury AIS ≥ 3	NISS >15: 76% of patients (mean NR)	Range 18-84 (mean/median NR)	Other study (National Study on Cost and Outcome of Trauma; NSCOT) Prospective	Various	SC: Level I trauma centres NSC: Large non-trauma centres Unclear whether investigator based at SC or NSC	Age, gender, NISS, mechanism of injury, comorbidities (Charlson score). Adjustment for NSC deaths before transfer: compared B2 patients transferred at various time points after NSC admission versus A patients alive at same time points after SC admission (i.e. excluded A patients dying before each time point)

Study	Dates, country (area), N centres	N patients	Inclusion/exclusion; definitions of groups	Severity (inclusion)	Severity (baseline): ISS and GCS	Age	Data source	System co-ordination	Description of centres	Adjustments
Biewener 2004[16]	1998-1999 Germany (Dresden) 1 SC, 6 NSCs	Total: 404 A: 210 B1: 102 B2: 92	Excluded deaths before SC/NSC arrival. Other exclusions: ISS >67; age >75 years. Note: Some transfers (B2) were level II to level I trauma centre. Group definitions: A (heli): helicopter to SC. A (amb): ground ambulance to SC. Unadjusted data includes all A (heli and amb); adjusted data includes A (heli) only	ISS > 15	ISS (mean): A (heli): 35.6 A (amb): 34.9 B1: 34.0 B2: 33.3	Mean (SD): A (heli): 37 (18) A (amb): 34 (18) B1: 39 (21) B2: 36 (18) All age ≤ 75	SC trauma registry (prospective); NSC data collection (retrospective)	NR	SC: Level I trauma centre, university hospital NSC: Regional (level II or III) hospitals Investigator based at SC	Age, ISS
Nardi 1994[17]	1992-1993 Italy (3 provinces in North-East) 4 SCs, 12 NSCs	Total: 222 A: 140 B1+B2: 82	Excluded deaths before arrival of first rescuers. Analyses including and excluding deaths before SC/NSC arrival/transfer. Group definitions: A1: direct to SC, also nearest hospital. A2: direct to SC via helicopter after stabilisation in field	ISS > 15 + SC ICU admission ≥ 48h + ventilatory support	ISS (mean, SD): A1: 33.4 (19.6) A2: 36.0 (17.8) B1+B2: 35.1 (18.2)	Mean: A1: 41 A2: 37 B1+B2: 43	Patients attended by EMS Prospective	Policy of severe trauma to trauma centre, either directly or via local hospital	SC: Trauma centres NSC: Nearest hospital for stabilisation Unclear whether investigator based at SC or NSC	None

Study	Dates, country (area), N centres	N patients	Inclusion/exclusion; definitions of groups	Severity (inclusion)	Severity (baseline): ISS and GCS	Age	Data source	System co-ordination	Description of centres	Adjustments
Transfer NSC to SC vs. direct triage to SC (excluding patients not transferred from NSC)										
Hsiao 2012a[28]	2010 Taiwan (south-central) 1 SC, NSCs	Total: 231 A: 156 B2: 75	Excluded deaths before SC arrival Other exclusions: loss of vital signs before SC arrival, stayed in the NSC for >6 hours, admitted to ward or ICU at NSC, not transported by EMS	ISS > 15	ISS (mean, SD): A: 27.7 (16.1) B2: 25.6 (11.7)	Mean (SD): A: 53.6 (21.1) B2: 49.9 (20.3)	Charts and EMS records Prospective	Exclusive; trauma system establishment began during study period; most patients sent to nearest hospital	SC: severe-grade emergency care ability hospital, similar rating to level 1 trauma centres. NSC: Non-trauma centres Investigator based at SC	Adjustments for: ISS score, hypotension, hypoxia, acidosis, coagulopathy, initial GCS score, haemoglobin, platelets
Garwe 2011a,[29] Garwe 2011b[30]	2006-2007 USA (Oklahoma) 1SC, NSCs	Total: 1998 A: 1398 B2: 600	Excluded deaths before arrival and deaths in ED within 2 hours of injury Other exclusions: length of stay <48 hours (for nonfatal cases), isolated orthopaedic injury to the extremities due to same level fall; overexertion injuries; submersions; poisonings; asphyxiation; injury from pre-existing condition, did not arrive at SC within 24 hours, transferred via more than one hospital, not transported by EMS, transferred from non-licensed, acute care or out of state facilities, those whose closest hospital was the SC.	AIS≥3 or ISS≥9 or TRISS survival probability <0.9 ISS≥16: A: 847 (60.6%) B: 397 (66.2%)	ISS (Mean, SD): A: 20.8 (11.5) B: 21.4 (11.5)	Mean (SD): A: 37 (19.2) B: 38.5 (23)	Oklahoma State Trauma Registry Retrospective	Inclusive trauma system	SC: Level 1 trauma centre NSC: Two level 2 trauma centres and a number of level 3 and 4 trauma centres in rural areas External investigator	Mortality hazard ratio adjusted for propensity to be transported directly to SC, time to SC, age, ISS, intubation in the ED, presence of severe head injury, comorbid condition and shock.
Koczirka 2011 [31]	1998-2007 USA (Delaware) 1SC, NSCs	Total: 2491 A: 1848 B2: 643	NR	ISS>24	NR	NR	Trauma system registry Retrospective	Inclusive trauma system	SC: Level 1 trauma centre NSC: other facilities	None

Study	Dates, country (area), N centres	N patients	Inclusion/exclusion; definitions of groups	Severity (inclusion)	Severity (baseline): ISS and GCS	Age	Data source	System co-ordination	Description of centres	Adjustments
Nirula 2010[18]	2004-2007 USA (various areas) 8 SCs, NSCs	Total: 1,105 A: 787 B2: 318	Excluded deaths before SC arrival. Other exclusions: arrival to hospital >6h after injury	Hypotension (<90) or elevated base deficit (≥ 6), transfusion within 12h, ≥ 1 injury AIS ≥ 2 (not brain), intact cervical spinal cord	ISS (mean, SD): A: 31 (13) B2: 31 (13)	Mean (SD): A: 41 (18) B2: 44 (20)	Glue Grant Trauma Database (severely injured patients) Prospective	Various	SC: Level I trauma centres NSC: Non-trauma centres Investigator based at SC	Age, ISS, time to SC arrival, comorbidities (APACHE II), crystalloid and blood infusion volumes, head injury, SC site
Clancy 2001[19]	1995-1996 USA (North Carolina) 9 SCs, NSCs	Total: 801 A: 358 B2: 443	Excluded deaths before SC arrival; included deaths in SC ED. Other exclusions: patients admitted for <24h Note: Some transfers (B2) may have been level II to level I trauma centre	ISS > 15	NR	A+B2, all severities (mean, SD): Level I SC: 34 (20) Level II SC: 36 (SD 20)	State trauma registry	NR	SC: 5 Level I and 4 level II trauma centres, > 600 beds each NSC: Other hospitals Investigator based at SC	None
O'Keefe 1999[20]	1986-1995 USA (Washington) 1 SC, NSCs	Total: 7,681 A: NR B2: NR	Excluded deaths before SC arrival and deaths in SC ED	ISS > 15	NR	All severities: mean 34	SC trauma registry Retrospective	Became inclusive trauma system during study period	SC: Level I trauma centre NSC: Other hospitals Investigator based at SC	Age, AIS (abdomen / chest / head), mechanism of injury, year of admission

Study	Dates, country (area), N centres	N patients	Inclusion/exclusion; definitions of groups	Severity (inclusion)	Severity (baseline): ISS and GCS	Age	Data source	System co-ordination	Description of centres	Adjustments
Sampalis 1999[21]	1992-1998 Canada (Montreal, Quebec City) 4 SCs, 95 NSCs	Total: 8,536 A: 4,680 B2: 3,856	Excluded deaths at the scene; included deaths in SC ED. Note: Some transfers (B2) were level II to level I trauma centre	ISS > 12 or one of: death from injury, PHI > 3, ≥ 2 injuries AIS ≥ 3, stay > 3 days	ISS ≥ 12: 94% patients Mean ISS 24.6-27.9 across study years	All study years: mean 46-54	Regional trauma registry; hospital &; EMS records Prospective	Became inclusive trauma system during study. Policy (1995+): severe trauma to level I trauma centre, either directly or via local hospital	SC: Level I trauma centres, trauma and neurosurgery cover at all times NSC: Level II or level III trauma centre Investigator based at SC	Age, ISS, trauma centre designation (level I, II or III), prehospital time, time to admission, phase of regionalisation of trauma system
Kam 1998[22]	1994-1996 Hong Kong 1 SC, 1 NSC	Total: 70 A: 43 B2: 27	Analyses including and excluding deaths before SC arrival and during transfer from NSC to SC	ISS > 15	% ISS 16-24, 25-40, 41-50, ≥ 51: A: 23%, 37%, 26%, 14% B2: 30%, 48%, 11%, 11%	All severities: >54 years: A: 15% B2: 18%	Medical records at SC Retrospective	Policy of transport to nearest hospital	SC: General hospital with trauma team; facilities and expertise between that of US level I and II trauma centres, 1200 beds NSC: District hospital of 200 beds; ED but no acute operative facilities Investigator based at SC	None
Sampalis 1997[23]	1993-1995 Canada (Montreal, Quebec City) 3 SCs, NSCs	Total: 1,755 A: 1,035 B2: 720	Excluded deaths before SC arrival. Other exclusions: injured outside city limits; not transported by EMS. Note: 27% transfers (B2) were level II to level I trauma centre	ISS > 12 and one of: death from injury; stay > 3 days; ICU admission	NR	All severities (mean, SD): A: 48 (23) B2: 42 (21)	State trauma registry; other study	Policy of severe trauma to level I trauma centre, either directly or via local hospital	SC: Level I trauma centres, neurosurgery available at all times NSC: Level II trauma centre (27% patients) or level III trauma centre (73% patients), specialists on call Investigator based at SC	None

Study	Dates, country (area), N centres	N patients	Inclusion/exclusion; definitions of groups	Severity (inclusion)	Severity (baseline): ISS and GCS	Age	Data source	System co-ordination	Description of centres	Adjustments
Young 1997[24]	1994-1995 USA (Virginia) 1 SC, NSCs	Total: 316 A: 165 B2: 151	Excluded deaths before SC arrival; included deaths in SC ED	ISS > 15	ISS (mean, SD): A: 24.8 (8.2) B2: 23.1 (7.2) GCS (mean, SD): A: 11.4 (4.9) B2: 11.4 (5.0)	Mean (SD): A: 44 (20) B2: 46 (21)	SC trauma registry; medical records Retrospective	NR	SC: Level I trauma centre NSC: Other hospitals Investigator based at SC	None
Boulanger 1993a[25]	1986-1990 Canada (Toronto, Ontario) 1 SC, NSCs	Total: 911 A: 226 B2: 685	Excluded deaths before SC arrival. Inclusion: victims of motor vehicle crashes (drivers or passengers), age >14 years	ISS > 15	ISS (mean, SD): A: 29.8 (12.2) B2: 31.5 (11.1) GCS (mean, SD): A: 10.8 (5.2) B2: 9.2 (5.3)	Mean (SD): A: 38 (18) B2: 34 (17)	SC trauma registry Prospective	Exclusive trauma system	SC: Regional trauma unit NSC: Non-trauma centres Investigator based at SC	None
Boulanger 1993b[25]	1986-1990 USA (Baltimore, Maryland) 1 SC, NSCs	Total: 1,852 A: 1,368 B2: 484	Excluded deaths before SC arrival. Inclusion: victims of motor vehicle crashes (drivers or passengers), age >14 years	ISS > 15	ISS (mean, SD): A: 28.8 (12.1) B2: 29.4 (14.0) GCS (mean, SD): A: 11.5 (4.4) B2: 11.9 (4.3)	Mean (SD): A: 33 (17) B2: 34 (18)	SC trauma registry Prospective	Inclusive trauma system	SC: Level I trauma centre NSC: Non-trauma centres Investigator based at SC	None
Head injury studies										
Transfer NSC to SC vs. direct triage to SC (excluding patients not transferred from NSC)										
Hsiao 2012b[40]	2003-2008 Taiwan (south-central) 1 SC, NSCs	Total: 254 A: 87 B2: 167	Excluded deaths before hospital arrival Other exclusions: loss of vital signs before arrival at hospital, multiple traumas, penetrating brain injury, <18 years of age, GCS>8 after drugs eliminated.	GCS 3-8 after initial resuscitation at the ED	GCS mean (SD) A: 5.4 (1.92) B2: 5.3 (1.71)	Median (range): A: 55 (20-91) B2: 48 (18-92)	Chart review Retrospective	Non-inclusive - patients bypass nearest hospital for SC at patient or family request	SC: "severe" class emergency care general hospital with neurosurgeons available 24h - similar to level 1 trauma centre NSC: Other hospitals Investigator based at SC	Age, initial GCS, hypotension, hypertension, hyperthermia, hyperglycaemia, surgical treatment

Study	Dates, country (area), N centres	N patients	Inclusion/exclusion; definitions of groups	Severity (inclusion)	Severity (baseline): ISS and GCS	Age	Data source	System co-ordination	Description of centres	Adjustments
Joosse 2012[41]	2006-2009 Netherlands (Amsterdam) 1 SC, NSCs	Total: 80 A: 56 B2: 24	Excluded deaths before hospital arrival Inclusion: severe head injury requiring neurosurgery (craniotomy, craniectomy, or operation on depressed skull fracture) within 6h of admission. Exclusion: Patients operated on solely for insertion of intracranial pressure monitor or external ventricular drain, or admitted for observation bur requiring neurosurgery after deterioration.	AIS ≥ 3 for head injury and requiring neurosurgical intervention	ISS (median, IQR): A: 25 (16-29) B2: 25 (16-25)	Median (IQR): A: 46 (31-56) B2: 53 (36-64)	Trauma registry at SC and NSC, electronic data at NSC, chart review. Prospective registry, retrospective study	Decision to present to SC made on-scene by ambulance nurses based on clinical presentation	SC: level 1 trauma centre with neurosurgical facilities NSC: district hospital without neurosurgical facilities Investigator based at SC	None
Lin 2012[42]	2008-2010 Israel (Naharia) 1 SC, 1 NSC	Total: 60 A: 29 B2: 31	Excluded deaths before hospital arrival Inclusion: aged >2 years, blunt intracranial injury diagnosed by CT and requiring neurosurgical intervention. Case-control study; subset of direct-to-SC patients selected at random. Exclusion: AIS>2 for other body system, received anticoagulation prior to injury, urgent non-neurosurgical operations, arrivals >24h after injury.	Requiring neurosurgical intervention	GCS mean (SD) A: 11.0 (2.8) B2: 10.4 (3.7)	Mean (SD): A: 31.7 (24.4) B2: 29.4 (23.2)	Trauma registry at SC and NSC, ER files and computerised medical records. Retrospective	Patients usually transported to nearest hospital	SC: Level 1 trauma centre NSC: trauma service but no neurosurgery Investigators based at SC and NSC	None
Simons 2010[33]	2001-2006 Canada (British Colombia) 1 SC vs. NSCs	Total: NR A: NR B2: NR	Excluded deaths before SC arrival	GCS ≤ 8	NR	NR	State trauma registry Retrospective	No bypass protocols; transport to nearest hospital	SC: Level I trauma centre with neurosurgery NSC: Local hospital, level V trauma services, no neurosurgery Investigator based at SC	None, but "similar patients" compared between groups (not reported how matched)

Study	Dates, country (area), N centres	N patients	Inclusion/exclusion; definitions of groups	Severity (inclusion)	Severity (baseline): ISS and GCS	Age	Data source	System co-ordination	Description of centres	Adjustments
Kejriwal 2009[34]	2004 New Zealand (Upper North Island) 1 SC, NSCs	Total: 170 A: 97 B2: 73	Excluded deaths before SC arrival Other exclusions: arrival at hospital >24h after injury	AIS ≥ 3 for head injury	ISS (median, IQR): A: 17 (9 to 50) B2: 16 (6 to 25)	Median (IQR): A: 40 (15-94) B2: 33 (20-49)	SC trauma registry Retrospective	Ad hoc trauma system; transport to nearest hospital; telemedicine	SC: City hospital, provides brain trauma care for population of two million NSC: Closest regional hospital Investigator based at SC	None
Moen 2009[35]	2004-2007 Norway (Trondheim) 1 SC, NSCs	Total: 88 A: 54 B2: 34	Excluded deaths before SC arrival Other exclusions: unsalvageable patients; deaths from other injuries; patients not receiving active treatment	GCS ≤ 8	ISS (median, range): A: 27 (9 to 50) B2: 26 (9 to 54) GCS (median, range): A: 5 (3 to 9) B2: 6 (3 to 9)	Median (range): A: 40 (7-94) B2: 45 (6-81)	SC data collection Retrospective	Well-developed transfer system; telemedicine	SC: University hospital department of neurosurgery NSC: Local hospitals Investigator based at SC	None
Moen 2008[36]	1998-2002 Norway (Trondheim) 1 SC, 8 NSCs	Total: 135 A: 75 B2: 60	Excluded deaths before SC arrival Other exclusions: unsalvageable patients; deaths within 24h of other injuries; patients not receiving active treatment	GCS ≤ 8	ISS (mean, range): A: 31.8 (9 to 75) B2: 27.0 (9 to 75) GCS (median, range): A: 5.5 (3 to 15) B2: 7 (3 to 15)	Median (range): A: 34 (1-82) B2: 34 (2-88)	Medical records, ambulance records Prospective	Air ambulance triage to SC or NSC, or ground ambulance transport to nearest hospital; telemedicine	SC: University hospital department of neurosurgery NSC: 7 local district hospitals and 1 central hospital Investigator based at SC	Mortality analysis only: Age, ISS, GCS, pupil dilation

Study	Dates, country (area), N centres	N patients	Inclusion/exclusion; definitions of groups	Severity (inclusion)	Severity (baseline): ISS and GCS	Age	Data source	System co-ordination	Description of centres	Adjustments
Tiesman 2007[37]	2002-2003 USA (Iowa) 9 SCs, 100+ NSCs	Total: 754 A: 375 B2: 379	Excluded deaths before transfer to SC	GCS ≤ 12	ISS (mean, SD): A: 26.3 (15.2) B2: 27.2 (11.9) GCS (mean, SD): A: 5.5 (3.3) B2: 5.2 (2.8)	NR	State trauma registry Retrospective	Inclusive trauma system; triage protocol	SC: 2 level I and 7 level II trauma centres with neurosurgery NSC: Community hospitals and lower level trauma centres Unclear whether investigator based at SC or NSC	None
Hartl 2006[38]	2000-2004 USA (New York State) 24 SCs, NSCs	Total: 1,118 A: 864 B2: 254	Excluded deaths before SC arrival, deaths in ED, and those brain dead on admission Other exclusions: arrival at SC >24h after injury; arrival at hospital <10 mins after injury; non-paralysed with GCS 3-4 and fixed & dilated pupils	GCS ≤ 8	GCS: A: 52% 3-5, 48% 6-8 B2: 47% 3-5, 53% 6-8	A: mean 36.5 B2: mean 34.4 A+B2: range 0-94	SC trauma registries	Inclusive trauma system	SC: 22 level I and II trauma centres enrolled in quality improvement programme NSC: Non-trauma centre Unclear whether investigator based at SC or NSC	Age, GCS, pupillary status, arterial hypotension
Sollid 2003[39]	1986-1995 Norway (North, Tromso) 1 SC, 10 NSCs	Total: 85 A: 47 B2: 38	Excluded deaths before surgery at SC Inclusion: Brain injury requiring neurosurgery for intracranial mass lesion Other exclusions: neurosurgery >48h after injury; operations for depressed or open skull fractures without intracranial mass lesions; operations with diagnostic burr holes; reoperations	Brain injury requiring neurosurgery for intracranial mass lesion	GCS (median): A: 7 B2: 7	Mean (range): A+B2: 41 (0-85)	Medical records, ambulance records Retrospective	NR	SC: University hospital (level I trauma centre) department of neurosurgery NSC: 9 district general hospitals and 1 central hospital Investigator based at SC	None

Study	Dates, country (area), N centres	N patients	Inclusion/exclusion; definitions of groups	Severity (inclusion)	Severity (baseline): ISS and GCS	Age	Data source	System co-ordination	Description of centres	Adjustments
Sampalis 1997[23]	1993-1995 Canada (Montreal, Quebec City) 3 SCs, NSCs	Total: 952 A: 466 B2: 486	Excluded deaths before SC arrival Other exclusions: injured outside city limits; not transported by EMS Note: 27% transfers (B2) were level II to level I SC	AIS ≥ 3 for head and one of: death due to injury; stay > 3 days; ICU admission	NR	Mean (SD) for all severities: A: 48 (23) B2: 42 (21)	State trauma registry plus other study	Policy of severe trauma to level I trauma centre, either directly or via local hospital	SC: Level I trauma centres, neurosurgery available at all times NSC: Level II trauma centre (27% patients) or level III trauma centre (73% patients), specialists on call Investigator based at SC	None

Abbreviations: AIS=Abbreviated Injury Scale; ALS=Advanced Life Support; BLS=Basic Life Support; ED=emergency department; EMS=emergency medical services; GCS=Glasgow Coma Scale; ICU=intensive care unit; IQR=interquartile range; ISS=Injury Severity Score; NR=not reported; NSC=non-specialist centre; SC=specialist centre; SD=standard deviation. Definitions of study groups: A=direct to SC and remained there; B1=direct to NSC and remained there; B2=to NSC initially then transferred to SC. In Nardi et al. (1994): A1=nearest hospital; A2=via helicopter after stabilisation.

Table 2: Mortality data (trauma and head injury)

	Trauma			Head injury		
Mortality analyses	**N studies (patients)**	**Refs**	**OR for triage to NSC vs. SC (95% CI)**	**N studies (patients)**	**Refs**	**OR for triage to NSC vs. SC (95% CI)**
Initial triage to NSC vs. SC (includes or adjusts for patients not transferred from NSC)						
Adjusted for age and severity	5 (19,910)	[13-15;26;27]	1.03 (0.85 to 1.23)	0	-	-
Unadjusted	6 (17,523)	[13;14;16;17;26;27]	1.04 (0.72 to 1.50)*	0	-	-
Transfers NSC to SC vs. direct triage to SC (excluding patients not transferred from NSC)						
Adjusted for severity (and generally age)	9 (34,266)	[13-16;18;20;21;28;30]	1.18 (0.96 to 1.44)*	3 (1,507)	[36;38;40]	0.74 (0.31 to 1.79)*
Unadjusted	15 (37,079)	[13-17;19;22-28;30;31]	0.83 (0.68 to 1.01)*	10 (3,671)	[23;34-42]	0.87 (0.62 to 1.23)*

*Significant heterogeneity ($I^2 \geq 50\%$). Higher ORs favour direct triage to SC. Abbreviations: CI=confidence interval; NSC=non-specialist centre; OR=odds ratio; SC=specialist centre.

Table 3: Morbidity data (head injury)

Study	N	Time of measurement	Transfer NSC to SC	Direct triage to SC	Comparison between groups
			GOS: median (range)		
Joosse 2012[41]	80	NR	3 (1-5)	3 (1-5)	p=0.866
Moen 2009[35]*	88	6 months	4 (1-5)	3 (1-5)	p=0.89
Moen 2008[36]	131	6 months	3 (1-5)	3 (1-5)	p=0.105
Sollid 2003[39]	85	2-76 months	4 (NR)	4 (NR)	p=Not sig
			N (%) with favourable GOS (score 4-5)		
Sollid 2003[39]	85	2-76 months	22/38 (58%)	25/47 (53%)	OR=1.21 (95% CI 0.51 to 2.87)
			N (%) discharged home		
Lin 2012[42]	60	NA	21/31 (68%)	16/29 (55%)	p=0.43 for discharge destination
Tiesman 2007[37]	754	NA	103/379 (27%)	115/375 (31%)	OR=0.84 (95% CI 0.62 to 1.161)

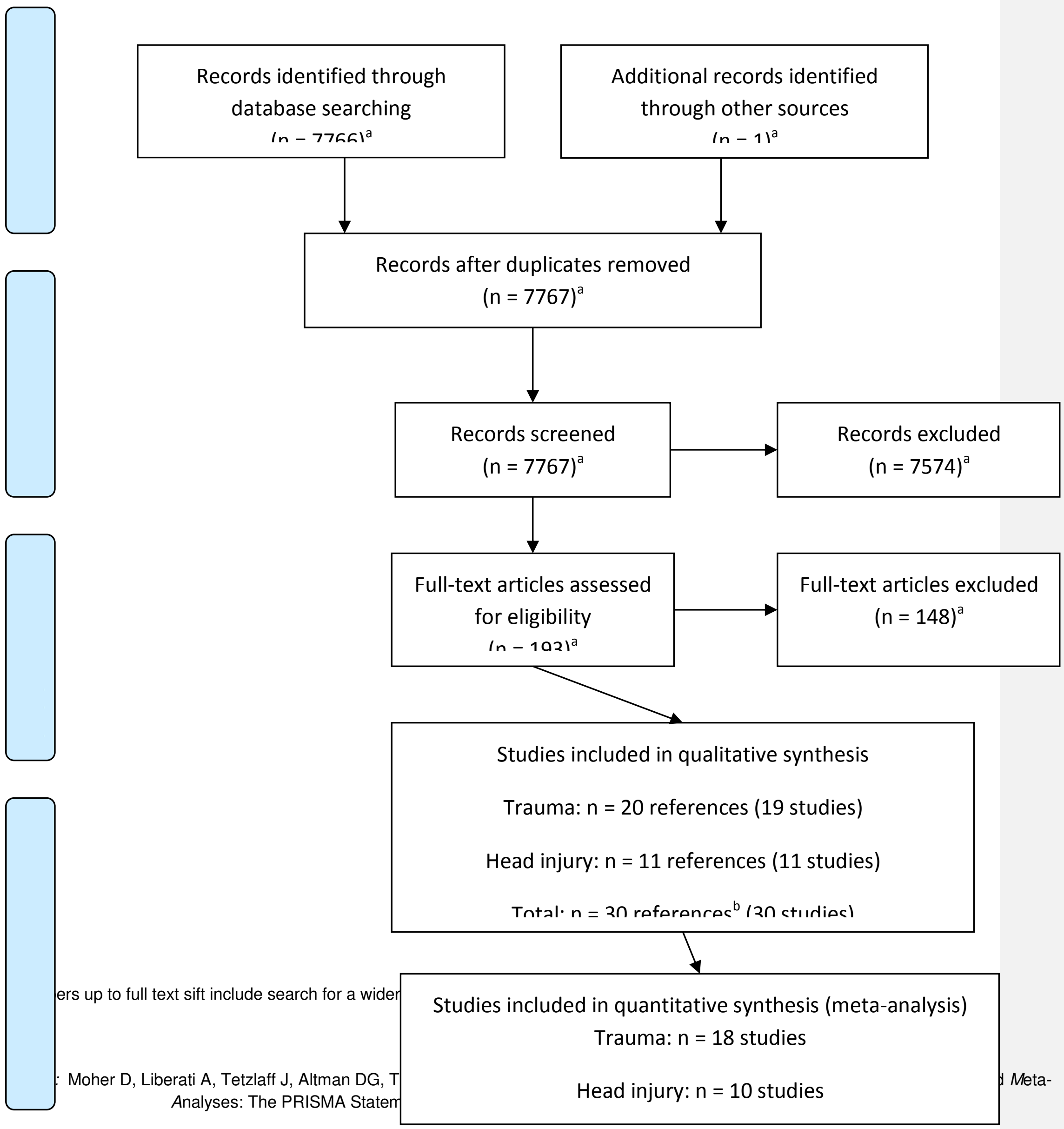
Abbreviations: CI=confidence interval; GOS=Glasgow Outcome Scale; NA=not applicable; NR=not reported; NSC=non-specialist centre; OR=odds ratio; SC=specialist centre; . Definitions of study groups: A=direct to SC and remained there; B1=direct to NSC and remained there; B2=to NSC initially then transferred to SC. *Moen et al. (2009) also report that there was no difference between groups in the proportion of patients with unfavourable GOS (1-3) at 6 months in an adjusted multiple regression analysis (no data reported).

Table 4: Length of stay (trauma and head injury)

Study	Mean/median	Hospital length of stay (days)			ICU length of stay (days)		
		Initial triage to NSC	**Direct to SC**	**Difference (NSC minus SC)**	**Initial triage to NSC**	**Direct to SC**	**Difference (NSC minus SC)**
Trauma							
Fatovich 2011a[26]	Median (IQR)	10 (5-20)	9 (3-19)	1	NR		
Fatovich 2011b[27]	Median (IQR)	12 (6-24)	9 (3-19)	3	5 (2-11)	4 (2-10)	1
Garwe 2011a,[29] Garwe 2011b[30]	Median (IQR)	7 (9)	6 (9)	1 (NS)	4 (8)	4 (8)	0 (NS)
Young 1997[24]	Mean (SD)	19.1 (20.6)	15.4 (21.3)	3.7 (NS)	12 (5.4)	10.1 (15.8)	1.9 (NS)
Nardi 1994[17]	Mean (SD)	NR	NR	NR	15 (NR)	A1: 13 (NR) A2: 11 (NR)	2.0 4.0
Boulanger 1993 (Canada)[25]	Mean (SD)	33.9 (NR)	26.2 (NR)	7.7	9.4 (NR)	8.4 (NR)	1.0
Boulanger 1993 (USA)[25]	Mean (SD)	23.7 (NR)	18.5 (NR)	5.2	18.5 (NR)	15.4 (NR)	3.1
Head injury		**Initial triage to NSC**	**Direct to SC**	**Difference (NSC minus SC)**	**Initial triage to NSC**	**Direct to SC**	**Difference (NSC minus SC)**
Lin 2012[42]	Mean (SD)	14.6 (14.9)	13.2 (9.0)	1.4 (p=0.52)	7.5 (6.9)	10.3 (8.8)	-2.8 (p=0.20)
Kejriwal 2009[34]	Median	7	7	0 (p=0.10)	3	1	2 (p=0.74)
Tiesman 2007[37]	Mean (SD)	12.7 (14.5)	8.8 (12.3)	3.9 (95% CI 2.0 to 5.8)	NR	NR	NR

Abbreviations: ICU=intensive care unit; NR=not reported; NS=non-significant (no further data reported); NSC=non-specialist centre; SC=specialist centre; SD=standard deviation. In Nardi et al. (1994): A1=nearest hospital; A2=via helicopter after stabilisation.

Appendix 1: PRISMA Flow Diagram



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Appendix 2: PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3-4
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	N/A
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	5
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	5
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5 (available on request)
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	5
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	5
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	5
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	6
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	6

Appendix 2: PRISMA Checklist

Section/topic	#	Checklist item	Reported on page #
Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	6
Section/topic	**#**	**Checklist item**	**Reported on page #**
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	N/A
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	p7, Appendix 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	p7-8, Tables 1-2
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	p8, Table 3
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	Tables 5-6, Figures 1-4
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	p8-11, Table 5, Figures 1-4
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	N/A
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	p8-11, Figures 1-4
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	12
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	12-13
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13-15
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	16

Appendix 2: PRISMA Checklist

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

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