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Helicopter emergency medical services for adults with major trauma (Review)

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[Intervention Review]

Helicopter emergency medical services for adults with major trauma

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ABSTRACT

Background

Although helicopters are presently an integral part of trauma systems in most developed nations, previous reviews and studies to date have raised questions about which groups of traumatically injured patients derive the greatest benefit.

Objectives

The purpose of this review is to determine if helicopter emergency medical services transport (HEMS) is associated with improved morbidity and mortality, compared to ground emergency medical services transport (GEMS), for adults with major trauma. The primary outcome was survival to hospital discharge. Secondary outcomes were quality-adjusted life years (QALYs) and disability-adjusted life years (DALYs).

Search methods

Searches were run in CENTRAL, MEDLINE, EMBASE, CINAHL (EBSCOhost), SCI-EXPANDED, CPCI-S, and ZETOC in January 2012. Relevant websites were also searched, including controlled trials registers, HSRProj, the World Health Organization (WHO) ICTRP, and OpenSIGLE. Searches were not restricted by date, language, or publication status. Attempts were made to contact authors in the case of missing data.

Selection criteria

Eligible trials included randomised controlled trials (RCTs) and non-randomised intervention studies. Non-randomised studies (NRS), including controlled trials and cohort studies, were also evaluated. Each study was required to have a GEMS comparison group. An injury severity score (ISS) > 15 or an equivalent marker for injury severity was required. Only adults aged 16 years or older were included.

Data collection and analysis

Three review authors independently extracted data and assessed the risk of bias of included studies. The Downs and Black quality assessment tool was applied for NRS. The results were analysed in a narrative review, and with studies grouped by methodology and injury type. A predefined subgroup was comprised of four additional studies that examined the role of HEMS versus GEMS for inter-facility transfer. Summary of findings tables were constructed in accordance with the GRADE Working Group criteria.

Main results

Twenty-five studies met the entry criteria for this review. Four additional studies met the criteria for a separate, predefined subgroup analysis of patients transferred to trauma centres by HEMS or GEMS. All studies were non-randomised studies; no RCTs were found. Survival at hospital discharge was the primary outcome. Data from 163,748 people from 21 of the 25 studies included in the primary analysis were available to calculate unadjusted mortality. Overall, considerable heterogeneity was observed and an accurate estimate of overall effect could not be determined. Based on the unadjusted mortality data from five trials that focused on traumatic brain injury, there was no decreased risk of death with HEMS (relative risk (RR) 1.02; 95% CI 0.85 to 1.23). Nine studies used multivariate regression to adjust for confounding, the five largest indicated a statistically significant increased odds of survival associated with HEMS. All Trauma-Related Injury Severity Score (TRISS)-based studies indicated improved survival in the HEMS group as compared to the Major Trauma Outcomes Study (MTOS) cohort; some studies showed survival benefits in both the HEMS and GEMS groups as compared to MTOS. No studies were found to evaluate the secondary outcome of morbidity as assessed by QALYs and DALYs. All four studies suggested a positive benefit when HEMS was used to transfer patients to higher level trauma centres. Overall, the quality of the included studies was very low as assessed by the GRADE Working Group criteria.

Authors' conclusions

Due to the methodological weakness of the available literature, and the considerable heterogeneity of effects and study methodologies, an accurate composite estimate of the benefit of HEMS could not be determined. Although five of the nine multivariate regression studies indicated improved survival associated with HEMS, the remainder did not. All were subject to a low quality of evidence as assessed by the GRADE Working Group criteria due to their non-randomised design. Similarly, TRISS-based studies, which all demonstrated improved survival, cannot be considered strong evidence because of their methodology, which did not randomize the use of HEMS. The question of which elements of HEMS may be beneficial for patients has not been fully answered. The results from this review provide motivation for future work in this area. This includes an ongoing need for diligent reporting of research methods, which is imperative for transparency and to maximise the potential utility of results. Large, multicentre studies are warranted as these will help produce more robust estimates of treatment effects. Future work in this area should also examine the costs and safety of HEMS, since multiple contextual determinants must be considered when evaluating the effects of HEMS for adults with major trauma.

PLAIN LANGUAGE SUMMARY

Helicopter emergency medical services for adults with major trauma

Trauma is a leading cause of death and disability worldwide and, since the 1970s, helicopters have been used to transport people with injuries to hospitals that specialise in trauma care. Helicopters offer several potential advantages, including faster transport to expert medical care and treatment en route to the hospital by providers who are specifically trained in trauma management. Twenty-five studies conducted internationally compared transport by helicopter emergency medical services to transport by ground emergency medical services (an ambulance), with both types of service aiming to improve either survival or disability for seriously injured patients. Some of these studies indicated some benefit of helicopter transport for survival after major trauma, but others did not. The studies were of varying sizes and different methods were used to determine if more patients survived when transported by helicopter versus ground ambulances. Some studies included helicopter teams that had specialised physicians on board whereas other helicopter crews were staffed by paramedics and nurses. Furthermore, patients transported by helicopter or ground emergency medical services had varying numbers and types of procedures en route to the trauma centre. The use of some of these procedures, such as the placement of a breathing tube, may have helped improve survival in some of the studies. Overall the quality of the included studies was low. Helicopter transport for some trauma patients may be beneficial for a variety of reasons and more research is required to determine what elements of helicopter transport help improve outcomes. The results from future research might help in better allocation of the helicopter transport resource with increased safety and decreased costs.

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SUMMARY OF FINDINGS

Summary of findings for the main comparison.

Helicopter emergency medical services compared with ground emergency medical services for adults with major trauma

Patient or population: adults (age>15) with major trauma (ISS>15)

Settings: Multinational

Intervention: Transportation to a trauma centre by helicopter emergency medical services (HEMS)

Comparison: Transportation to a trauma centre by ground emergency medical services (GEMS)

Outcomes	**Illustrative comparative risks* (95% CI)**		**Relative effect (95% CI)**	**No of Participants (studies)**	**Quality of the evidence (GRADE)**	**Comments**
	Assumed risk	**Corresponding risk**				
	GEMS	**HEMS**				
Overall unadjusted mortality	**Low risk population**		**RR 1.00** (0.76 to 1.30)	163,748	⊕⊝⊝⊝ **very low**	Results could not be reliably combined for meta-analysis due to considerable heterogeneity. The relative effect calculated here reflects ***unadjusted mortality*** only for studies that reported data enabling the calculation of a risk ratio. See text and Figure 3 (Analysis 1.1) for details.
	--	--				
	Medium risk population					
	--	--				
	High risk population					
	--	--				
Quality-adjusted life years (QALY)	--	--	--	--	--	No studies examining QALY as an outcome met the inclusion criteria for this review.
Disability-adjusted life years (DALY)	--	--	--	--	--	No studies examining DALY as an outcome met the inclusion criteria for this review.

*The basis for the **assumed risk** (e.g. the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).

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CI: Confidence interval; **RR:** Risk Ratio.

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.
Very low quality: We are very uncertain about the estimate.

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BACKGROUND

Description of the condition

Worldwide, unintentional injuries are responsible for over 3.9 million deaths and over 138 million disability-adjusted life-years (Chandran 2010). Trauma currently accounts for 12% of the world's burden of disease and annually there are more than five million deaths due to injuries worldwide (CDC 2010; Krug 2002; Murray 1996). By 2020, it is estimated that 1 in 10 people will die from injuries (CDC 2010; Murray 1996).

Description of the intervention

Early reports from the Korean and Vietnam wars suggested a 2% increase in survival for casualties as the time to definitive care improved from five hours to one hour with prompt transport by helicopter to forward-deployed surgical theatres (Baxt 1983; Baxt 1985; Bledsoe 2006; Cowley 1973; McNabney 1981; Shatz 2004; Taylor 2010). Based on the results of these wartime experiences, civilian helicopters were used for the first time in the 1970s to transport traumatically injured patients to trauma centres (Kerr 1999; Wish 2005). In Germany, the *Christoph 1* helicopter entered service in 1970, and services rapidly expanded to over seven rescue bases (Seegerer 1976). Today, the use of helicopter emergency medical services (HEMS) for the transportation of trauma patients is commonplace in most developed nations (Butler 2010; Champion 1990; Kruger 2010; Ringburg 2009). Helicopters are capable of transporting patients with major trauma significantly faster than ground units and the speed benefit is more pronounced as the distance from a trauma centre increases. Nevertheless, recent research has questioned which traumatically injured patients derive the greatest benefit from the utilization of this limited and resource-intensive transportation modality (Bledsoe 2005; Bledsoe 2006; Cunningham 1998; DiBartolomeo 2005; Ringburg 2009).

How the intervention might work

The use of HEMS is largely predicated on the concept of the 'golden hour' (Cowley 1979). Time may play a crucial role in the treatment of adults with major trauma, and delays in management could worsen prognosis. Helicopter transport can decrease transport times and may facilitate earlier, definitive treatment. Several studies have established that timely and advanced trauma care may help improve mortality figures by reversing hypoperfusion to vital organs (Cowley 1979; Sampalis 1999). In one study, the risk of death was found to be significantly increased for every 10-minute increase in out-of-hospital time (Sampalis 1999). However, the origins and scientific evidence for the 'golden hour', while intuitively appealing, have been questioned as has the role of HEMS in the chain of survival for critically injured trauma patients (Lerner 2001).

Mortality from motor vehicle crashes has been shown to be reduced when an organized system of trauma care is implemented, of which HEMS is often an important component (Nathans 2000). The risk of death may be reduced by 15% to 20% when care is provided in a trauma centre (MacKenzie 2006; MacKenzie 2007). A level I trauma centre provides the highest level of surgical and critical care for trauma patients. Level I trauma centres have 24-hour surgical coverage, including in-house coverage by orthopaedic surgeons, neurosurgeons, plastic surgeons, and other specialists, in addition to an active research program and a commitment to regional trauma education. Patients with major trauma who require an operation may benefit from management at a level I trauma centre, but it is unclear if earlier intervention and rapid assessment alone fully explain the survival benefit (Haas 2009). The mortality benefits resulting from admission to a level I trauma centre may be due to the definitive surgical expertise available at these centres (Haut 2006) in addition to the advanced resources for critical care and rehabilitation services (Haut 2009). Furthermore, speed may not be the only contributory effect of HEMS in terms of mortality benefits for adults with major trauma. HEMS crews are typically composed of highly trained personnel, including experienced paramedics, critical care nurses, respiratory therapists, and in some cases physicians. Hence, any HEMS-associated outcome benefit is likely to be the result of some combination of speed, expertise, and the role that HEMS programs have as part of integrated trauma systems (Thomas 2003). Transport of injured patients remains a major goal for most HEMS programs (Thomas 2002); beneficial effects of specialized trauma care regarding morbidity and mortality may be mediated by HEMS.

Why it is important to do this review

Results supporting mortality benefits for adults transported by HEMS for major trauma have been inconsistent (Thomas 2002; Thomas 2004; Thomas 2007; Ringburg 2009), resulting in substantial controversy in both the medical literature and the transportation safety arena. Many HEMS outcome studies suffer from the limitations of small sample sizes, significant heterogeneity, and other inadequate statistical methodologies. Some overviews of the literature have pointed to a clear positive effect on survival associated with HEMS transport (Ringburg 2009) while others have maintained persistent skepticism about the beneficial impact of HEMS (Bledsoe 2006). The use of HEMS is not without potential risk. In addition to the risk to patients, HEMS flight crews have one of the highest mortality risks of all occupations (Baker 2006). For these reasons, a systematic review of the literature is warranted so that structured evidence may be produced to inform and improve clinical interventions, triage decisions, and public policies regarding HEMS. The results from this review may inform the design of subsequent randomised or non-randomised trials through the identification of relevant subgroups of trauma patients who may benefit from HEMS transport.

OBJECTIVES

To determine if helicopter emergency medical services (HEMS) transport, compared to ground emergency medical services (GEMS) transport, is associated with improved morbidity and mortality for adults with major trauma.

METHODS

Criteria for considering studies for this review

Types of studies

Eligible trials included randomised controlled trials (RCTs) and non-randomised intervention studies.

Evidence for benefit or harm of HEMS was not hypothesized to be found with randomised trials because HEMS has become a highly integrated component of many trauma systems; therefore, non-randomised studies (NRS) were also evaluated, which is in accordance with the Cochrane guidance for including NRS (Reeves

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2011). NRS included non-randomised controlled trials and cohort studies. Since case-control studies are susceptible to different types of biases than other observational studies and allocation to groups is by outcome, which introduces further bias, these types of studies were excluded. Evidence from RCTs was not combined with that from NRS.

As NRS cover a wide variety of fundamentally different designs, only studies utilizing the best available designs were included. Studies had to include a comparison group consisting of a GEMS group with or without a comparison via a Trauma-Related Injury Severity Score (TRISS)-based analysis. TRISS is a logistic regression model that compares outcomes to a large cohort of patients in the Major Trauma Outcomes Study (MTOS) (Champion 1990). As first utilized by Baxt in 1983 (Baxt 1983), TRISS-based comparisons are made with a three-step process. First, the actual mortality of HEMS-transported patients is compared to TRISS-predicted mortality. Next, the mortality of GEMS-transported patients is compared to TRISS-predicted mortality. Finally, the null hypothesis that actual survival is no different than TRISS-predicted survival is tested for the HEMS cohort versus the GEMS cohort. For non-United States (US) TRISS-based studies, use of the standardized *W* statistic was required because the *M* statistic for non-US populations may be below the cutoff for non-standardized TRISS (Schluter 2010). An *M* statistic > 0.88 is considered acceptable for comparing non-US populations to the MTOS cohort, based on case-mix and injury severity. A *W* statistic indicates the number of survivors expected per 100 patients treated. Non-US TRISS-based studies that failed to report the *W* statistic were tracked and examined with a sensitivity analysis. TRISS studies reporting the *Z* statistic were also included. A *Z* statistic > 1.96 indicates a potential survival benefit when one population is compared to the MTOS cohort (Champion 1990).

Studies were included if other techniques such as regression modelling or stratification were used to control for confounding. Each included study had to provide a description of how the groups were formed. If the study did not compare two or more groups of participants, it was excluded. Groups were defined based on time or location differences or by naturally occurring variations in treatment decisions. For example, some studies examined groups with different crew configurations, different equipment, or different capabilities to perform invasive interventions.

Both prospective and retrospective NRS were included. If parts of a retrospective study were conducted prospectively, these studies were only included if the study was described in sufficient detail to discern this. Included studies had to describe comparability between the groups assessed. For instance, the injury severity score (ISS) varied between HEMS and GEMS groups in some studies.

There are many potential confounders that may be responsible for any positive or detrimental effect of HEMS. Potential confounders that were considered included:

- different types of prehospital interventions (i.e. needle thoracentesis, cricothyrotomy, rapid-sequence endotracheal intubation);
- different levels of care at the receiving trauma centre (e.g. integrated trauma system versus isolated rural hospital);
- varying expertise of HEMS versus ground EMS providers (i.e. different crew configurations);
- age, gender of patients;
- injury stratification (i.e. Injury Severity Score (ISS) or other score);
- type of traumatic injury (i.e. blunt versus penetrating trauma; isolated traumatic brain injury versus other types of trauma);
- scene transport versus inter-facility transport.

Types of participants

Adults with major trauma and aged 16 years or older.

Major trauma was defined by an ISS greater than or equal to 15. An ISS of 15 or greater has previously been shown to be associated with a greater need for trauma care (Baker 1976; Kane 1985). In the event that the ISS was not reported, we considered alternative scoring systems or other definitions for major trauma such as a New Injury Severity Score (NISS) greater than or equal to 15 (Osler 1997). Since any individual Abbreviated Injury Scale (AIS) of four or greater will result in an ISS greater than 15, this was also used to indicate major trauma if studies only reported AIS (Wyatt 1998). Individuals reported to have sustained 'major trauma', or a similar description that was nearly equivalent to an ISS greater to or equal than 15, were included. Trauma centres were defined by level, whenever possible, as defined by the American College of Surgeons Committee on Trauma (ACS-COT 1999). Briefly, a level I trauma centre represents the highest level of possible trauma care, including 24-hour multispeciality surgical coverage. Level I trauma centres are also required to have an active research program and are expected to be regional leaders in trauma education. Level II trauma centres supplement the clinical expertise of a level I centre, and also have 24-hour multispeciality coverage, but are not required to have an active research program. Level III to level V centres represent descending capabilities with fewer available specialties and a focus on stabilization for transfer to higher level trauma centres.

Types of interventions

Transport of patients with major trauma by helicopter emergency medical services (HEMS) compared with transport by ground emergency medical services (GEMS).

Types of outcome measures

Primary outcomes

Survival, as defined by discharge from the hospital.

Survival is the most consequential, most consignable, and least ambiguous variable used to express outcome in HEMS studies (Ringburg 2009).

Secondary outcomes

Secondary outcomes included quality-adjusted life years (QALYs) and disability-adjusted life years (DALYs).

Since the focus of this review was the evaluation of the benefits of HEMS in terms of morbidity and mortality, economical outcomes were not considered. The financial costs and benefits associated with HEMS are complex and sufficiently important to warrant a separate study.

Search methods for identification of studies

Searches were not restricted by date, language, or publication status.

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Electronic searches

We searched the following databases:

- Cochrane Injuries Group Specialised Register (24 January 2012);
- Cochrane Central Register of Controlled Trials (CENTRAL) (issue 1 of 12, 2012);
- MEDLINE (OvidSP) (1950 to 24 January 2012);
- EMBASE (OvidSP) (1980 to 24 January 2012);
- CINAHL (EBSCOhost) (1982 to 24 January 2012);
- ISI Web of Science: Science Citation Index Expanded (SCI-EXPANDED) (1970 to January 2012);
- ISI Web of Science: Conference Proceedings Citation Index-Science (CPCI-S) (1990 to January 2012);
- ZETOC (24 January 2012).

Searches were based on the MEDLINE search strategy and were adapted, where necessary, for use in other databases.

Searching other resources

We searched the reference lists of all relevant material found in order to identify additional published and unpublished studies. Handsearches of secondary references were also performed.

We searched (24 January 2012) the following web-based trials registers for published and unpublished studies:

- Clinicaltrials.gov (www.clinicaltrials.gov);
- Controlled Trials metaRegister (www.controlled-trials.com);
- National Library of Medicine's Health Services Research Projects in Progress (HSRProj) (http://wwwcf.nlm.nih.gov/hsr_project/home_proj.cfm);
- World Health Organization (WHO) Clinical Trials Registry Platform (ICTRP) (http://apps.who.int/trialsearch/);
- OpenSIGLE (System for Information on Grey Literature in Europe) (http://opensigle.inist.fr/).

Data collection and analysis

The search results werecollated and merged into a single bibliographic database. Duplicates were identified and removed before screening the titles and abstracts.

Selection of studies

Two authors (SG and EH) examined the electronic search results in order to reject material that did not meet any of the inclusion criteria. Three review authors (SG, CS, and DS) independently screened the remaining titles and abstracts for reports of possibly relevant trials. Each study was marked as 'exclude', 'include', or 'uncertain'.

All titles or abstracts classified as 'exclude' were cross-reviewed by one of the other three authors and the reasons for exclusion were documented. If a title was not clearly relevant, a full-text version was retrieved. Reasons for exclusion included studies not pertaining to traumatically-injured adults, studies with non-original data, single case reports, the lack of a control group or description of a comparison group, or other reasons, based on the rationale described above.

All titles or abstracts classified as 'include' or 'uncertain' were retrieved in full and assessed using the recommendations provided in Chapter 13 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Reeves 2011).

Disagreements were resolved by group consensus (SG, CS, EH, ST). If further clarification was required, attempts were made to contact the authors.

Data extraction and management

Three authors (SG, CS, and EH) were each assigned one-third of the included articles and independently extracted information on study characteristics and the results. Any uncertainty about study inclusion was resolved by group consensus. Data extraction and study quality forms were developed, pilot tested, and used by the group. Data to be extracted included: last name and first initial of the first author, publication year, study design, participants, duration of follow-up, definition of patient population, data for each intervention-outcome comparison, estimate of effect with confidence intervals and P values, key conclusions of study authors, and review author's comments. Data were put into Review Manager 5.1 software.

Assessment of risk of bias in included studies

Risk of bias for included RCTs was assessed by two review authors (SG and CS). There was very good agreement between the two review authors (kappa = 0.92). Six domains were evaluated: sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and other sources of bias. The risk of bias in each category was judged as high risk, low risk, and unclear according to guidance in Chapter 8 of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). Any disagreements were resolved by group consensus. Risk of bias for all NRS conducted entirely prospectively was assessed in the same manner but using the domains defined by the Downs and Black quality assessment scale (Downs 1998).

For NRS not conducted entirely prospectively, risk of bias was assessed with the Downs and Black quality assessment scale (Downs 1998). This tool is considered an acceptable tool for evaluating NRS (Deeks 2003). The Downs and Black assessment tool has five items for evaluating risk of bias in NRS. All five subscales from this tool were utilized. The total number of points for each subscale was 11 for reporting bias, three for external validity, seven for internal validity, six for internal validity confounding and selection bias, and five for power. Thresholds were established to define 'low', 'unclear', and 'high' levels of bias. Scores met the definition for a 'low' risk of bias if the scores were: > 8/11 for reporting bias, 3/3 for external validity, > 5/7 for internal validity, > 5/6 for internal validity confounding and selection bias, and > 4/5 for power. Studies were considered to be at 'high' risk of bias if the scores were: < 6/11 for reporting bias, < 1/3 for external validity, < 4/7 for internal validity, < 3/6 for internal validity confounding and selection bias, and < 2/5 for power. Scores between the 'low' and 'high' bias thresholds were scored as 'unclear'.

Measures of treatment effect

For the dichotomous outcome of mortality, we calculated summary relative risks (RR) or log relative risks using the generic inverse-variance method, but only if the included studies had similar

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design features. For the continuous secondary outcomes (QALYs and DALYs), mean differences (MD) were calculated.

Unit of analysis issues

The unit of analysis was the individual patient.

Dealing with missing data

We attempted to contact the authors of included studies to request missing data. If the authors failed to respond, we considered the data missing.

Assessment of heterogeneity

We explored possible sources of heterogeneity between studies, and a forest plot was constructed. The forest plot was visually assessed for heterogeneity by examining overlap of confidence intervals. We calculated an I^2 statistic to determine the proportion of variation due to heterogeneity; we considered a value greater than 50% as an indicator of significant statistical heterogeneity and a value greater than 90% as an indicator of considerable heterogeneity. We also calculated a Chi^2 statistic for heterogeneity, with a P value < 0.05 suggestive of significant heterogeneity.

Assessment of reporting biases

A funnel plot was generated and examined visually to assess for potential publication bias. We anticipated difficulty in showing that all relevant studies could be identified because of poor indexing and inconsistent use of design labels by HEMS researchers. We read full papers to determine eligibility of studies that came into question.

Data synthesis

We presented a narrative synthesis of our review by summarizing the design characteristics, risk of bias, and results of the included studies. We commented extensively on how each study design or quality attribute affected the quantitative result. Potential sources of bias in our review were discussed, in addition to our methods used to control for these potential biases.

We hypothesized that several factors relating to different study designs may have a significant effect on the results from individual studies. We anticipated that some studies may have used a TRISS-based analysis, which is based on a population from the Major Trauma Outcomes Study (MTOS), as a control group. The TRISS analysis, which is used extensively in trauma research, is the most commonly used tool for benchmarking trauma outcomes but the coefficients have not been updated within the last 14 years (Schluter 2010). TRISS is a weighted combination of patient age, ISS, and Revised Trauma Score (RTS), and was developed to predict a patient's probability of survival after sustaining a traumatic injury. As trauma care may have improved over time, the data from which the original coefficients were derived may not reflect present day survival. Furthermore, TRISS-based studies may not be wholly representative of all trauma injury populations (Champion 1990). These limitations were considered in all of our interpretations and analyses of TRISS-based studies. Since 1996, the Trauma Audit and Research Network in the United Kingdom has been used to collect and analyse data for trauma patients (Gabbe 2011). The developers of this trauma registry have formulated a case-mix adjustment model which addresses some of the limitations of the TRISS model (TARN 2011). Like the TRISS, the probability of survival (Ps) for each patient can be accurately calculated using age, gender, Glasgow Coma Score (GCS), ISS, and an interaction term for age and gender (TARN 2011).

Subgroup analysis and investigation of heterogeneity

Any salutary effect of HEMS is likely to be the result of some combination of speed, crew configuration (that is medical expertise), and the fact that HEMS programs are often an integral part of a comprehensive trauma system (Thomas 2003).

Sensitivity analysis

A sensitivity analysis was planned to examine the effect of excluding studies judged to be inadequate. We also considered a sensitivity analysis to investigate how different aspects of the observed heterogeneity may have impacted our overall results. Non-US TRISS-based studies that failed to report the *W* statistic were recorded and compared in a separate sensitivity analysis.

Preplanned subgroup analyses were performed, when possible, to determine whether results differed by the following.

Population

i. Older versus younger age (e.g. age greater than 65 years)

ii. Urban versus rural helicopter and ground emergency medical services systems

Type of injury

i. Blunt versus penetrating trauma

ii. Studies limited to traumatic brain injuries only

iii. Injury severity (e.g. ISS of 15 to 25, 26 to 49, > 50)

iv. Comorbidities (e.g. patients with different levels of preexisting medical conditions; such as previously healthy patients versus patients with preexisting medical conditions such as coronary artery disease, diabetes, etc.)

Intervention

i. Crew configuration (e.g. physician-staffed, paramedic only, nurse and paramedic)

ii. HEMS disposition (e.g. transfer to level 1 versus level 2 trauma centre)

iii. Interfacility transfers versus primary scene transports

iv. HEMS and GEMS interventions (e.g. intubations, chest decompressions)

RESULTS

Description of studies

See: Characteristics of included studies.

Each study was scored according to the five domains of the Downs and Black risk of bias assessment tool (Downs 1998). Domain scores for each study are reported as the numerator in the risk of bias tables, with the denominator representing the maximum score for each domain.

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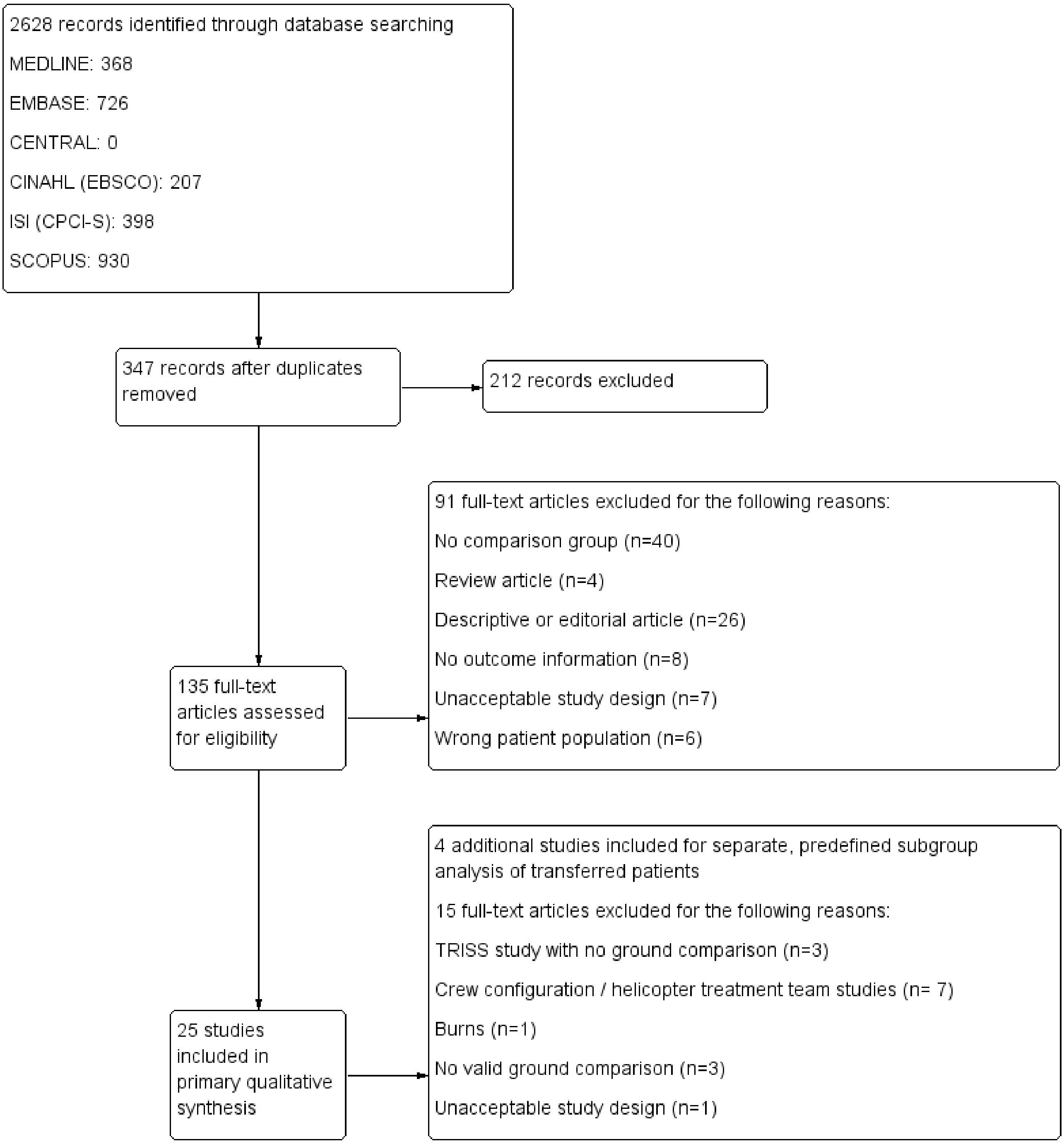
Results of the search

See: Figure 1.

Figure 1. Study flow diagram.



Twenty-five studies met the entry criteria for this review. Four additional studies met the criteria for a separate, predefined subgroup analysis of patients transferred to trauma centres by HEMS or GEMS.

Included studies

All studies were non-randomised studies; no RCTS were found. Nine studies included in the primary analysis used logistic regression to control for known confounders (Braithwaite 1998; Brown 2010; Cunningham 1997; Frey 1999; Koury 1998; Newgard 2010; Sullivent 2011; Talving 2009; Thomas 2002). Six studies in the primary analysis used TRISS methods (Biewener 2004; Buntman 2002;

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Frink 2007; Nicholl 1995; Phillips 1999; Schwartz 1990). Two studies (Nardi 1994; Weninger 2005) did not use TRISS methods or regression but relied on stratification to control for confounding factors. In Nardi 1994, all patients had an ISS > 15, and only data from HEMS and GEMS patients transported to a level I centres were used. Weninger 2005 used extensive stratification by physiological parameters such as blood pressure, heart rate, respiratory rate, oxygen saturation, and AIS to evaluate HEMS and GEMS patients.

Studies evaluating HEMS versus GEMS for blunt trauma or traumatic brain injury were evaluated separately in preplanned subgroup analyses. Three studies examined outcomes for patients sustaining blunt trauma (Bartolacci 1998; Baxt 1983; Thomas 2002). Of the three blunt trauma studies, two used TRISS-based methods (Bartolacci 1998; Baxt 1983) and one used logistic regression (Thomas 2002). Five studies focused on traumatic brain injury (Baxt 1987; Berlot 2009; Davis 2005; Di Bartolomeo 2001; Schiller 1988). Of these studies, two were TRISS-based (Baxt 1987; Di Bartolomeo 2001) and one used logistic regression (Davis 2005); the remaining two traumatic brain injury studies reported unadjusted mortality without stratification (Berlot 2009; Schiller 1988).

Four additional studies examining the role of HEMS versus GEMS for transferred patients met the inclusion criteria for a subgroup analysis that was planned a priori (Brown 2011; McVey 2010; Mitchell 2007; Moylan 1988). One transfer study used logistic regression (Brown 2011) and two used TRISS-based methods (McVey 2010; Mitchell 2007). Another transfer study stratified patients according to trauma score (Moylan 1988).

Excluded studies

Seven HEMS studies examined the effect of physician-based helicopter treatment teams (HTTs). HTTs, used extensively in European systems in Germany and the Netherlands, rarely transport the patient in the helicopter and these studies were excluded since the main objective of this review was to determine the effect of HEMS versus GEMS transport for traumatically injured adults. Only one study examined burns patients, and this study was excluded. Three studies used TRISS to compare HEMS patient outcomes to the MTOS cohort, but not GEMS, and these studies were excluded since these studies violated the TRISS methods for comparing HEMS to GEMS as originally described by Baxt 1983. Additional study exclusions are described in Figure 1.

Risk of bias in included studies

See: Figure 2 and Figure 3.

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Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

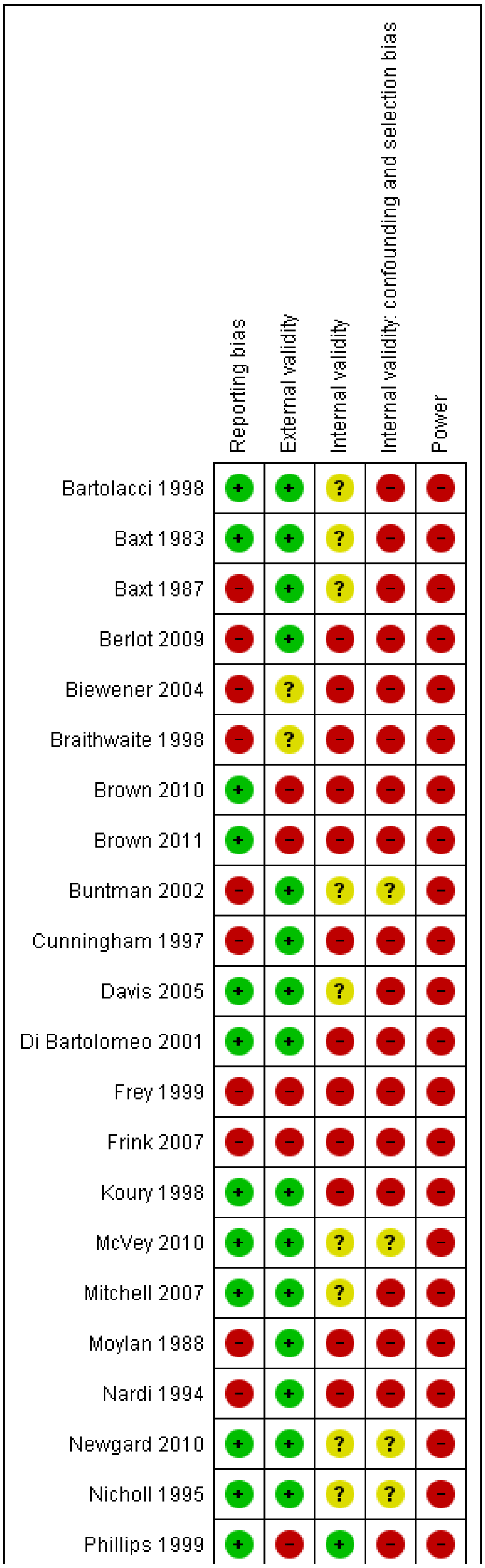

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Figure 2. (Continued)

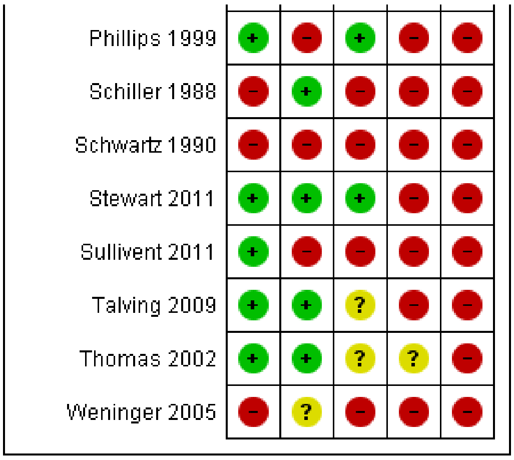
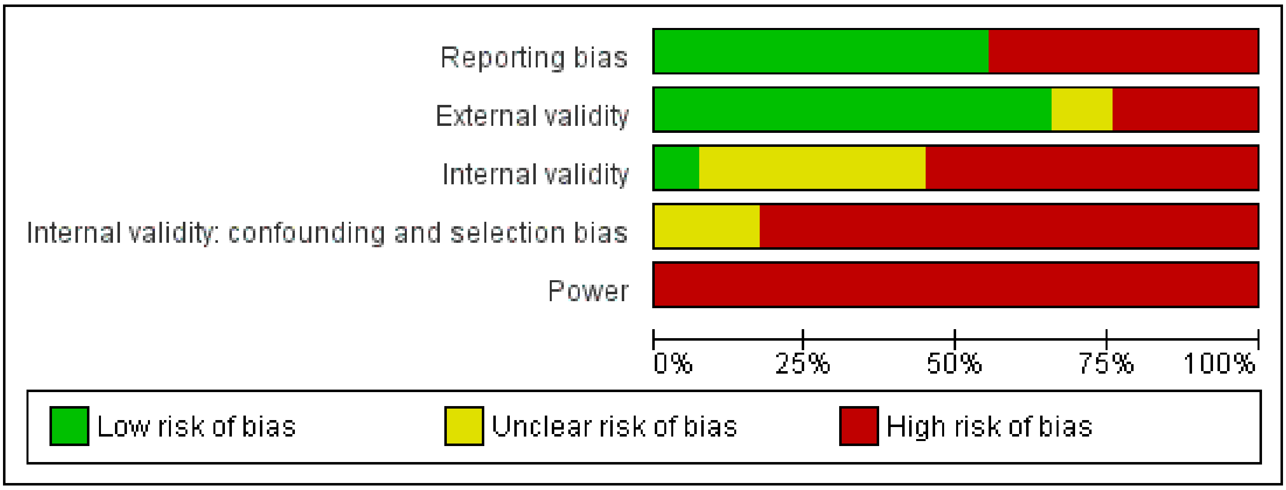


Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



Risk of bias was assessed with the Downs and Black assessment tool (Downs 1998). The highest possible score was 32. The mean overall quality score for all included studies was 14.9 (range 7 to 22). Overall, the majority of studies were of low methodological quality and not a single study had an overall 'low' risk of bias. Not a single study included a valid power calculation. Only five studies had an overall quality score of greater than 19 (Baxt 1983; Davis 2005; Di Bartolomeo 2001; Newgard 2010; Nicholl 1995; Stewart 2011; Thomas 2002).

Allocation

All studies had an unclear or high level of selection bias. This was not a surprising finding considering the nature of the included studies; selection bias is an inherent risk of NRS.

One potential source of selection bias was injury severity; not all studies used ISS > 15 as an inclusion criterion, and some studies used other measures of injury severity. For example, in Braithwaite 1998 the mean ISS was 13.8 in the GEMS group versus 19.1 in the HEMS group (P < 0.01). Although the ISS was below our inclusion criterion cutoff of 15, this study was included because a regression analysis was used to control for injury severity. In Phillips 1999, patients were stratified by probability of survival rather than ISS and, therefore, we only included patients with a probability of survival less than 50% in our review. The study by Talving 2009 consisted of a patient population that had an ISS < 15 in 74% of individuals; we only used data from the subgroup in this study with an ISS > 15. In Cunningham 1997, the mean ISS was lower than 15 in the GEMS group, but patients were stratified by ISS and logistic regression was used to adjust for differences in injury severity. In Moylan 1988, although ISS was not used we included this study because patients were stratified by trauma score, and the mean trauma score was 8.7 for HEMS patients and 9.2 for GEMS patients (P value not reported).

Most studies included in this review attempted to control for confounding. Of the 25 studies in the primary analysis, and the four transfer studies in the predetermined subgroup analysis, a total of 12 studies (39%) used multivariable logistic regression. Only three studies reported regression diagnostics to ensure that the regression model was specified correctly (Newgard 2010; Sullivent 2011; Thomas 2002). Four studies used advanced regression

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techniques including propensity scores (Davis 2005; Stewart 2011), instrumental variables (Newgard 2010), and techniques to control for clustering by trauma centre (Thomas 2002).

Ten of the total studies relied on a TRISS-based analysis to compare both HEMS and GEMS outcomes against the MTOS cohort; however, TRISS-based statistics were not reported consistently. The validity of TRISS methods has been questioned because the MTOS was established nearly two decades ago (Champion 1990) and changes in injury prevention and trauma care may preclude valid comparisons over time. Patients in the MTOS might have had a worse prognosis or different injury severity than contemporary trauma patients. To adjust for these potential differences, investigators using TRISS are encouraged to report an *M* statistic to ensure that severity and case-mix is comparable (Schluter 2010). Only one study included in this review reported an *M* statistic (Buntman 2002). Four TRISS studies were published after 2000 and it is possible that these populations might have differed significantly from the original MTOS cohort (Biewener 2004; Buntman 2002; Di Bartolomeo 2001; Frink 2007). Di Bartolomeo 2001 attempted to control for case-mix differences by comparing patients to an Italian MTOS cohort. The *W* statistic was only reported by four studies (Bartolacci 1998; Di Bartolomeo 2001; McVey 2010; Mitchell 2007). Only four studies reported a *Z* statistic (Baxt 1983; Biewener 2004; Phillips 1999; Schwartz 1990) and three studies failed to formally report any TRISS statistics (Baxt 1987; Frink 2007; Nicholl 1995).

Crew configuration varied widely between studies and this may have had an effect on mortality since HEMS or GEMS patients might have been preferentially exposed to potential life-saving interventions. For example, in one of the earliest and best-known HEMS studies, Baxt 1983 reported a 52% reduction in mortality for the HEMS group. In this study the HEMS crews consisted of an acute care physician who could perform advanced airway interventions, while the prehospital interventions authorized for the GEMS group were limited to advanced first aid and placement of an oesophageal obturator airway (EOA). HEMS and GEMS crew configurations were not described in all studies and less than half of all studies included in the primary analysis described the type and frequency of prehospital interventions. Crew configurations are described for the studies that provided this information in the Characteristics of included studies table. Twelve studies included in the primary analysis had physicians as part of the HEMS crew (Bartolacci 1998; Baxt 1983; Baxt 1987; Berlot 2009; Davis 2005; Di Bartolomeo 2001; Frink 2007; Nardi 1994; Nicholl 1995; Schwartz 1990; Thomas 2002; Weninger 2005). Eleven studies did not describe the crew configuration for HEMS or GEMS (Biewener 2004; Braithwaite 1998; Brown 2010; Cunningham 1997; Frey 1999; Newgard 2010; Schiller 1988; Stewart 2011; Sullivent 2011). Nine studies described the frequency and types of prehospital interventions performed between the HEMS and GEMS groups (Bartolacci 1998; Berlot 2009; Biewener 2004; Davis 2005; Di Bartolomeo 2001; Nardi 1994; Phillips 1999; Schwartz 1990; Weninger 2005), whereas three studies (Braithwaite 1998; Stewart 2011; Talving 2009) only described the frequency of endotracheal intubation.

Blinding

None of the included studies attempted to blind study participants to the intervention of HEMS versus GEMS. None of the included studies made an attempt to blind those measuring the main outcome of the intervention (HEMS versus GEMS). This resulted in either an 'unclear' or 'high' degree of bias, indicating poor levels of internal validity, for over 90% of the included studies. Detection bias was possible in the majority of included studies due to the retrospective nature of the study designs and because for patients with an ISS > 15 mortality is more likely. It is also possible that deaths were recorded more frequently in the trauma registries that served as a primary source of data for most of the included studies. Survivors lost to follow-up might not have been captured in the registries, biasing the results. Furthermore, mortality definitions differed amongst studies. Thirty-day mortality may be different from 60-day mortality, and this outcome is often difficult to assess. Most studies did not provide information on duration of follow-up.

Incomplete outcome data

Studies with incomplete outcome data were not included in this review; however, attrition bias could not be accurately assessed due to the retrospective nature of the study designs. None of the studies adjusted the analyses for different lengths of follow-up, and it is possible that not all outcomes were available. Losses to patient follow-up were not taken into account in any of the included studies and this explains why over 80% of included studies were at high risk of bias in terms of internal validity. For the unadjusted analysis (Analysis 1.1), data were available for 21 of the 25 studies. Four studies (Brown 2010; Frey 1999; Newgard 2010; Schwartz 1990) did not provide raw data for inclusion in the analysis; attempts to contact authors for this data were unsuccessful.

Selective reporting

Not a single study fully controlled for all known confounders; 50% of all included studies had a low level of reporting bias and the remaining 50% had a high level of reporting bias. Publication bias was assessed with a funnel plot (Figure 4). Trials were seen both to the right and left of the point of no effect, with no trials clustered around the line indicating no difference. An empty zone in the lower right quadrant of the plot was observed. Therefore, it is possible that publication bias was present. This result might also be explained by the considerable clinical heterogeneity amongst the included studies. It is possible that smaller studies with non-significant results were not published.

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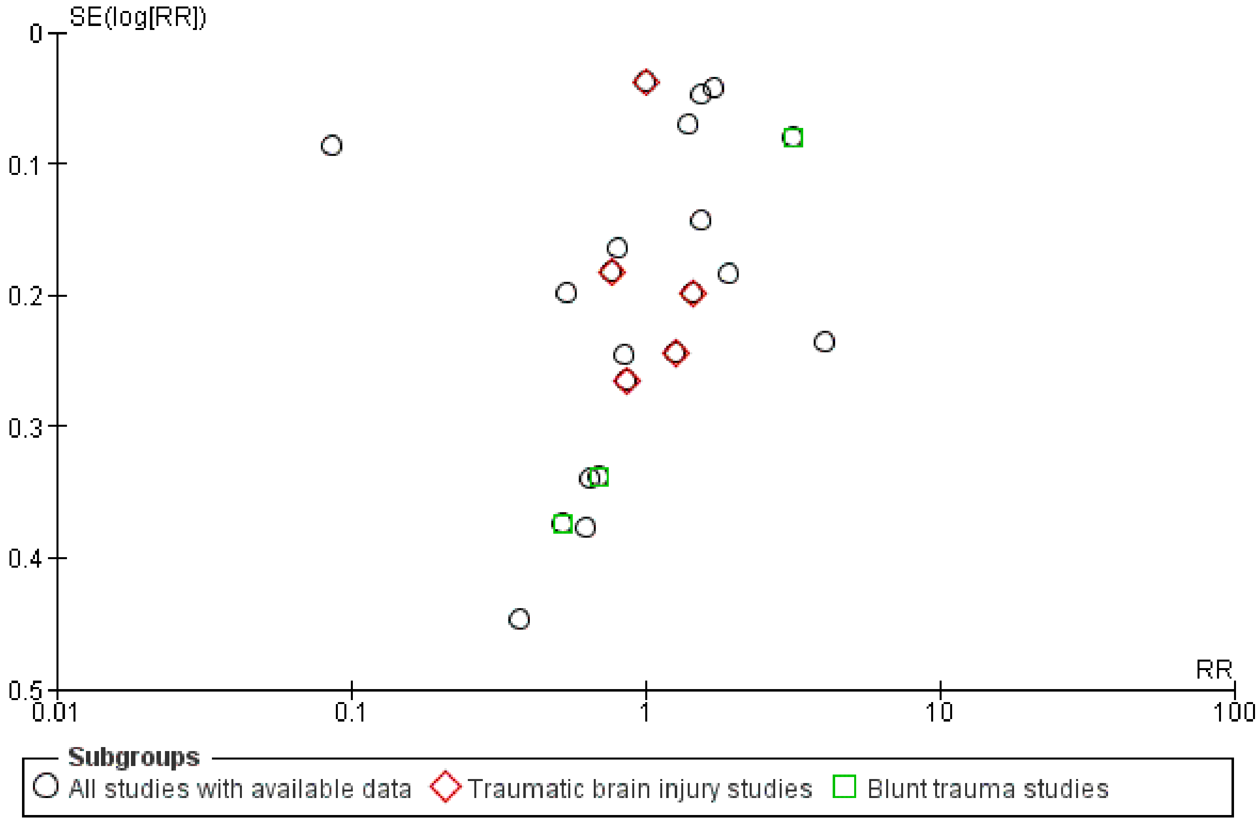
Figure 4. Funnel plot of comparison: HEMS versus GEMS, outcome: 1.1 Overall unadjusted mortality.



Other potential sources of bias

Eleven studies had a minority of paediatric patients included in the patient mix; however, the mean age in all of these studies was reported to be greater than 25 years. One study had 74% of patients with an ISS < 15 (Talving 2009); only the results from the subgroup with an ISS > 15 were included.

Effect estimates, and associated confidence intervals in studies using regression techniques, might be inaccurate based on the availability of the data used to specify the regression model. For instance, the National Trauma Data Bank was used in three studies (Brown 2010; Brown 2011; Sullivent 2011) and this data source is known to have a high proportion of missing data, especially for the physiological variables that the authors included as covariates (Roudsari 2008).

Effects of interventions

See: **Summary of findings for the main comparison**

See: Summary of findings for the main comparison.

Primary outcome measure

Twenty-one of the included studies had extractable data on unadjusted mortality (Analysis 1.1). Considerable heterogeneity was observed as evidenced by an I^2 value of 98% and a highly statistically significant Chi^2 test for heterogeneity ($P < 0.00001$).
Combining the results from these unequally sized and heterogeneous studies in a meta-analysis would be likely to lead to a Yule-Simpson effect (that is Simpson's paradox) and flawed conclusions. For example, when certain groups are combined without accounting for injury severity and other confounders a correlation may be present. This correlation may disappear when the groups are stratified or when analysed with regression techniques. Such a phenomenon appears to be evident in Analysis 1.1. Three studies that appeared to show a pronounced benefit for GEMS based on unadjusted mortality (Stewart 2011; Sullivent 2011; Thomas 2002) had opposite and statistically significant greater odds of survival for HEMS patients after adjusting for confounders with multivariable logistic regression (Table 1). Another study that appeared to significantly favour GEMS based on unadjusted mortality showed no statistical difference between HEMS and GEMS after adjustment with regression (Cunningham 1997). Similarly, based on the unadjusted mortality from Buntman 2002 one would infer that GEMS is superior to HEMS. However, after TRISS methods were applied HEMS was shown to improve survival by 21.43% (Buntman 2002). Alternatively, several studies that appeared to clearly support HEMS based on unadjusted mortality suffered from small sample sizes and the results from these studies might have been biased (Bartolacci 1998; Baxt 1983; Baxt 1987; Koury 1998; Nardi 1994).

Additonally, it is important to understand that four studies (Brown 2010; Frey 1999; Newgard 2010; Schwartz 1990) did not provide raw data for calculation of unadjusted mortality, and this may have influenced the overall relative risk of unadjusted mortality. Three of these studies were regression-based and all three indicated a statistically significantly improved odds of survival (Brown 2010;

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Frey 1999; Newgard 2010). Schwartz 1990 used a TRISS analysis to demonstrate an improvement in predicted survival for HEMS but not GEMS, a finding that was contrary to the results from an unadjusted analysis. Due to the considerable clinical and methodological heterogeneity found in the included studies, a pooled estimate of effect is not presented.

To investigate the effects of the interventions more precisely, studies were evaluated as two subgroups with a precisely defined patient population (adults with blunt trauma or traumatic brain injury), studies that employed multivariate regression techniques, studies that used TRISS-based methods, and studies that met inclusion criteria but used other methods.

See: Table 1.

Studies that used multivariate regression methods

Ten studies used multivariate regression techniques to adjust for known confounders (Braithwaite 1998; Brown 2010; Cunningham 1997; Frey 1999; Koury 1998; Newgard 2010; Stewart 2011; Sullivent 2011; Talving 2009; Thomas 2002). The results from three of these studies focused exclusively on blunt trauma patients (Braithwaite 1998; Schwartz 1990; Thomas 2002) and these studies are summarized in the following section. The effect estimates and 95% confidence intervals (CIs) from these studies are summarized in Table 1 (effect estimates and CIs were not available for Cunningham 1997).

Brown 2010 analysed 41,987 HEMS transports and 216,400 GEMS transports from the 2007 National Trauma Data Bank. When adjusting for ISS, age, gender, injury mechanism, vital signs, type of trauma centre, and urgency of operation, HEMS was associated with a statistically significant greater odds of survival to hospital discharge (OR 1.22; 95% CI 1.18 to 1.27; P < 0.01).

Cunningham 1997 found that HEMS was associated with statistically significant survival benefit for patients with mid-range, but not higher, acuity. Patients with an ISS of 21 to 30 had 56% survival in the HEMS group versus 37.4% survival in the GEMS group. For patients with an ISS of 31 to 40, 80% of HEMS patients survived versus 62.8% of GEMS patients. However, for the most severely injured patients with a probability of survival less than 90%, HEMS patients had 66.9% survival versus the GEMS patients who had 81.9% survival.

Frey 1999 reported in an abstract on 12,233 motor vehicle crash victims admitted to trauma centres in Pennsylvania, PA, USA. A non-significant association with improved survival was found for HEMS in this study (OR 1.34; 95% CI 0.91 to 1.80; P value not reported). Reasons for a lack of statistical significance in Frey et al may be due to residual confounding, transport of lower severity patients, and the fact that this study included only motor vehicle crash patients. Recent advances in vehicle safety may partially explain why no benefit was found when HEMS was compared to GEMS.

A retrospective cohort study by Koury 1998 found a non-statistically significant trend for survival in patients with an ISS > 25 and transported by HEMS (OR 1.6; 95% CI 0.77 to 3.34; P = 0.24). This study controlled for confounding factors such as age, type of trauma, ISS, hospital length of stay, and length of emergency department stay. This study also included some paediatric patients (14% to 16.7%) and inter-facility transfers, although these factors were adjusted for in the regression model. The relatively small number of patients in Koury et al (N = 272) may explain the wide CI for the effect estimate. Moreover, a higher ISS cutoff was used (≥ 25) and the authors acknowledged that the study was likely to be underpowered to find a difference between HEMS and GEMS.

Newgard 2010 conducted a secondary analysis of a prospective cohort registry study of adult trauma patients transported by 146 EMS agencies to 51 level I and II trauma centres in North America. A multivariate regression model using instrumental variables was used to study the association of EMS intervals and mortality among trauma patients with field-based physiological abnormalities, using distance from a trauma centre as the instrument. HEMS had a non-significant trend towards improved survival (OR 1.41; 95% CI 0.68 to 2.94; P value not reported) in the multivariate model. The primary objective of this study was to test the association of EMS intervals and mortality among trauma patients (for example. the 'golden hour' concept) and HEMS was only analysed as one independent variable that might have influenced outcome.

Stewart 2011 calculated a propensity score based on prehospital variables (age, gender, mechanism of injury, respiratory rate, anatomic triage criteria, intubation, level of prehospital care, road distance to a trauma centre) and hospital variables (RTS on ED arrival, ISS, time from receipt of EMS call to ED arrival, time in minutes from receipt of the first EMS call to time of death). This study included 10,184 patients in the state of Oklahoma, USA who were admitted to a single level I trauma centre or one of two level II trauma centres. The propensity score was used as a single confounding covariate in a Cox multivariable proportional hazards regression model to determine the association between mode of transport and mortality. Overall, HEMS patients had a statistically significantly higher hazard ratio for survival compared to GEMS patients (hazard ratio for improved survival (HR) 1.49; 95% CI 1.19 to 1.89; P = 0.001). In the most severely injured patients (RTS of three or less at the scene), the mode of transport was not associated with improved survival.

Sullivent 2011 used multivariate logistic regression to examine the association between mortality and transportation between HEMS and GEMS. The 2007 National Trauma Data Bank was used for this study, with 148,270 records of patients treated at 82 participating trauma centres in the USA. The authors stratified the regression analysis results by three age categories: ≥18 years, 18 to 54 years, and ≥ 55 years. Overall, HEMS transport conferred a statistically significant mortality benefit (OR 1.64; 95% CI 1.45 to 1.87; P < 0.0001), although in the age category ≥ 55 years there was a non-significant association with improved survival (OR 1.08; 95% CI 0.88 to 1.75; P = 0.42).

Talving 2009 retrospectively examined 1836 patients transported by HEMS or GEMS in a predominantly urban environment. In the subgroup of patients with an ISS > 15, HEMS transport was found to have a non-statistically significant trend towards improved survival (OR 1.81; 95% CI 0.55 to 5.88; P = 0.33). An analysis of four high risk subgroups was conducted in this study. Patients with ISS > 15, penetrating trauma, a head AIS > 4, or systolic blood pressure < 90 mmHg did not experience a statistically significantly benefit from HEMS transport in a multivariable analysis adjusting for age, vital signs, injury mechanism, and injury severity. The lack of benefit in this study may be due to the geographical location of the HEMS program that was studied. The region serviced by HEMS was predominantly urban and HEMS was used when transport times exceeded 30 minutes. Thirty minutes may not be a clinically

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important cutoff to justify HEMS use, and patient over-triage was likely in this study.

Studies that used Trauma-Related Injury Severity Score (TRISS)-based methods

Eight studies (Bartolacci 1998; Baxt 1983; Biewener 2004; Buntman 2002; Frink 2007; Nicholl 1995; Phillips 1999; Schwartz 1990) used TRISS-based methods to compare survival for HEMS versus GEMS against the standard of the MTOS cohort. The results from Bartolacci 1998 are discussed in the preceding section. A significant difference between observed and expected survivors was found for HEMS patients (Z = 3.38; P < 0.0001). The W statistic reported in this study was 11.88, which suggests nearly 12 expected survivors for every 100 patients flown; but the M statistic was 0.52, which is less than the acceptable 0.88 threshold for comparing populations (Schluter 2010). The non-significant M statistic indicated that there was a higher proportion of patients with a low probability of survival in the HEMS group compared with the MTOS cohort.

Baxt 1983 studied 300 consecutive HEMS and GEMS transports to a level I trauma centre over a 30-month period. Although the actual Z statistic was not reported, a 52% reduction in predicted mortality was found with the HEMS group (P < 0.001). Overall, 20.62 patients were predicted to die in the HEMS group based on a comparison with the MTOS cohort, but only 10 patients died. In the GEMS group, 14.79 were predicted to die but 19 died. Major improvements in survival were most pronounced for the more seriously injured patient groups. For patients with a ≤ 24% chance of survival, four HEMS patients died when 7.03 were predicted to die; in the GEMS group, six patients died when 7.03 were predicted to die.

Biewener 2004 assessed the impact of rural HEMS versus urban GEMS in 403 trauma patients in the Dresden region in Germany. TRISS-based methods were only used to compare HEMS versus GEMS for patients transported directly from the scene to a level I trauma centre. No TRISS statistics were reported in this study. In the HEMS groups, the TRISS analysis identified 27 unexpected survivors and 4 unexpected deaths out of the 140 HEMS patients; 13 unexpected survivors and 2 unexpected deaths were found in the GEMS group. Although the TRISS evaluation failed to demonstrate any statistically significant differences between HEMS and GEMS group survival, in a multivariate regression model patients in the GEMS group had a trend for decreased odds of survival (OR 0.94; 95% CI 0.38 to 2.34; P value not reported).

Buntman 2002 reported the results from a prospective database analysis of 428 HEMS and GEMS patients in South Africa. Survival rates in the HEMS and GEMS groups were compared with TRISS predicted survival rates, and patients with a probability of survival less than 65% were more likely to survive if transported by HEMS. Overall, 38.15 HEMS patients were expected to die and 39 actually died (Z = 0.223); 38.96 GEMS patients were predicted to die and 51 actually died (Z = 2.939). The difference in the Z statistic between the HEMS and GEMS groups was 1.921 (P < 0.05) indicating a greater chance for survival in the HEMS group than the GEMS group. It should be noted that the M statistic reported in this study was 0.618 for the HEMS group and 0.867 for the GEMS group; both groups failed to meet the threshold for accurate comparison to the MTOS cohort.

Frink 2007 retrospectively evaluated 7534 HEMS and GEMS patients in Germany and used a TRISS prediction of survival to demonstrate a survival benefit for patients transported by HEMS, though no specific TRISS statistics were reported in this study. Overall mortality was 34.9% in the HEMS group versus 40.1% in the GEMS group (P < 0.01), but this difference was only found in patients with an ISS < 61.

Nicholl 1995 compared 337 HEMS patients and 466 GEMS patients in the UK using the TRISS methodology. The number of HEMS deaths exceeded the MTOS norms by 15.6% compared with an excess of 2.4% in the GEMS group. No TRISS-specific statistics were reported and overall mortality for patients with an ISS > 15 was 51% in the HEMS group and 44% in the GEMS group (not statistically significant, P value not reported). In this study, non-significant trends for improved survival with HEMS compared to GEMS were found for patients with an ISS of 16 to 24 (OR for improved survival 1.25; 95% CI 0.44 to 3.33) and an ISS of 25 to 40 (OR for improved survival 1.11; 95% CI 0.83 to 1.43). In both of these ISS groups there were less than 60 patients in each group, thus the wide CIs are likely to be due to the relatively small number of patients within each subgroup.

Phillips 1999 used the TRISS methodology to compare mortality rates of 792 trauma patients transported by HEMS or GEMS in Texas, USA. The Z statistic was not significant for actual versus predicted deaths for HEMS (Z = 0.40) or GEMS (Z = 0.151). The HEMS group sustained 15 deaths compared with a TRISS-predicted rate of 16.44 deaths; the GEMS group sustained 41 deaths compared with a TRISS-predicted rate of 39.11 deaths; neither result was statistically significant.

Schwartz 1990 reported on a series of blunt trauma patients transported by either HEMS or GEMS to a single level I trauma centre in Connecticut, USA, between 1987-1988. TRISS methodology was used in this cohort, but W, Z, and M statistics were not reported. HEMS crews were comprised of highly trained providers, including a physician, nurse, and respiratory therapist, while GEMS crews were comprised of an EMT and paramedic. HEMS patients had a probability of survival of 2.23 standard deviations better than the national norm, while GEMS patients had a survival -2.69 standard deviations below the national norm. More HEMS patients were intubated (42% vs 3%) and more HEMS patients were treated with a pneumatic anti-shock garment (56% vs 30%). There was no significant difference in the prehospital times for either HEMS or GEMS once crews had arrived at the scene.

Studies using other methods to adjust for confounding

Two additional studies that did not use regression techniques or a TRISS-based analysis met the inclusion criteria (Nardi 1994; Weninger 2005). The results from Nardi 1994 are summarized in the blunt trauma section. These studies did not utilize TRISS-based methods or regression techniques. In Weninger et al, HEMS and GEMS patients were similar in age, sex, and injury severity (Weninger 2005). HEMS patients had more frequent administration of intravenous fluids, endotracheal intubation, and chest tube placement than GEMS patients. Twenty of 104 HEMS patients died (19.2%) versus 39 of 172 GEMS patients (22.7%) (P value not reported).

Traumatic brain injury studies

Five studies focused on the role of HEMS versus GEMS transport for traumatic brain injury (Baxt 1987; Berlot 2009; Davis 2005; Di Bartolomeo 2001; Schiller 1988). A total of 11,528 patients were

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analysed from these studies and data were available from all five studies to calculate unadjusted mortality. Moderate heterogeneity was observed in this subgroup (Chi^2=6.80; I^2 =41%). Based on the raw mortality data from these five trials, no significant association with improved survival was found (RR 1.02 in favour of HEMS; 95% CI 0.85 to 1.23).

A total of 10,314 HEMS and GEMS patients were studied by Davis 2005. Propensity scores were used to account for the variability in selection of patients undergoing HEMS versus GEMS transport and a multivariate regression model was used to adjust for age, sex, mechanism of injury, hypotension, Glasgow Coma Score (GCS), AIS, and ISS. An improved odds of survival was found for HEMS patients (OR 1.90; 95% CI 1.60 to 2.25; P < 0.0001) after adjustment for potential confounders. When stratified by GCS, a statistically significant survival benefit was only observed for the GCS group with a score of 3 to 8 (OR 1.84; 95% CI 1.51 to 2.23; P < 0.001).

Di Bartolomeo 2001 utilized a population-based, prospective cohort design to investigate the effect of two different patterns of prehospital care in the Fiuli Venezia Giulia region of Italy. The HEMS group was staffed by a physician and the GEMS group was staffed by a nurse. Significantly more patients in the HEMS group received chest tube placement, placement of intravenous lines, and advanced modes of ventilation, including endotracheal intubation. After controlling for transport mode, gender, age, ISS, and Revised Trauma Score (RTS), no significant difference was found between HEMS and GEMS (OR not reported; P = 0.68). For patients requiring urgent neurosurgery, a non-significant trend towards improved mortality was found for HEMS (OR 1.56; 95% CI 0.38 to 6.25; P value not reported).

In a retrospective cohort of 606 patients by Schiller 1988, unadjusted mortality was statistically significantly higher for HEMS (18%) versus GEMS (13%) (P < 0.05). All patients in this cohort had blunt trauma and 80% had a traumatic brain injury. All patients had an ISS between 20 and 39. While all patients were transported to a level I trauma centre in this study, crew configurations were not described. The study was conducted in a primarily urban setting in Phoenix, AZ, USA.

Baxt 1987 studied the impact of HEMS versus GEMS for 128 consecutive patients with traumatic brain injury in San Diego, CA, USA. HEMS crews consisted of an attending physician and nurse, and GEMS crews consisted of emergency medical technicians (EMTs) capable of providing only basic life support. Overall unadjusted mortality was 31% in the HEMS group and 40% in the GEMS group (P < 0.0001). For GCS scores of five, six, or seven the GEMS group had improved mortality; however for GCS scores of three or four, mortality was statistically significantly lower for the HEMS group (52%) versus the GEMS group (64%) (P value not reported for this subgroup).

Berlot 2009 retrospectively compared HEMS versus GEMS outcomes in 194 patients with an AIS-head ≥ 9 and an ISS ≥ 15. HEMS crews consisted of two nurses and an anaesthesiologist. GEMS crews consisted of a physician capable of providing only basic life support and two nurses trained in emergency care. HEMS patients had an unadjusted mortality of 21% versus 25% in the GEMS group (P < 0.05); 54% of HEMS patients survived with only minor neurologic disability compared to 44% of GEMS patients (P < 0.05).

Blunt trauma studies

Six studies consisted of a population of adults with blunt trauma (Bartolacci 1998; Baxt 1983; Braithwaite 1998; Nardi 1994; Schwartz 1990; Thomas 2002). Heterogeneity in this subgroup was considerable (Chi^2=39.53; I^2 =95%). All three studies provided data to estimate unadjusted mortality but due to the heterogeneity a reliable effect estimate, and associated CI, could not be estimated. These data, when considered collectively, suggest an overall benefit of HEMS versus GEMS for adults with major trauma, although meta-analysis could not be performed to provide a precise estimate of the effect size.

In Bartolacci 1998, HEMS patients were treated by an anaesthesiologist and a paramedic whereas GEMS patients were treated by an acute care physician and a paramedic. All patients were transported to a level I trauma centre in Sydney, Australia. Major blunt trauma was defined by the mechanism of injury and an ISS > 15. A *W* statistic of 12.18 was calculated (95% CI 5.29 to 19.07). This indicated that there were 12 more survivors in the HEMS group than expected for every 100 patients transported, based on a comparison with the MTOS cohort.

Thomas 2002 studied 16,699 blunt trauma patients treated in the New England, USA area from 1995 to 1998; 2292 patients were treated by HEMS and 14,407 patients were treated by GEMS. Although the unadjusted mortality was 9.4% for HEMS versus 2.0% for GEMS, after adjusting for age, sex, transport year, receiving hospital, ISS, mission type, and prehospital level of care HEMS was found to be associated with a lower odds of death compared to GEMS (OR 0.76; 95% CI 0.59 to 0.98; P = 0.031). Some HEMS crews consisted of a physician and nurse while others consisted of paramedics or nurses only.

Baxt 1983 included 150 HEMS and 150 GEMS patients in the San Diego, CA, USA area who sustained major blunt trauma. The authors employed a TRISS analysis, comparing expected versus actual survival based on comparison to the MTOS cohort. In the HEMS group, 20.6 patients were predicted to die but only 10 died; in the GEMS group 14.8 patients were expected to die but 19 died. Although the actual *Z* statistic was not reported, HEMS versus GEMS patients were 52% more likely to survive when patient groups were stratified by injury severity (P < 0.001).

Braithwaite 1998 performed a retrospective study of 16,699 blunt trauma patients with a categorization of the ISS into five groups: 0 to 15, 16 to 30, 31 to 45, 46 to 60, and > 60. A statistically significant overall beneficial effect on survival for HEMS compared to GEMS could not be confirmed, but a statistically significant interaction between HEMS transport and mortality was found in the middle ISS groups (16 to 30, 31 to 45, 31 to 45) thus demonstrating a survival benefit for patients with moderate to severe injuries.

Schwartz 1990 retrospectively analysed data from a Connecticut, USA EMS system, comparing 126 blunt trauma patients transported by either HEMS or GEMS with TRISS methodology. HEMS patients were statistically significantly more likely to survive compared to the MTOS cohort (Z = 2.23) and GEMS patients had a lower survival rate than predicated by MTOS (Z = -2.69).

Nardi 1994 prospectively collected data on 222 blunt trauma patients, with mean ISS greater than 30, in Italy. Patients transported directly to a trauma centre by HEMS had an unadjusted

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mortality rate of 12% versus a mortality rate of 32% for GEMS patients transported directly to a trauma centre; 14% of HEMS patients had a chest tube placed and 81% were intubated, no patients in the GEMS comparison group had a chest tube placement or intubation. The HEMS crew consisted of an anaesthesiologist with at least 10 years' experience and two nurses with intensive care unit experience. GEMS crews consisted of two nurses with basic trauma life support training and an occasional emergency department physician who was not allowed to intubate.

Secondary outcome measures

No studies measuring QALYs or DALYs met the inclusion criteria for this review.

Subgroup analysis

Four studies that met inclusion criteria focused on the role of HEMS versus GEMS for inter-facility transfers to higher levels of trauma care (Brown 2011; McVey 2010; Mitchell 2007; Moylan 1988).

Brown 2011 examined 74,779 patients transferred to trauma centres by either HEMS (20%) or GEMS (80%). Multivariate regression was used to determine whether transport modality was an independent predictor of survival while adjusting for age, gender, mechanism of injury, ISS, hypotension, severe traumatic brain injury, abnormal respiratory rate, mechanical ventilation, emergent operations, intensive care unit (ICU) admission, and trauma centre designation. HEMS transportation for patients with an ISS > 15, when used as the modality to transfer patients to a higher level of trauma care, was independently associated with statistically significantly improved survival (OR 1.09; 95% CI 1.02 to 1.17; P = 0.01).

Moylan et al examined the impact of HEMS versus GEMS on inter-hospital transportation to a level I trauma centre for 330 severely injured patients (Moylan 1988). HEMS patients were more likely to receive blood transfusions (32% versus 10.5%), be intubated (50% versus 25%), or have medical anti-shock trousers (MAST) applied (60.2% versus 34.9%). HEMS patients also received significantly more mean amounts of intravenous fluid (3.34 L per patient) than GEMS patients (2.1 L per patient). For patients with a trauma score between 10 and 5, 54 of 101 GEMS patients survived (53.5%) compared to 53 of 64 HEMS patients (82.8%). This result was statistically significant, favouring HEMS in terms of a survival advantage (P < 0.001).

Mitchell 2007 compared outcomes for 823 patients with an ISS > 12 in Nova Scotia, Canada; 84% of HEMS patients and 43.5% of GEMS patients were transferred from a primary or distant trauma centre to the equivalent of a level I trauma centre. A TRISS-based regression analysis was performed with reporting of the Z statistic W score. For the HEMS group, the Z statistic was 2.77 versus a Z statistic of -1.97 for the GEMS group. The W score for HEMS was 6.40 indicating that there were 6.4 more survivors than expected per 100 patients, as compared in the MTOS cohort. In comparison, the W score for the GEMS group was -2.40 indicating that there were 2.4 unexpected non-survivors per every 100 patients. Crew configuration, in-flight interventions, and stabilizing procedures at the primary and distant trauma centres were not described.

In another Canadian study, McVey 2010 compared outcomes of trauma patients transported by HEMS or GEMS, with a mean ISS > 20. This study was described as a "natural experiment" since a group of GEMS patients consisted of patients initially designated to be flown by helicopter but who were eventually transported by land due to weather or other aviation-related reasons. A TRISS analysis was performed, with calculation of Z statistics and W scores. The majority of HEMS missions in this study were inter-facility transfers (79.6%). In the HEMS group, the Z statistic was 3.37 and the W score indicated 5.61 survivors for every 100 patients transported. In the GEMS group, the Z statistic was -2.71 and the W score indicated that there were two additional unexpected non-survivors for every 100 patients transported. Neither Mitchell 2007 or McVey 2010 reported an M statistic and although these studies were performed in a North American system comparability with the original MTOS cohort may not be entirely valid.

DISCUSSION

Summary of main results

This review included 25 studies that examined survival for HEMS compared to GEMS for adults with major trauma. An additional four studies met inclusion criteria for analysis as a subgroup of patients transferred to trauma centres. Most of the available studies did not use methodology that allowed for the ability to assess whether HEMS gave trauma patients who were not in proximity to specialty care the same chance of survival as those patients to whom care was immediately available Floccare 2002. Due to the considerable heterogeneity of effects and study methodologies, an accurate estimate of composite effect could not be determined. The quality of evidence, which reflects the extent of confidence that an estimate of effect is correct, was very low as assessed by the GRADE Working Group criteria thus making comparisons difficult.

Overall completeness and applicability of evidence

This review included studies from all regions of the world, but it should be noted that HEMS systems are predominantly located in high-income countries. Thus, the findings from this review may only be generalisable for a number of settings. This review used a comprehensive search strategy that did not exclude non-English articles. We used a formal protocol that omitted studies known to be more susceptible to bias, and we searched for, and included when appropriate, published abstracts as well as journal articles. Seven of the 29 studies that were included were European. Single studies from Australia and South Africa were included, and two studies from Canada. Seven European HEMS studies that were excluded were helicopter treatment team (HTT) studies. Many European HEMS systems are different from North American systems. For instance, in most European HEMS programs physicians are mandatory crew members, whereas in the United States most HEMS programs are staffed by critical care nurses and paramedics. Moreover, in Europe the helicopter is used in many systems to transport the treatment team to the scene of the injury, and in countries such as the Netherlands the helicopter is rarely used for patient transport. Finally, the majority of HEMS studies in this review failed to isolate the strict benefit of HEMS. Any salutary effect of HEMS is likely due to some combination of crew expertise, prehospital interventions, and timely access to a high-level trauma centre.

Quality of the evidence

The overall quality of studies in this review was low as assessed by the Downs and Black risk of bias tool and very low according to the GRADE Working Group guidelines for evaluating the impact

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of healthcare interventions. Most studies had a high risk of bias across all domains. All studies had either an unclear or high risk of bias due to selection bias, confounding, and failure to determine the amount of power required to estimate statistically significant effects. Furthermore, most studies did not report the validity of their measurement methods for assessing outcomes; the majority of studies relied on local or national trauma registries, where the quality of data from these sources is not well known. Not all studies provided data on prehospital interventions and, in some studies, HEMS groups were disproportionally comprised of more highly trained providers, including physicians. It should be noted that the relative effect for mortality calculated for the GRADE analysis reflects unadjusted mortality; it only included studies that reported data that enabled the calculation of a risk ratio.

Potential biases in the review process

One of the co-authors of this study (ST) was the primary author for one of the higher-quality studies included in this review (Thomas 2002). Nevertheless, this study was carefully subjected to the risk of bias assessment and the author did not partake in the risk of bias assessment process. Several of the authors of this review maintain active roles as HEMS administrators and policy advisors (ST, DF, EH, JH). Data regarding safety were not available in any of the included studies, and helicopter mishaps may represent an adverse effect associated with the intervention.

Agreements and disagreements with other studies or reviews

Six different reviews have been published on HEMS over the last decade (Bledsoe 2006; Butler 2010; Ringburg 2009a; Taylor 2010; Thomas 2002; Thomas 2003; Thomas 2007). Thomas et al published a series of annotated reviews of the HEMS outcomes literature in 2002, 2003, and 2007 (Thomas 2002; Thomas 2003; Thomas 2007). The goal of the 2002 and 2007 reviews was to provide a reference for outcomes-based literature. Neither of these papers were formal systematic reviews. In 2003, Thomas and Biddinger authored a brief review that highlighted the problems in identifying patients who will benefit from HEMS prospectively (Thomas 2003). This study was not a formal systematic review and the goal of the paper was to address studies published since 2001; only four studies were discussed.

Bledsoe 2006 published a meta-analysis to determine the percentage of trauma patients transported from the scene by helicopter with non-life threatening injuries. Twenty-two studies were included in the final analysis, though the study was not, by definition, a meta-analysis because effects were not pooled. Five of the studies included in our review (Bartolacci 1998; Baxt 1983; Braithwaite 1998; Cunningham 1997; Phillips 1999) were also evaluated by Bledsoe et al. Two of these studies had over 50% of patients with an ISS < 15 (Bartolacci 1998; Cunningham 1997). In our study, data were only abstracted from the subgroups of patients in these studies with an ISS > 15. Furthermore, TRISS (Bartolacci 1998) and logistic regression (Cunningham 1997) were used to adjust for severity of injury. Bledsoe 2006 concluded that the majority of trauma patients transported from the scene have non-life threatening injuries; 25.8% of all patients analysed were discharged within 24 hours after arrival at the trauma centre.

Ringburg 2009a performed a literature review in 2009. Sixteen studies were reviewed. This study was not a systematic review and the authors concluded that HEMS appeared to be beneficial, but only when rigorous statistical methodology was applied. In 2010, Taylor et al conducted a systematic review of the literature to determine the economic costs of HEMS and the relationship of costs to outcomes (Taylor 2010). A limited search strategy was employed and 15 studies met the inclusion criteria. This review also included non-trauma patients. It highlighted a lack of high-quality studies. The authors concluded that the "weight of observational evidence" supports an association between HEMS and improved survival in selected trauma patients, but effects could not be pooled due to the considerable differences in the cost and effectiveness of HEMS between studies (Taylor 2010).

A recent systematic review was conducted by Butler 2010 with the goal of determining whether HEMS is beneficial for trauma patients. A meta-analysis was not conducted due to the inconsistencies in patient inclusion criteria and outcome measures. Studies were limited to the English language and there was no cutoff for injury severity. Twenty-three eligible studies were evaluated in an evidence table. Studies examining the effect of helicopter treatment teams were included. All studies were moderate to low level evidence as assessed using the Oxford Centre of Evidence Based Medicine guidelines. Fourteen studies reported results that demonstrated a survival benefit for HEMS compared to GEMS. The authors included helicopter treatment team (HTT) studies. Butler et al attributed HEMS benefits to four potential factors: 1) transport of advanced airway skills to the scene, 2) transport of a team experienced in managing trauma patients to the scene, 3) expeditious transport of patients from the scene to a hospital, and 4) triage to a definitive trauma centre. Differences in study design, treatment protocols, triage guidelines, and crew configuration were acknowledged as limiting factors that barred the authors from establishing any resolutions about the role of HEMS for trauma patients. The authors acknowledged the importance of considering the benefits of a helicopter treatment team separately from the benefits associated with HEMS transport.

With the exception of the review focused on non-life threatening injuries (Bledsoe 2006), there are no overall disagreements with any of the previous reviews. Our protocol used a comprehensive search strategy that was devised with the help of a methodologist from the Cochrane Injuries Group. In all previous studies, the use of electronic databases was more limited than our comprehensive search strategy. Our strategy was designed to identify as many relevant studies as possible in order to minimize bias and to estimate reliable effects (Reeves 2011). Through the use of strict inclusion criteria, a thorough quality assessment, and a narrative synthesis we are confident that all pertinent HEMS studies of adults with major trauma were identified and analysed at the time the available literature for this review was assessed as up to date.

AUTHORS' CONCLUSIONS

Implications for practice

Due to the methodological weakness of the available literature, and the considerable heterogeneity of effects and study methodologies, an accurate composite estimate of the benefit of HEMS could not be determined. The question of which elements of HEMS are most beneficial for patients has not been fully answered, and any HEMS-associated benefit could be the result of some combination of crew expertise, decreased prehospital time, and the fact that HEMS are an integral part of organized trauma systems in many developed

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countries (Thomas 2003). Moreover, HEMS-associated benefits may include physician adjudicated launching criteria based on severity injury and mechanism, centrally coordinated launching algorithms with selected HEMS deployment, trauma volumes at receiving trauma centres, and the ability of the helicopter to transport patients in areas inaccessible by ground vehicles or prohibitively distant from trauma centres. This review stresses the importance of triage criteria since the benefits of HEMS may be greatest for patients with serious but potentially survivable injuries. Ideal dispatch criteria and triage guidelines to ensure the efficient use of helicopters remain elusive.

Implications for research

The results from this review will motivate future work in this area, including the ongoing need for diligent reporting of research methods, which is imperative for transparency and to maximise the potential utility of results. Given the infeasibility and ethical concerns about performing RCTs for HEMS, the use of advanced methods for observational research, such as propensity scores and instrumental variables, should be considered the standard for analysing the data from future HEMS studies. Furthermore, correct specification of logistic regression models is vital since effect estimates will be biased if the assumptions for these models are violated. Other outcomes of interest including morbidity, disability, and health-related quality of life after HEMS versus GEMS transport should be also be measured to assess potential HEMS-associated benefits. Large, multicentre studies are warranted in the future and this will help produce more robust estimates of treatment effects; it is likely that large numbers of patients will be required to accurately quantify outcomes. Finally, the costs and safety of HEMS cannot be ignored, and future studies need to consider multiple contextual determinants if the use of HEMS is to be supported.

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REFERENCES

References to studies included in this review

Bartolacci 1998 *{published data only}*

Bartolacci RA, Munford BJ, Lee A, McDougall PA. Air medical scene response to blunt trauma: Effect on early survival. *The Medical Journal of Australia* 1998;**169**:612-6.

Baxt 1983 *{published data only}*

Baxt WG, Moody P. The impact of a rotorcraft aeromedical emergency care service on trauma mortality. *JAMA* 1983;**249**(22):3047-51.

Baxt 1987 *{published data only}*

Baxt WG, Moody P. The impact of advanced prehospital emergency care on the mortality of severely brain-injured patients. *The Journal of Trauma: Injury, Infection, and Critical Care* 1987;**27**(4):365-9.

Berlot 2009 *{published data only}*

Berlot G, LaFata C, Bacer B, Biancardi B, Viviani M, Lucangelo U, et al. Influence of prehospital treatment on the outcome of patients with severe blunt traumatic brain injury: A single-centre study. *European Journal of Emergency Medicine* 2009;**16**:312-7.

Biewener 2004 *{published data only}*

Biewener A, Aschenbrenner U, Rammelt S, Grass R, Zwipp H. Impact of helicopter transport and hospital level on mortality of polytrauma patients. *The Journal of Trauma: Injury, Infection, and Critical Care* 2004;**56**:94-8.

Braithwaite 1998 *{published data only}*

Braithwaite CE, Rosko M, McDowell R, Gallagher J, Proenca J, Spott MA. A critical analysis of on-scene helicopter transport on survival in a statewide trauma system. *The Journal of Trauma: Injury, Infection, and Critical Care* 1998;**45**(1):140-6.

Brown 2010 *{published data only}*

Brown JB, Stassen NA, Bankey PE, Sangosanya AT, Cheng JD, Gestring ML. Helicopters and the civilian trauma system: National utilization patterns demonstrate improved outcomes after traumatic injury. *The Journal of Trauma: Injury, Infection, and Critical Care* 2010;**69**:1030-6.

Brown 2011 *{published data only}*

Brown JB, Stassen NA, Bankey PE, Sangosanya AT, Cheng JD, Gestring ML. Helicopters improve survival in seriously injured patients requiring interfacility transfer for definitive care. *The Journal of Trauma: Injury, Infection, and Critical Care* 2011;**70**:310-4.

Buntman 2002 *{published data only}*

Buntman AJ, Yeomans KA. The effect of air medical transport on survival after trauma in Johannesburg, South Africa. *South African Medical Journal* 2002;**92**:807-11.

Cunningham 1997 *{published data only}*

Cunningham P, Rutledge R, Baker C, Clancy TV. A comparison of the association of helicopter and ground ambulance transport with the outcome of injury in trauma patients transported from the scene. *The Journal of Trauma: Injury, Infection, and Critical Care* 1997;**43**(6):940-6.

Davis 2005 *{published data only}*

Davis DP, Peay J, Serrano JA, Buono C, Vilke GM, Sise MJ, et al. The impact of aeromedical response to patients with moderate to severe traumatic brain injury. *Annals of Emergency Medicine* 2005;**46**:115-22.

Di Bartolomeo 2001 *{published data only}*

Di Bartolomeo S, Sanson G, Nardi G, Scian F, Michelutto V, Lattuada L. Effects of 2 patterns of prehospital care on the outcome of patients with severe head injury. *Archives of Surgery* 2001;**136**:1293-300.

Frey 1999 *{published data only}*

Frey C, Dula D, Escalante M. Outcomes associated with helicopter and ambulance transport of motor vehicle accident victims to trauma centers. *American Journal of Epidemiology* 1999;**149**(11):79.

Frink 2007 *{published data only}*

Frink M, Probst C, Hildebrand F, Richter M, Hausmanninger C, Wiese B, et al. The influence of transportation mode on mortality in olytraumatized patients. An analysis based on the German Trauma Registry [German]. *Unfallchirug* 2007;**110**:334-40.

Koury 1998 *{published data only}*

Koury SI, Moorer L, Stone K, Stapczynski JS, Thomas SH. Air vs ground transport and outcome in trauma patients requiring urgent operative interventions. *Prehospital Emergency Medical Care* 1998;**2**:289-92.

McVey 2010 *{published data only}*

McVey J, Petrie DA, Tallon JM. Air versus ground transport of the major trauma patient: A natural experiment. *Prehospital Emergency Care* 2010;**14**:45-50.

Mitchell 2007 *{published data only}*

Mitchell AD, Tallon JM, Sealy B. Air versus ground transport of major trauma patients to a tertiary trauma centre: a province-wide comparison using TRISS analysis. *Canadian Journal of Surgery* 2007;**50**(2):129-33.

Moylan 1988 *{published data only}*

Moylan JA, Fitzpatrick KT, Beyers J, Georgiade GS. Factors improving survival in multisystem trauma patients. *Annals of Surgery* 1988;**207**(6):679-83.

Nardi 1994 *{published data only}*

Nardi G, Massarutti D, Muzzi R, Kette F, Demonte A, Carnelos GA, et al. Impact of emergency medical helicopter service on mortality for trauma in north-east Italy. *European Journal of Emergency Medicine* 1994;**1**:69-77.

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Newgard 2010 *{published data only}*

Newgard CD, Schmicker RH, Hedges JR, Trickett JP, Davis DP, Bulger EM, et al. Emergency medical services intervals and survival in trauma: Assessment of the "Golden Hour" in a North American prospective cohort. *Annals of Emergency Medicine* 2010;**55**:235-46.

Nicholl 1995 *{published data only}*

Nicholl JP, Brazier JE, Snooks HA. Effects of London helicopter emergency medical service on survival after trauma. *BMJ* 1995;**311**:217-22.

Phillips 1999 *{published data only}*

Phillips RT, Conaway C, Mullarkey D, Owen JL. One Year's trauma mortality at Brooke Army Medical Center: Is aeromedical transportation of trauma patients necessary?. *Military Medicine* 1999;**164**(5):361-5.

Schiller 1988 *{published data only}*

Schiller WR, Knox R, Zinnecker H, Jeevanandam M, Sayre M, Burke J, Young DH. Effect of helicopter transport of trauma victims on survival in an urban trauma center. *The Journal of Trauma: Injury, Infection, and Critical Care* 1988;**28**(8):1127-33.

Schwartz 1990 *{published data only}*

Schwartz RJ, Lenworth MG, Juda RJ. A comparison of ground paramedics and aeromedical treatment of severe blunt trauma patients. *Connecticut Medicine* 1990;**54**(12):660-2.

Stewart 2011 *{published data only}*

Stewart KE, Cowan LD, Thompson DM, Sacra JC, Albrecht R. Association of direct helicopter versus ground transport and in-hospital mortality in trauma patients: A propensity score analysis. *Academic Emergency Medicine* 2011;**18**:1208-16.

Sullivent 2011 *{published data only}*

Sullivent EE, Faul M, Wald MW. Reduced mortality in injured adults transported by helicopter emergency medical services. *Prehospital Emergency Care* 2011;**15**:295-302.

Talving 2009 *{published data only}*

Talving P, Teixeira PGR, Barmparas G, DuBose J, Inaba K, Lam L, Demetriades D. Helicopter evacuation of trauma victims in Los Angeles: Does it improve survival?. *World Journal of Surgery* 2009;**33**:2469-76.

Thomas 2002 *{published data only}*

Thomas SH, Harrison TH, Buras WR, Ahmed W, Cheema F, Wedel SK. Helicopter transport and blunt trauma mortality: A multicenter trial. *The Journal of Trauma: Injury, Infection, and Critical Care* 2002;**52**:136-45.

Weninger 2005 *{published data only}*

Weninger P, Trimmel H, Herzer G, Nau T, Aldrian S, Vecsei V. Prehospital trauma care provided by HEMS or ground EMS: Does it make a difference? [German]. *Notfall & Rettungsmedizin* 2005;**8**(3):171-81.

Additional references

ACS-COT 1999

American College of Surgeons, Committee on Trauma. Resources for optimal care of the injured patient: 1999. Chicago: American College of Surgeons, 1998.

Baker 1976

Baker SP, O'Neill B. The injury severity score: an update. *The Journal of Trauma* 1976;**16**(11):882-5.

Baker 2006

Baker SP, Grabowski JG, Dodd RS, Shanahan DF, Lamb MW, Li G. EMS helicopter crashes: What influences fatal outcome?. *Annals of Emergency Medicine* 2006;**47**:351-6.

Baxt 1985

Baxt WG, Moody P, Clevland HC, Fischer RP, Kyes FN, Leicht MJ, et al. Hospital-based rotorcraft aero medical emergency care services and trauma mortality: a multicenter study. *Annals of Emergency Medicine* 1985;**14**(9):859-64.

Bledsoe 2005

Bledsoe BE, Smith MG. Medical helicopter accidents in the United States: a 10-year review. *Journal of Trauma* 2004;**56**(6):1325-8.

Bledsoe 2006

Bledsoe BE, Wesley AK, Eckstein M, Dunn TM, O'Keefe MF. Helicopter scene transport of trauma patients with non life-threatening injuries: a meta-analysis. *The Journal of Trauma* 2006;**60**(6):1257-65.

Butler 2010

Butler DP, Anwar I, Willett K. Is it the H or the EMS in HEMS that has an impact on trauma patient mortality? A systematic review of the evidence. *Emergency Medicine Journal* 2010;**27**:692-701.

CDC 2010

Centers for Disease Control and Prevention. 10 leading causes of death, United States. 1999-2006, all races, both sexes. Centers for Disease Control and Prevention 2010:(http://webappa.cdc.gov/sasweb/ncipc/leadcaus10.html).

Champion 1990

Champion HR, Copes WS, Sacco WJ, Lawnick MM, Keast SL, Bain LW, et al. The Major Trauma Outcome Study: establishing national norms for trauma care. *The Journal of Trauma* 1990;**30**(11):1356-65.

Chandran 2010

Chandran A, Hyder AA, Peek-Asa C. The global burden of unintentional injuries and an agenda for progress. *Epidemiologic Reviews* 2010;**32**(1):110-20.

Cowley 1973

Cowley R, Hudson F, Scanlan E, Gill W, Lally RJ, Long W, Kuhn AO. An economical and proved helicopter program for transporting the emergency critically ill and injured patient in Maryland. *The Journal of Trauma* 1973;**13**(12):1029-38.

Copyright © 2013 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Cowley 1979

Cowley RA, Mergner WJ, Fisher RS, Jones RT, Trump BF. The subcellular pathology of shock in trauma patients: studies using the immediate autopsy. *The American Journal of Surgery* 1979;**45**(4):255-69.

Cunningham 1998

Cunningham P, Rutledge R, Baker CC, Clancy TV. A comparison of the association of helicopter and ground ambulance transport with the outcome of injury in trauma patients transported from the scene. *The Journal of Trauma* 1997;**43**(6):940-6.

Deeks 2003

Deeks JJ, Dinnes J, D'Amico R, Sowden AJ, Sakarovitch C, Song F, et al. Evaluating non-randomised intervention studies. *Health Technology Assessment* 2003;**7**(27):139.

DiBartolomeo 2005

DiBartolomeo S, Sanson G, Nardi G, Michelutto V, Scian F. HEMS vs Ground-BLS care in traumatic cardiac arrest. *Prehospital Emergency Care* 2005;**9**:79-84.

Downs 1998

Downs SH, Black N. The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions. *Journal of Epidemiology and Community Health* 1998;**52**:377-84.

Floccare 2002

Floccare DJ, Hankins DG. Chapter 50: Air Services. In: Kuehl AE editor(s). Prehospital Systems and Medical Oversight. 3rd Edition. Lenexa, KS, USA: National Association of EMS Physicians, 2002:567-75.

Gabbe 2011

Gabbe BJ, Lecky FE, Bouamra O, Woodford M, Jenks T, Coats TJ, Cameron PA. 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**:138-43.

Haas 2009

Haas B, Jurkovich GJ, Wang J, Rivara FP, MacKenzie EJ, Nathens AB. Survival advantage in trauma centres: expeditious intervention or experience?. *Journal of the American College of Surgeons* 2009;**208**(1):28-36.

Haut 2006

Haut ER, Chang DC, Efron D, Cornwell 3rd EE. Injured patients have lower mortality when treated by "full-time" trauma surgeons vs. surgeons who cover trauma "part-time". *The Journal of Trauma* 2006;**61**(2):272-9.

Haut 2009

Haut ER, Chang DC, Hayanga AJ, Efron DT, Haider AH, Cornwell 3rd EE. System-based and surgeon-based influences on trauma mortality. *Archives of Surgery* 2009;**8**:759-64.

Higgins 2011

Higgins JPT, Altman DG, Sterne JAC (editors). Chapter 8: Assessing risk of bias in included studies. In: Higgins JPT, Green S (editors) Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration 2011. Available from www.cochrane-handbook.org.

Kane 1985

Kane G, Engelhardt R, Celentano J, Koenig W, Yamanaka J, McKinney P, et al. Empirical development and evaluation of prehospital trauma triage instruments. *The Journal of Trauma* 1985;**25**(6):482-9.

Kerr 1999

Kerr WA, Kerns TJ, Bissell RA. Differences in mortality rates among trauma patients transported by helicopter and ambulance in Maryland. *Prehospital and Disaster Medicine* 1999;**14**(3):159-64.

Krug 2002

Krug EG, Dhalberg LL, Mercy JA, Zwi AB, Lozano R (editors). World report on violence and health. World Health Organization 2002:1-19.

Kruger 2010

Kruger AJ, Skogvoll E, Castren M, Kurola J, Lossius HM, the ScanDoc Phase 1a Study Group. Scandinavian pre-hospital physician-manned emergency medical services--same concept across borders?. *Resuscitation* 2010;**81**:427-33.

Lerner 2001

Lerner EB, Moscati RM. The golden hour: scientific fact or medical urban legend. *Academic Emergency Medicine* 2001;**8**(7):758-60.

MacKenzie 2006

MacKenzie EJ, Rivara FP, Jurkovich GJ, Nathens AB, Frey KP, Egleston BL, et al. A national evaluation of the effect of trauma-centre care on mortality. *The New England Journal of Medicine* 2006;**354**(4):366-78.

MacKenzie 2007

MacKenzie EJ, Rivara FP, Jurkovich GJ, Nathens AB, Frey KP, Egleston BL, et al. The National Study on Costs and Outcomes of Trauma. *The Journal of Trauma* 2007;**63**:S54-S67.

McNabney 1981

McNabney WK. Vietnam in context. *Annals of Emergency Medicine* 1981;**10**(12):659-61.

Murray 1996

Murray CJ, Lopez A. The global burden of disease: I. A comprehensive assessment of mortality and disability from diseases, and injuries and risk factors in 1990 and projected to 2020. Cambridge, MA, USA: Harvard University Press, 1996.

Nathens 2000

Nathens AB, Jurkovich GJ, Rivara FP, Maier RV. Effectiveness of state trauma systems in reducing injury-related mortality: a national evaluation. *The Journal of Trauma* 2000;**48**(1):25-30.

Copyright © 2013 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

Osler 1997

Osler T, Baker SP, Long W. A modification of the injury severity score that improves accuracy and simplifies scoring. *The Journal of Trauma* 1997;**43**(6):922-5.

Reeves 2011

Reeves BC, Deeks JJ, Higgins JPT, Wells G. Chapter 13: Including non-randomised studies. In: Higgins JPT, Green S (editors) Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (updated March 2011). The Cochrane Collaboration. Available from www.cochrane-handbook.org 2011.

Ringburg 2009

Ringburg AN, Polinder S, Meulman TJ, Styerberg WE, van Lieshout EM, Patka P, et al. Cost-effectiveness and quality-of-life analysis of physician-staffed helicopter emergency medical services. *The British Journal of Surgery* 2009;**96**(11):1365-70.

Ringburg 2009a

Ringburg AN, Thomas SH, Steyerberg EW, van Lieshout EMM, Patka P, Schipper IB. Lives saved by helicopter emergency medical services: An overview of literature. *Air Medical Journal* 2009;**28**(6):298-302.

Roudsari 2008

Roudsari B, Field C, Caetano R. Clustered and missing data in the US National Trauma Data Bank: implications for analysis. *Injury Prevention* 2008;**14**:96-100.

Sampalis 1999

Sampalis JS, Denis R, Lavoie A, Frechette P, Boukas S, Nikolis A, et al. Trauma care regionalization: a process-outcome evaluation. *The Journal of Trauma* 1999;**46**(4):565-79.

Schluter 2010

Schluter PJ, Nathens A, Neal ML, Gobel S, Cameron CM, Davey TM, McClure RJ. Trauma and Injury Severity Score (TRISS) coefficients 2009 revision. *The Journal of Trauma* 2010;**68**(4):761-70.

Seegerer 1976

Seegerer K. 10 years of the Munich Emergency Medical Service: organization and technic. *MMW Muenchener medizinische Wochenschrift* 1976;**118**(18):573-8.

Shatz 2004

Shatz DV, Delgado J. Civilian use of rotor wing medical transport has had its opponents. *The Journal of Trauma* 2004;**56**(6):1325-8.

TARN 2011

The Trauma Audit and Research Network. Ps09: An improved approach to outcome predictions. Retrieved on 24 March 2011 from: https://www.tarn.ac.uk/Content.aspx?c=1894.

Taylor 2010

Taylor CB, Stevenson M, Jan S, Middleton PM, Fitzharris M, Myburgh JA. A systematic review of the costs and benefits of helicopter emergency medical services. *Injury* 2010;**41**(1):10-20.

Thomas 2003

Thomas SH, Biddinger PD. Helicopter trauma transport: an overview of recent outcomes and triage literature. *Current Opinions in Anaesthesiology* 2003;**16**(2):153-8.

Thomas 2004

Thomas SH. Helicopter emergency medical services transport outcomes literature: annotated review of articles published 2000-2003. *Prehospital Emergency Care* 2004;**8**(3):322-33.

Thomas 2007

Thomas SH. Helicopter emergency medical services transport outcomes literature: annotated review of articles published 2004-2006. *Prehospital Emergency Care* 2007;**11**:477-88.

Wish 2005

Wish JR, Long WB, Edlich RF. Better trauma care. How Maryland does it. *Journal of Long-Term Effects of Medical Implants* 2005;**15**(1):79-89.

Wyatt 1998

Wyatt JP, Beard D, Busuttil A. Quantifying injury and predicting outcome after trauma. *Forensic Science International* 1998;**95**(1):57-66.

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Bartolacci 1998

Methods	Retrospective cohort, TRISS-based (W statistic reported)
Participants	Blunt trauma only, ISS > 15, New South Wales, Australia
Interventions	HEMS versus GEMS transport to a trauma centre
Outcomes	Mortality
Notes	HEMS crews: physicians (anaesthesiologist), GEMS crews: paramedics

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Bartolacci 1998 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Reporting bias	Low risk	8/11
External validity	Low risk	3/3
Internal validity	Unclear risk	4/7
Internal validity: confounding and selection bias	High risk	3/6
Power	High risk	0/5

Baxt 1983

Methods	Retrospective cohort, ground comparison group only
Participants	Blunt trauma patients only in San Diego, USA, over a 30 month period
Interventions	HEMS versus GEMS transport to a trauma centre
Outcomes	Mortality
Notes	HEMS crews: physician and nurse, GEMS crews: paramedic and EMT

Risk of bias

Bias	Authors' judgement	Support for judgement
Reporting bias	Low risk	8/11
External validity	Low risk	3/3
Internal validity	Unclear risk	4/7
Internal validity: confounding and selection bias	High risk	3/6
Power	High risk	0/5

Baxt 1987

Methods	Retrospective cohort, TRISS-based (W, Z, M statistics not reported)
Participants	Traumatic brain injury patients in California, USA
Interventions	HEMS versus GEMS transport to a single level I trauma centre

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Baxt 1987 *(Continued)*

Outcomes	Mortality
Notes	HEMS crews administered medications and provided advanced life support; GEMS crews rendered mostly basic life support (10% of GEMS units were staffed by a paramedic)

Risk of bias

Bias	Authors' judgement	Support for judgement
Reporting bias	High risk	5/11
External validity	Low risk	3/3
Internal validity	Unclear risk	4/7
Internal validity: confounding and selection bias	High risk	2/6
Power	High risk	0/5

Berlot 2009

Methods	Retrospective cohort, ground comparison group only
Participants	Traumatic brain injury patients in the Fruli-Venezia Giulia region, Italy, 2002-2007
Interventions	HEMS versus GEMS transport to one of two speciality hospitals for traumatic brain injury
Outcomes	Mortality
Notes	HEMS crews had advanced-life support-capable physicians and two nurses, GEMS crews had a non-advanced life support physician and two nurses; HEMS patients were treated more aggressively

Risk of bias

Bias	Authors' judgement	Support for judgement
Reporting bias	High risk	7/11
External validity	Low risk	3/3
Internal validity	High risk	4/7
Internal validity: confounding and selection bias	High risk	1/6
Power	High risk	0/5

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Biewener 2004

Methods	Retrospective cohort, TRISS (W, Z, M statistics not reported)
Participants	Polytrauma patients in Germany between January 1998-December 1999
Interventions	HEMS versus GEMS transfer to a local hospital versus trauma centre
Outcomes	Mortality
Notes	4 pathways: HEMS to trauma centre, GEMS to trauma centre, GEMS to local hospital, GEMS followed by late inter hospital transfer to a trauma centre

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Reporting bias	High risk	7/11
External validity	Unclear risk	2/3
Internal validity	High risk	4/7
Internal validity: confounding and selection bias	High risk	2/6
Power	High risk	0/5

Braithwaite 1998

Methods	Retrospective cohort, ground comparison group only
Participants	Trauma patients in the Pennsylvania Trauma Outcome study, 1978-1995, USA
Interventions	HEMS versus GEMS transport to trauma centres
Outcomes	Mortality
Notes	Not all hospitals were level I trauma centres, types of injuries not described

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Reporting bias	High risk	5/11
External validity	Unclear risk	2/3
Internal validity	High risk	4/7
Internal validity: confounding and selection bias	High risk	3/6
Power	High risk	0/5

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Brown 2010

Methods	Retrospective cohort, ground comparison group only
Participants	Trauma patients in the 2007 National Trauma Data Bank, USA
Interventions	HEMS versus GEMS transport to trauma centres
Outcomes	Mortality
Notes	Higher baseline ISS in HEMS group compared to GEMS group

Risk of bias

Bias	Authors' judgement	Support for judgement
Reporting bias	Low risk	8/11
External validity	High risk	0/3
Internal validity	High risk	3/7
Internal validity: confounding and selection bias	High risk	2/6
Power	High risk	0/5

Brown 2011

Methods	Retrospective cohort, ground comparison group only
Participants	Trauma patients in the 2007 National Trauma Data Bank, USA
Interventions	HEMS versus GEMS inter-facility transfer to higher level trauma centres
Outcomes	Mortality
Notes	Crew configurations unknown

Risk of bias

Bias	Authors' judgement	Support for judgement
Reporting bias	Low risk	8/11
External validity	High risk	1/3
Internal validity	High risk	4/7
Internal validity: confounding and selection bias	High risk	2/6

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Brown 2011 *(Continued)*

Power	High risk	0/5

Buntman 2002

Methods	Retrospective cohort, TRISS-based (Z and M statistic reported)
Participants	Trauma patients admitted to one of two trauma centres in Johannesburg, South Africa, September 1999-January 2000
Interventions	HEMS versus GEMS transport to a trauma centre
Outcomes	Mortality
Notes	Crew configurations and types of injuries not described

Risk of bias

Bias	Authors' judgement	Support for judgement
Reporting bias	High risk	6/11
External validity	Low risk	3/3
Internal validity	Unclear risk	3/7
Internal validity: confounding and selection bias	Unclear risk	2/6
Power	High risk	0/5

Cunningham 1997

Methods	Retrospective cohort, ground comparison group only
Participants	Trauma patients in North Carolina, 1987-1993
Interventions	HEMS versus GEMS transport to level I or level II trauma centres
Outcomes	Mortality
Notes	Crew configurations not described

Risk of bias

Bias	Authors' judgement	Support for judgement
Reporting bias	High risk	6/11
External validity	Low risk	3/3
Internal validity	High risk	3/7

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Cunningham 1997 *(Continued)*

Internal validity: confounding and selection bias	High risk	2/6
Power	High risk	0/5

Davis 2005

Methods	Retrospective cohort, ground comparison group only
Participants	Traumatic brain injury patients in the San Diego area, California, USA, 1987-2003
Interventions	HEMS versus GEMS transport to level I or level II trauma centres
Outcomes	Mortality
Notes	GEMS crews could not intubated, but HEMS crews could; HEMS crews: nurse, paramedic, physician, GEMS crews: two paramedics

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Reporting bias	Low risk	11/11
External validity	Low risk	3/3
Internal validity	Unclear risk	5/7
Internal validity: confounding and selection bias	High risk	3/6
Power	High risk	0/5

Di Bartolomeo 2001

Methods	Retrospective cohort, TRISS-based (W, Z, M statistics not reported)
Participants	Traumatic brain injury patients in the Fruli-Venezia Giulia region of Italy, March 1998 - February 1999
Interventions	HEMS with physician versus GEMS with nurse, transport to a speciality hospital for traumatic brain injury
Outcomes	Mortality
Notes	HEMS patients received advanced ventilation including endotracheal intubation (64/92), chest tubes (4/92), and intravenous lines (92/92); GEMS patients only received bag-mask ventilation, no chest tubes, and 74/92 had intravenous lines placed

Risk of bias

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Di Bartolomeo 2001 *(Continued)*

Bias	Authors' judgement	Support for judgement
Reporting bias	Low risk	10/11
External validity	Low risk	3/3
Internal validity	High risk	4/7
Internal validity: con-founding and selection bias	High risk	3/6
Power	High risk	0/5

Frey 1999

Methods	Retrospective cohort, ground comparison group only
Participants	12,244 motor vehicle crash patients admitted to trauma centres in Pennsylvania, USA
Interventions	HEMS versus GEMS transport to trauma centres
Outcomes	Mortality
Notes	Crew configurations and types of injuries not described; Levels of trauma centres not described

Risk of bias

Bias	Authors' judgement	Support for judgement
Reporting bias	High risk	4/11
External validity	High risk	0/3
Internal validity	High risk	1/7
Internal validity: con-founding and selection bias	High risk	1/6
Power	High risk	0/5

Frink 2007

Methods	Retrospective cohort, TRISS-based (W, Z, M statistics not reported)
Participants	Poly trauma patients admitted to trauma centres in Germany, Switzerland, Austria, Netherlands, 1993-2003
Interventions	HEMS versus GEMS transport to trauma centres
Outcomes	Mortality

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Frink 2007 *(Continued)*

Notes	Both HEMS and GEMS had physician crews; patients were admitted to different types (level) of trauma centres

Risk of bias

Bias	Authors' judgement	Support for judgement
Reporting bias	High risk	5/11
External validity	High risk	0/3
Internal validity	High risk	3/7
Internal validity: confounding and selection bias	High risk	2/6
Power	High risk	0/5

Koury 1998

Methods	Retrospective cohort, ground comparison group only
Participants	Trauma patients in Kentucky, USA, 1990-1994
Interventions	HEMS versus GEMS transported to a single trauma centre (level I)
Outcomes	Mortality
Notes	HEMS crews: nurse and paramedic, GEMS crews: paramedic only; ISS higher in HEMS group (22.3 vs. 15.9)

Risk of bias

Bias	Authors' judgement	Support for judgement
Reporting bias	Low risk	9/11
External validity	Low risk	2/3
Internal validity	High risk	4/7
Internal validity: confounding and selection bias	High risk	3/6
Power	High risk	0/5

McVey 2010

Methods	Retrospective cohort, TRISS-based, W and Z statistic reported

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McVey 2010 *(Continued)*

Participants	Trauma patients in Nova Scotia, Canada, 1997-2003
Interventions	HEMS versus GEMS inter-facility transport to a level I trauma centre
Outcomes	Mortality
Notes	79.6 % of HEMS were inter-facility transfers; 41.6% of all GEMS were inter-facility transfers; 90% of all trauma patients had blunt trauma

Risk of bias

Bias	Authors' judgement	Support for judgement
Reporting bias	Low risk	8/11
External validity	Low risk	3/3
Internal validity	Unclear risk	4/7
Internal validity: confounding and selection bias	Unclear risk	3/6
Power	High risk	0/5

Mitchell 2007

Methods	Retrospective cohort, TRISS-based, W and Z score reported
Participants	Trauma patients with an ISS > 12 in Novia Scotia, Canada, 1998-2002
Interventions	HEMS versus GEMS transfer to a level I trauma centre
Outcomes	Mortality
Notes	84% of all HEMS were inter-facility transfers; 43.5% of all GEMS were inter-facility transfers; quality score: 18

Risk of bias

Bias	Authors' judgement	Support for judgement
Reporting bias	Low risk	8/11
External validity	Low risk	3/3
Internal validity	Unclear risk	4/7
Internal validity: confounding and selection bias	High risk	3/6
Power	High risk	0/5

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Moylan 1988

Methods	Retrospective cohort, ground comparison group only
Participants	Polytrauma patients in North Carolina, USA, 1985-1986
Interventions	HEMS versus GEMS inter-facility transfer to a level I trauma centre
Outcomes	Mortality
Notes	Types of injuries not described

Risk of bias

Bias	Authors' judgement	Support for judgement
Reporting bias	High risk	6/11
External validity	Low risk	3/3
Internal validity	High risk	2/7
Internal validity: confounding and selection bias	High risk	3/6
Power	High risk	0/5

Nardi 1994

Methods	Prospective 7-month cohort, 2 ground comparison groups (GEMS to regional centre, GEMS to Level I trauma centre)
Participants	Trauma patients in three Italian provinces, 7 month period
Interventions	HEMS versus GEMS transport to a trauma centre (all HEMS went to a level I trauma centre)
Outcomes	Mortality
Notes	HEMS crews: anaesthesiologist and two intensive care nurses, GEMS crews:two nurses with basic trauma life support training and one emergency physician who could not intubate; HEMS only operated in daytime

Risk of bias

Bias	Authors' judgement	Support for judgement
Reporting bias	High risk	4/11
External validity	Low risk	2/3
Internal validity	High risk	1/7

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Nardi 1994 *(Continued)*

Internal validity: confounding and selection bias	High risk	0/7
Power	High risk	0/5

Newgard 2010

Methods	Secondary analysis of a prospective cohort of trauma patients, instrumental variables analysis
Participants	Trauma patients from 10 sites across North America, 2005-2007
Interventions	HEMS versus GEMS transport to level I and level II trauma centres
Outcomes	Mortality
Notes	Unknown crew configurations

Risk of bias

Bias	Authors' judgement	Support for judgement
Reporting bias	Low risk	9/11
External validity	Low risk	2/3
Internal validity	Unclear risk	4/7
Internal validity: confounding and selection bias	Unclear risk	4/6
Power	High risk	0/5

Nicholl 1995

Methods	Retrospective cohort, TRISS-based (W, Z, M statistics not reported)
Participants	Trauma patients in Greater London area, UK, 1991-1993
Interventions	HEMS versus GEMS transport to a trauma centre
Outcomes	Mortality
Notes	Type of injuries not described; HEMS crews: physician, GEMS crews: did not always have a physician

Risk of bias

Bias	Authors' judgement	Support for judgement
Reporting bias	Low risk	9/11

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Nicholl 1995 *(Continued)*

External validity	Low risk	3/3
Internal validity	Unclear risk	4/7
Internal validity: confounding and selection bias	Unclear risk	4/6
Power	High risk	0/5

Phillips 1999

Methods	Retrospective cohort, ground comparison group only
Participants	Trauma patients in San Antonio, TX, USA, October 1995 - September 1996
Interventions	HEMS versus GEMS transport to a single level I trauma centre
Outcomes	Mortality
Notes	HEMS crews: nurse and paramedic, GEMS crews: two paramedics

Risk of bias

Bias	Authors' judgement	Support for judgement
Reporting bias	Low risk	9/11
External validity	High risk	1/3
Internal validity	Low risk	5/7
Internal validity: confounding and selection bias	High risk	3/6
Power	High risk	0/5

Schiller 1988

Methods	Retrospective cohort, ground comparison group only
Participants	Traumatic brain injury patients in Arizona, USA, 1983-1986
Interventions	HEMS versus GEMS transport to a single level I trauma centre
Outcomes	Mortality
Notes	Unclear if GEMS had advanced life support capabilities; blunt traumatic brain injuries only

Risk of bias

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Schiller 1988 *(Continued)*

Bias	Authors' judgement	Support for judgement
Reporting bias	High risk	6/11
External validity	Low risk	3/3
Internal validity	High risk	2/7
Internal validity: confounding and selection bias	High risk	2/6
Power	High risk	0/5

Schwartz 1990

Methods	Retrospective cohort, TRISS-based (W, Z, M statistics not reported)
Participants	Blunt trauma patients in Connecticut, USA, July 1987 - June 1988
Interventions	HEMS versus GEMS transport to a single level I trauma centre
Outcomes	Mortality
Notes	HEMS crews:physician, nurse, respiratory therapist, GEMS crews: paramedic and EMT; No definition for "severe blunt trauma"

Risk of bias

Bias	Authors' judgement	Support for judgement
Reporting bias	High risk	3/11
External validity	High risk	1/3
Internal validity	High risk	1/7
Internal validity: confounding and selection bias	High risk	3/6
Power	High risk	0/5

Stewart 2011

Methods	Retrospective cohort
Participants	10,184 blunt or penetrating trauma patients admitted to trauma centres in the state of Oklahoma, USA, between Jan 2005 - December 2008
Interventions	HEMS versus GEMS transport to a single level I trauma centre or transport to one of two Level II trauma centres; % intubated was also tabulated

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Stewart 2011 *(Continued)*

Outcomes	24 hour and 2-week mortality
Notes	Propensity score analysis: the propensity score was used as a confounding covariate in a Cox proportional hazards model (hazard ratios calculated)

Risk of bias

Bias	Authors' judgement	Support for judgement
Reporting bias	Low risk	9/11
External validity	Low risk	3/3
Internal validity	Low risk	5/7
Internal validity: confounding and selection bias	High risk	2/6
Power	High risk	2/5

Sullivent 2011

Methods	Retrospective cohort, ground comparison only
Participants	Trauma patients in the 2007 National Trauma Data Bank, USA
Interventions	HEMS versus GEMS transport to 82 different trauma centres
Outcomes	Mortality
Notes	Crew configuration not described; type of trauma centre (level) not described; type of injuries not described

Risk of bias

Bias	Authors' judgement	Support for judgement
Reporting bias	Low risk	8/11
External validity	High risk	0/3
Internal validity	High risk	2/7
Internal validity: confounding and selection bias	High risk	2/6
Power	High risk	0/5

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Talving 2009

Methods	Retrospective cohort, ground comparison only (ground group with > 30 minutes transport time)
Participants	Trauma patients in the Los Angeles area, CA, USA, 1998-2007
Interventions	HEMS versus GEMS transport to a single level I trauma centre
Outcomes	Mortality
Notes	HEMS crews: paramedic and nurse, GEMS crews: two paramedics

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Reporting bias	Low risk	8/11
External validity	Low risk	3/3
Internal validity	Unclear risk	4/7
Internal validity: confounding and selection bias	High risk	3/6
Power	High risk	0/5

Thomas 2002

Methods	Retrospective cohort, ground comparison group only
Participants	Blunt trauma patients only, in New England, USA, 1995-1998
Interventions	HEMS versus GEMS transport to one of five level I trauma centres
Outcomes	Mortality
Notes	HEMS crews: all had a nurse, some had a physician, GEMS crews: paramedics and nurses

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Reporting bias	Low risk	9/11
External validity	Low risk	3/3
Internal validity	Unclear risk	4/7
Internal validity: confounding and selection bias	Unclear risk	3/6
Power	High risk	0/5

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Weninger 2005

Methods	Retrospective cohort, ground comparison group only
Participants	Trauma patients in Germany
Interventions	HEMS versus GEMS transport to a single level I trauma centre
Outcomes	Mortality
Notes	Types of injuries not described; both HEMS and GEMS staffed by physicians but different prehospital interventions performed between the groups

Risk of bias

Bias	Authors' judgement	Support for judgement
Reporting bias	High risk	6/11
External validity	Unclear risk	2/3
Internal validity	High risk	1/7
Internal validity: confounding and selection bias	High risk	2/6
Power	High risk	0/5

DATA AND ANALYSES

Comparison 1. HEMS

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Unadjusted mortality	21		Risk Ratio (IV, Random, 95% CI)	Totals not selected
1.1 All studies with available data	21		Risk Ratio (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.2 Traumatic brain injury studies	5		Risk Ratio (IV, Random, 95% CI)	0.0 [0.0, 0.0]
1.3 Blunt trauma studies	3		Risk Ratio (IV, Random, 95% CI)	0.0 [0.0, 0.0]

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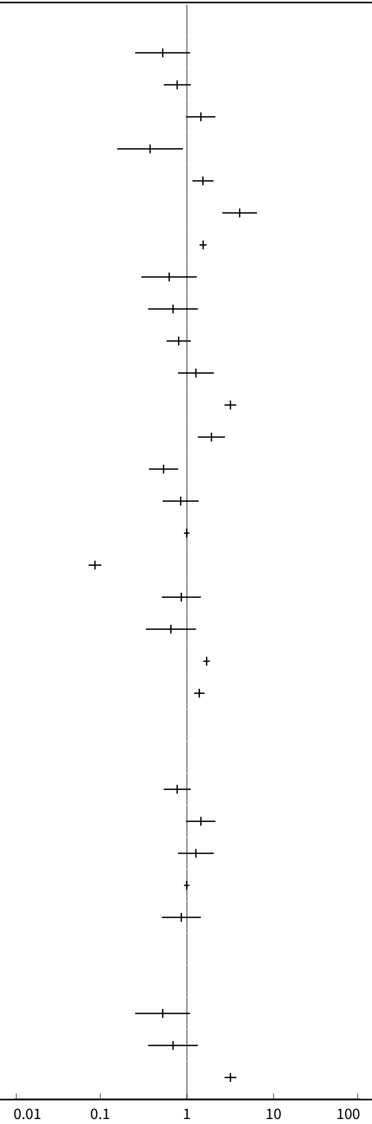
Analysis 1.1. Comparison 1 HEMS, Outcome 1 Unadjusted mortality.

Study or subgroup	HEMS n/N	GEMS n/N	Risk Ratio IV, Random, 95% CI
1.1.1 All studies with available data			
Baxt 1983	10/150	19/150	0.53[0.25,1.09]
Baxt 1987	32/104	51/128	0.77[0.54,1.11]
Schiller 1988	64/347	33/259	1.45[0.98,2.13]
Nardi 1994	5/42	31/98	0.38[0.16,0.9]
Nicholl 1995	79/288	72/402	1.53[1.16,2.03]
Cunningham 1997	23/565	73/7277	4.06[2.56,6.43]
Braithwaite 1998	1931/14967	516/6148	1.54[1.4,1.69]
Koury 1998	9/32	9/20	0.63[0.3,1.3]
Bartolacci 1998	9/77	52/308	0.69[0.36,1.34]
Phillips 1999	11/15	31/34	0.8[0.58,1.11]
Di Bartolomeo 2001	28/92	22/92	1.27[0.79,2.05]
Thomas 2002	215/2292	425/14407	3.18[2.72,3.72]
Buntman 2002	39/122	51/306	1.92[1.34,2.75]
Biewener 2004	31/140	42/102	0.54[0.36,0.79]
Weninger 2005	20/104	39/172	0.85[0.52,1.37]
Davis 2005	759/3017	1845/7295	0.99[0.92,1.07]
Frink 2007	135/3870	1469/3664	0.09[0.07,0.1]
Berlot 2009	19/89	26/105	0.86[0.51,1.45]
Talving 2009	25/478	12/150	0.65[0.34,1.27]
Sullivent 2011	682/10049	1874/46695	1.69[1.55,1.84]
Stewart 2011	274/2717	540/7467	1.39[1.21,1.6]
1.1.2 Traumatic brain injury studies			
Baxt 1987	32/104	51/128	0.77[0.54,1.11]
Schiller 1988	64/347	33/259	1.45[0.98,2.13]
Di Bartolomeo 2001	28/92	22/92	1.27[0.79,2.05]
Davis 2005	759/3017	1845/7295	0.99[0.92,1.07]
Berlot 2009	19/89	26/105	0.86[0.51,1.45]
1.1.3 Blunt trauma studies			
Baxt 1983	10/150	19/150	0.53[0.25,1.09]
Bartolacci 1998	9/77	52/308	0.69[0.36,1.34]
Thomas 2002	215/2292	425/14407	3.18[2.72,3.72]



Favours HEMS Favours GEMS

ADDITIONAL TABLES

Table 1. Studies that utilized multivariate logistic regression to adjust for potential confounders.

Study	Number of patients	Odds Ratio for Survival	95% Confidence Interval	P value
Braithwaite 1998	HEMS: 15,938 GEMS: 6,473	Not reported (1)	Not reported (1)	< 0.01 (2)
Brown 2010	HEMS: 41,987	1.22	1.18-1.27	< 0.01

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Table 1. Studies that utilized multivariate logistic regression to adjust for potential confounders. *(Continued)*

	GEMS: 216,400			
Cunningham 1997	HEMS: 1,346 GEMS: 17,144	Not reported (1)	Not reported (1)	
Frey 1999	HEMS: Not reported GEMS: Not reported	1.34	0.91-1.8	N.S. (3)
Koury 1998	HEMS: 168 GEMS: 104	1.6	0.77-3.34	0.24
Newgard 2010 (4)	HEMS: 158 GEMS: 3,498	1.41	0.68-2.94	N.S. (3)
Stewart 2011 (5)	HEMS: 2,739 GEMS: 6,473	1.49	1.19-1.89	0.001
Sullivant 2011	HEMS: 10,049 GEMS: 46,695	1.64	1.45-1.87	< 0.0001
Talving 2009 (6)	HEMS: 1,836 GEMS: 1,537	1.81	0.55-5.88	0.33
Thomas 2002	HEMS: 2,292 GEMS: 14,407	1.32	1.03-1.71	0.031

(1) Effect estimate and 95% confidence interval not reported
(2) Statistically significant effect on survival (in favour of HEMS) when HEMS analysed as interaction between HEMS and ISS ranges from 16-60
(3) P value not reported
(4) Instrumental variables analysis
(5) Cox proportional hazards regression, including a propensity score as a confounding covariate
(6) Adjusted odds ratio for subgroup with ISS> 15

APPENDICES

Appendix 1. Search strategies

MEDLINE (OvidSP) 1950 to 24 January 2012

1.exp Air Ambulances/
2.(helicopter* adj3 (ES or EMS or emergency or emergencies or service*)).ab,it.
3.(helicopter* or rotor craft or rotor wing or rotary wing or helicopter* or rotor?craft or rotor?wing or rotary?wing or Helicopter emergency medical service* or HEMS or Air emergency medical service* or AEMS).ab,ti.
4.exp Emergency Medical Services/
5.exp "Transportation of Patients"/
6.4 or 5
7.(Air* or helicopter* or rotorcraft or rotorwing or rotarywing or rotor?craft or rotor?wing or rotary?wing).ab,ti.
8.6 and 7
9.1 or 2 or 3 or 8
10.exp "Wounds and Injuries"/
11.exp Fracture Fixation/

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12.exp Pelvis/in [Injuries]
13.exp Pelvic Bones/in [Injuries]
14.exp Femur Head/in [Injuries]
15.((spine* or spinal) adj3 (fracture* or injury* or broke*)).ti,ab.
16.((head or crani* or cerebr* or brain* or skull*) adj3 (injur* or trauma* or damag* or wound* or fracture*)).ti,ab.
17.((femur* or femoral*) adj3 (fracture* or injur* or trauma* or broke*)).ti,ab.
18.((pelvis or pelvic) adj3 (fracture* or injur* or trauma* or broke*)).ti,ab.
19.((crush* or burn*) adj3 (injur* or trauma*)).ti,ab.
20.10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19
21.9 and 20
22.((injur* or wound* or sick or trauma* or patient*) adj3 (transport* or transfer*) adj3 (air* or helicopter* or rotorcraft or rotorwing or rotarywing or rotor?craft or rotor?wing or rotary?wing or sky)).ab,ti.
23.21 or 22
24.clinical trials as topic.sh.
25.randomi?ed.ti,ab.
26.randomized controlled trial.pt.
27.controlled clinical trial.pt.
28.(controlled adj3 (('before and after') or trial* or study or studies or evaluat*)).ab,ti.
29.randomized.ab.
30.placebo.ti,ab.
31.((before adj3 after) or (interrupted adj3 time)).ab,ti.
32.randomly.ab.
33.trial.ti.
34.groups.ti,ab.
35.(observed or observation*).mp.
36.exp device approval/
37.((compar* or intervention or evaluat*) adj3 (trial* or stud*)).ab,ti.
38.(random* adj3 allocat*).ab,ti.
39.exp prospective studies/
40.exp follow-up studies/
41.exp comparative study/
42.exp cohort studies/
43.exp evaluation studies/
44.exp treatment outcome/
45.or/24-44
46.exp animals/
47.exp humans/
48.46 not (46 and 47)
49.45 not 48
50.23 and 49

CONTRIBUTIONS OF AUTHORS

SG, ST, and CS helped to design and write the protocol. DF, EH, JH, and PP helped review the protocol.

DECLARATIONS OF INTEREST

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Studies including burn patients were originally planned for inclusion but, after further deliberation, our research team decided to exclude these types of injuries. Only one burns study (Hallock 1985) would have met the inclusion criteria for this review.

The original protocol stated that TRISS-based studies would be included even if a GEMS comparison group was not specified. Three studies did not have a GEMS comparison group and were excluded. The approach to TRISS studies should have been described in more detail in the original protocol. Briefly, analysis of HEMS versus GEMS TRISS-based studies relies on a three-step process as originally described by Baxt et al (Baxt 1983). The methods section of this paper was modified to describe this process in more detail.

Originally, we planned on using 30-day mortality as the primary outcome of interest. The vast majority of studies only reported survival to discharge, so survival to hospital discharge was used instead.

INDEX TERMS

Medical Subject Headings (MeSH)

*Air Ambulances; Disability Evaluation; Injury Severity Score; Quality-Adjusted Life Years; Regression Analysis; Survival Analysis; Wounds and Injuries [complications] [*mortality]

MeSH check words

Adult; Female; Humans; Male

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