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**Patient-centred outcomes for prehospital trauma trials: a systematic review and patient involvement exercise**

Journal:	<i>Trauma</i>
Manuscript ID	TRA-18-0043.R1
Manuscript Type:	Original Article
Keywords:	Trauma, Prehospital, Patients, Trials, Outcomes, Research
Abstract:	<p><b>Introduction</b> Outcome measures are used in clinical trials to determine efficacy of interventions. We aimed to determine which outcome measures in prehospital major trauma trials have been reported in the literature, and which of these are most patient-centred.</p> <p><b>Methods</b> A systematic review identified outcomes reported in prehospital clinical trials of major trauma patients. A search was undertaken using Medline, Embase, clinicaltrials.gov, Web of Science and Google Scholar. Data were summarized by dividing outcomes into common themes. These were presented to a Patient and Public Involvement (PPI) group consisting of trauma survivors and their relatives. This group ranked the categories of outcomes in order of most importance, and to agree some consensus statements regarding these outcome measures.</p> <p><b>Results</b> There were 27 eligible studies, including 9,537 patients. Outcome measures were divided into 9 categories: quality of life (QoL); length of stay; mortality/survival; physiological parameters fluid/blood product requirements; complications; health economics; safety and feasibility; and intervention success. Of these, mortality/survival was the most common reported category, but in multiple timescales. The PPI group agreed that the most important category was QoL, and that mortality/survival should only be reported if concurrently reported with longer term QoL. Length of stay and health economics were not considered important.</p> <p><b>Conclusions</b> Outcome measures in prehospital clinical trials in major trauma have been heterogeneous, inconsistent, and not necessarily patient-centred. Trauma survivors considered QoL and mortality most important when combined. Consensus is required for consistent, patient-centred, outcome measures in order to investigate interventions of meaningful impact to patients.</p>

**Table 1. Patient characteristics from included studies**

Author	Year	Country	Age	% male	ISS	MOI (% blunt trauma)
Baker	2009	Canada (Toronto)	42.5	60	36.2	
Baxt	1987	USA (San Diego)	27.8		13.9	100
Bernard	2010	Australia (Melbourne)	40	75	30.5	100
Bickell	1985	USA (Houston)				17.1
Bickell	1987	USA (Houston)			22.5	0
Bickell	1994	USA (Houston)	31	88	26	0
Bulger	2008	USA (Seattle)	41	62.7	28	
Bulger	2010	USA (Seattle)	38.9	76.3	26.9	98.6
Bulger	2011	USA (Seattle)	37.7	77.3	22.8	60.9
Chang	1995	USA (Wichita)	34.5	77.9	25.9	48.4
Cooper	2004	Australia (Melbourne)	38	66	38	
Garner <sup>‡</sup>	2015	Australia (Sydney)	42*	76	26*	
Helm et al	2003	Germany (Ulm)	38.4	70.2	32.2	
Junger	2013	USA (Boston)	39.1	86.4	25.5*	95.5
Maningas	1989	USA (San Francisco)	33		16.6	0
Mattox	1989	USA (Houston)			20	
Mattox	1991	USA (Houston)	34	83	19	26
Moore <sup>‡</sup>	2009	USA (Denver)	35.9	77	20.1	47
Morrison	2011	Canada (Toronto)	46	60	31	100
Rhee	1994	USA (Omaha)	31	75		
Sayre	1996	USA (Cincinnati)	29	95	25	
Schreiber	2015	USA (Portland)	41.9	75	9.5*	66.7
Turner	2000	UK (Sheffield)		64.4		98.3
Vassar	1991	USA (Sacramento)	29*		27*	84.3
Vassar	1993	USA (Sacramento)	32		19	
Vassar	1993	USA (Sacramento)	31		32	
Watts	1999	USA (Falls Church)			9	

ISS: injury severity score; MOI: mechanism of injury;

**Central tendency values for age and ISS are presented exactly as extracted from individual studies, and represent mean values unless indicated with an asterisk as median. Gaps in the table represent unavailable data.**

<sup>‡</sup>Data taken from revised criteria

<sup>‡</sup>From "as treated" data

**Table 2. Outcomes reported in included studies according to individual categories**

Outcome category	Number of studies (references)			
	Primary	N	Secondary	N
<b>Quality of life</b>		<b>6</b>		<b>1</b>
Extended Glasgow Outcome Score (6 month)	(10, 15, 18, 21)	4		
Glasgow Outcome Score (6 month)	(19)	1		
Morbidity (6 month)	(30)	1		
Cerebral Performance Category (discharge)			(26)	1
<b>Length of stay</b>		<b>7</b>		<b>4</b>
Scene time	(12)	1		
Length of stay (in hospital)	(12, 13, 17)	3	(19, 30)	2
Length of stay (intensive care)	(12, 13)	2	(19, 29)	2
Time in Emergency Centre	(12)	1		
<b>Mortality/survival</b>		<b>16</b>		<b>11</b>
Non-specified time-frame	(17, 23, 33)	3	(23, 30)	2
24 hours	(24)	1	(25)	1
48 hours			(26)	1
28 days	(14, 16)	2	(15, 16, 21)	3
30 days	(24-26)	3	(19, 25)	2
6 months	(30)	1		
In-hospital			(29)	1
Survival to discharge	(13, 31, 32)	3	(15)	1
Predicted vs actual survival	(9, 32)	2		
Time to death	(12)	1		
<b>Physiological Parameters</b>		<b>8</b>		<b>12</b>
Change in SBP (2 hr period)	(28)	1		
Correlation of biomarkers with neurological outcome	(8)	1		
Rate of hypotension (SBP <90mmHg)			(19)	1
Rate of hypoxia (SpO <sub>2</sub> <90mmHg)			(19)	1
Increase in blood pressure	(31, 32)	2		
Intracranial pressure			(15)	1
Change in temperature during transport	(34)	1		
PaCO <sub>2</sub> (ED arrival)	(20)	1		
Trauma Score (ED arrival)	(11, 12)	2		
Physiological parameters of organ dysfunction			(15, 16)	2
Improvement in physiological status (24 hours)			(24)	1
Change in pulse rate			(28)	1
Urinary output			(28)	1
Admission vital signs and blood chemistries			(29)	1
Admission haematologic assays			(29)	1
Renal performance (RIFLE classification)			(29)	1
Change in Triage Revised Trauma Score			(30)	1
<b>Fluid/blood product requirements</b>		<b>3</b>		<b>7</b>
Estimated intraoperative blood loss	(13)	1		
Perioperative transfusion (units of PRBCs)	(12)	1		
Early crystalloid volume	(29)	1		
Fluid/blood requirement in first 24 hours			(15, 16, 29)	3
Fluid/blood requirement			(21)	1
Decreased fluid volume resuscitation requirement			(24)	1
Allogeneic blood use (first 24 hours)			(25)	1
Volume of IV solution administered			(28)	1
<b>Complications</b>		<b>0</b>		<b>12</b>
Development of Multi Organ Dysfunction Syndrome			(14)	1
Development of nosocomial infections (28 days)			(14)	1
Development of nosocomial infections			(15, 16)	2
Evidence of Infection			(21)	1

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3	Incidence of Multi Organ Failure (30 days)		(25)	1
4	Multiple Organ Dysfunction Score		(15, 16)	2
5	Reduced post injury complications		(24)	1
6	Ventilator free days		(29)(36)	1
7	Any complications		(30)	1
8	Admission to Intensive Care		(30)	1
9	<b>Health economics</b>		<b>1</b>	<b>0</b>
10	Hospital costs	(12)	1	
11	<b>Safety and feasibility</b>		<b>3</b>	<b>2</b>
12	Adherence to protocol	(22)	1	
13	Logistical problems encountered	(22)	1	
14	Reported safety issues	(22)	1	
15	Safety of interventions		(24)	1
16	Protocol violations		(29)	1
17	<b>Intervention success</b>		<b>1</b>	<b>1</b>
18	Intubation success rate	(27)	1	
19	Time of intubation		(27)	1

SBP: systolic blood pressure; RIFLE: Risk, Injury, Failure, Loss of kidney function, and End-stage kidney disease  
 Studies that report versions of "survival" or "mortality" are grouped together, in subgroups according to timescale.

**Table 3. Primary outcomes reported according to type of intervention**

Primary Outcome*	Type of intervention						
	Fluid resuscitation (hypovolaemia)	Fluid resuscitation (TBI)	Anti-shock garment	Grade of clinician	Prehospital intubation	Ventilation strategy	Temperature management
Quality of life	(30)	(15, 18, 21)		(19)	(9)		
Length of stay	(13)		(12, 17)				
Mortality/survival	(14-16, 24, 25, 30-33)	(26)	(17, 23)	(9)			
Physiological parameters	(31, 33)	(8, 28)	(11, 12)			(20)	(34)
Fluid/blood product requirement	(13, 29)		(12)				
Health economics			(12)				
Safety and feasibility	(22)						
Intervention success					(27)		

\*There is no row for the category of "complications" because this was not a primary outcome in any included study

**Table 4. Consensus statements made by the group after discussion, summarised for each category of outcome measure.**

<b>Outcome measure</b>	<b>Consensus statements</b>
<b>Mortality and survival</b>	Mortality/survival should only be reported if it is also accompanied by a measure of longer term quality of life outcome
<b>Quality of life</b>	This is the most important outcome measure to us
<b>Complications</b>	It is important to know the number and seriousness of complications, especially infections
<b>Safety &amp; feasibility</b>	These are important but should not be the main focus of a study
<b>Physiological parameters</b>	These parameters are only important if they affect the treatment of patients
<b>Intervention success</b>	We consider this important for clinical trials
<b>Fluid/blood product requirements</b>	These parameters are only important if they affect the wellbeing of patients
<b>Length of stay</b>	This is of little importance. We are more interested in the success of treatments than how long is spent in hospital
<b>Health economics</b>	Cost is not considered important to individuals, but is an important factor for society

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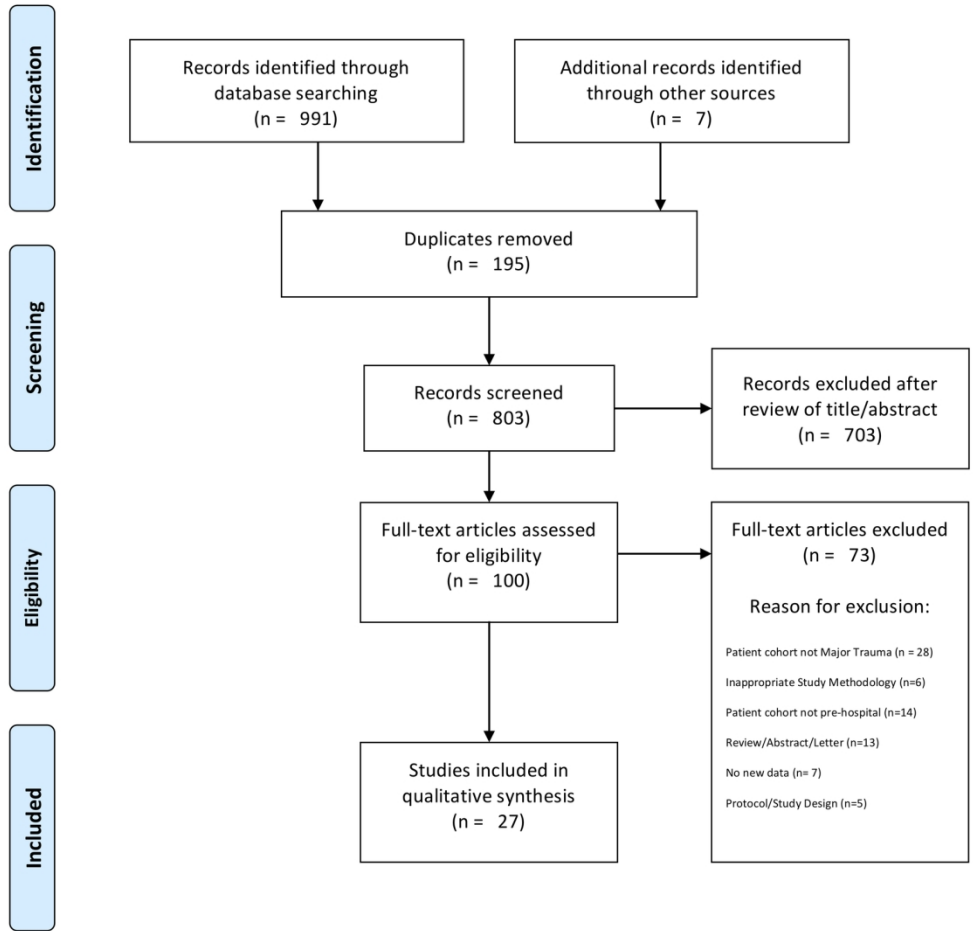
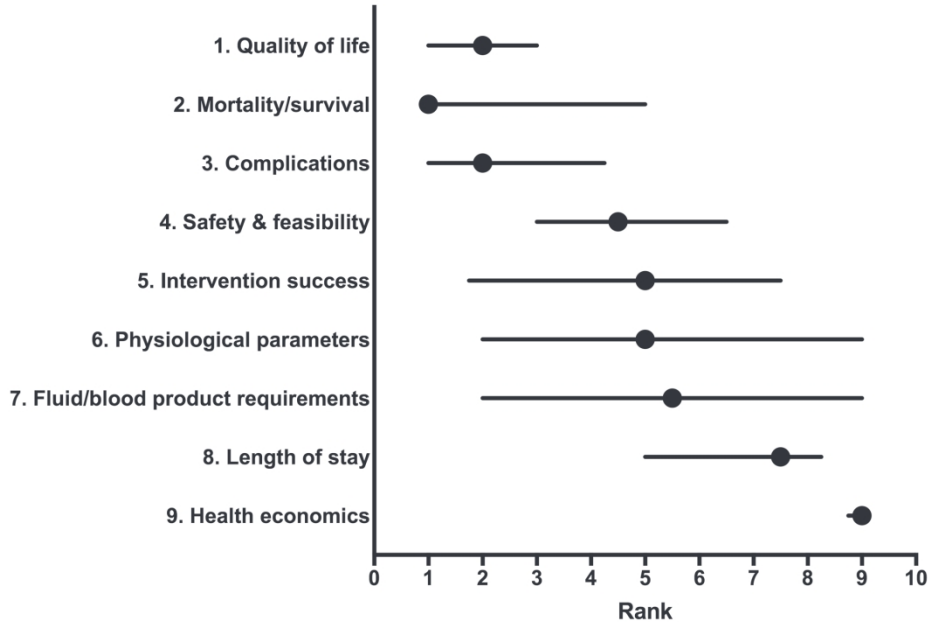


Fig 1. PRISMA diagram of search results

156x148mm (300 x 300 DPI)



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Outcome categories shown in rank order according to the Patient and Public Involvement group consensus, with median individual ranks also illustrated (interquartile ranges are shown as horizontal bars around the median)

184x118mm (300 x 300 DPI)

**Supplementary Table 1. Example of Medline database using OVID SP search strategy**

<b>Prehospital</b>	1. exp Emergency Medical Services/ or prehospital.mp.
	2. emergency medical technician.mp. or exp Emergency Medical Technician/
	3. out of hospital.mp.
	4. ambulance.mp. or exp Ambulances/
	5. pre-hospital.mp.
	6. air ambulance.mp. or exp Air Ambulances/
	7. helicopter.mp. or exp Aircraft/
	8. hems.mp. or exp "Transportation of Patients"/
	9. paramedic.mp.
	10. 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9
<b>Major Trauma</b>	11. injured.mp.
	12. injuries.mp.
	13. injury.mp. or exp "Wounds and Injuries"/
	14. wound.mp.
	15. exp Wounds, Penetrating/ or exp Wounds, Gunshot/ or wounded.mp.
	16. trauma.mp.
	17. exp Multiple Trauma/ or major trauma.mp.
	18. 11 or 12 or 13 or 14 or 15 or 16 or 17
<b>Randomized Controlled Trial</b>	19. randomized controlled trial.pt.
	20. exp Random Allocation/ or exp Randomized Controlled Trials as topic/ or randomised controlled trial*.MP.
	21. randomized controlled trial.mp. or exp Randomized Controlled Trial/
	22. 19 or 20 or 21
	23. 10 and 18 and 22
	24. limit 23 to (english and humans)

# Patient-centred outcomes for prehospital trauma trials: a systematic review and patient involvement exercise

Running title: *patient-centred prehospital trauma trials*

## Abstract

### Introduction

Outcome measures are used in clinical trials to determine efficacy of interventions. We aimed to determine which outcome measures in prehospital major trauma trials have been reported in the literature, and which of these are most patient-centred.

### Methods

A systematic review identified outcomes reported in prehospital clinical trials of major trauma patients. A search was undertaken using Medline, Embase, clinicaltrials.gov, Web of Science and Google Scholar. Data were summarised by dividing outcomes into common themes which were presented to a Patient and Public Involvement (PPI) group consisting of trauma survivors and their relatives. This group ranked the categories of outcomes in order of most importance, and agreed consensus statements regarding these outcome measures.

### Results

There were 27 eligible studies, including 9,537 patients. Outcome measures were divided into nine categories: quality of life (QoL); length of stay; mortality/survival; physiological parameters fluid/blood product requirements; complications; health

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3 economics; safety and feasibility; and intervention success. Of these,  
4  
5 mortality/survival was the most commonly reported category, but over multiple  
6  
7 timescales. The PPI group agreed that the most important category was QoL, and  
8  
9 that mortality/survival should only be reported if concurrently reported with longer  
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11 term QoL. Length of stay and health economics were not considered important.  
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## 17 **Conclusions**

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19 Outcome measures in prehospital clinical trials in major trauma have been  
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21 heterogeneous, inconsistent, and not necessarily patient-centred. Trauma survivors  
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23 considered QoL and mortality most important when combined. Consensus is  
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25 required for consistent, patient-centred, outcome measures in order to investigate  
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27 interventions of meaningful impact to patients.  
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## Introduction

Major trauma is the leading cause of death in the UK of people aged under 40, with over 20,000 cases and 5,400 deaths every year [1]. Research that aims to improve trauma patient outcomes may be undertaken during the prehospital period, so that earlier interventions, closer to the point of wounding can be investigated. A register of studies in prehospital trauma care [2], concluded that there was a paucity of Randomised Controlled Trials (RCTs) in this setting, and there have been calls for further prehospital research because of the deficit of high quality evidence [3].

Outcome measures reported in RCTs measure the difference in effects between interventions and controls and must be both biologically appropriate and clinically meaningful in order to assess the overall effect of any intervention, and should be selected based on what can be answered given the selected study design and methodology [4]. Furthermore, outcome measures should be patient-centred so that they have a translatable value on patients' lives after injury, treatment and rehabilitation.

The Trauma Audit Research Network (TARN) collects data relating to patients suffering major trauma across England and Wales. It states that "outcomes (survival or death) after trauma are best measured by the number of those who actually survived compared with the number who are expected to survive". TARN records 30-day survival data and when combined with other demographic and clinical variables is used to generate a probability of survival (Ps) to enable comparison of survival outcomes between centres. In addition to survival outcomes, and as part of an extended pilot project, TARN also collects Patient Reported Outcome Measures (PROMs) [5]. There has however been no international consensus on which outcome measures should be reported, and in which circumstances in major trauma

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3 trials. It is timely therefore, to gain insight into which outcome measures have been  
4 reported in the literature so far, and to assess whether these are considered  
5 important by trauma patients.  
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10 The two , mary research questions for the current study were what outcome  
11 measures are reported in prehospital RCTs of major trauma patients and which of  
12 these outcome measures are patient-centred? It aimed to answer these questions  
13 by using a combination of systematic review methodology and a qualitative focus  
14 group exercise involving trauma survivors and their relatives.  
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## 25 **Methods**

### 26 **Study design**

27 This study was undertaken in two parts. Firstly, a systematic review of the literature  
28 was performed in order to find all outcome measures used in prehospital clinical  
29 trials involving trauma patients. Secondly, those outcome measures were  
30 summarised and presented to a Patient and Public Involvement (PPI) group in order  
31 to determine which outcome measures they found to be relevant and important to  
32 them. The intention was to determine which commonly reported outcome measures  
33 were most patient-centred, in order to inform future study investigators and research  
34 centres.  
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### 51 **Systematic review of the literature**

52 A systematic review was undertaken using standard systematic review methodology  
53 and the Preferred Reporting Items for Systematic Reviews and Meta-Analyses  
54 (PRISMA) guidelines [6]. No meta-analysis was planned, since the systematic  
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3 search was intended to be informative rather than to compare outcomes for any  
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5 intervention.  
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### 10 ***Inclusion and exclusion criteria***

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12 The inclusion and exclusion criteria for included studies were decided *a priori*.  
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14 Clinical RCTs that included adult major trauma patients (ISS  $\geq$  16, or if described  
15 as “major trauma”)during the prehospital phase of care that reported at least one  
16  
17 primary outcome measure were eligible for inclusion. There was no limitation on  
18  
19 publication date. Studies who reported data from patients who had sustained “minor  
20  
21 trauma” were excluded, as were studies where data was reported exclusively from  
22  
23 non-trauma patients or if there was a mixed caseload of trauma and non-trauma  
24  
25 where data pertaining to the trauma patients could not be extracted separately. Due  
26  
27 to the known marked differences that exist between how children and adults interpret  
28  
29 and report on their health [7], studies that included only paediatric patients were  
30  
31 excluded. The search was restricted to humanstudies published in English.  
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### 40 ***Search Strategy***

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42 A search strategy was developed to capture all relevant literature. The Medline and  
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44 Embase databases were searched using the OVID SP interface; the terms being  
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46 used for the searches included MeSH terms and also free text terms such as “injury”,  
47  
48 “injuries”, “injured”, “wound”, “wounds”, “wounded”, “trauma”, “prehospital”, “pre-  
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50 hospital”, “Emergency Medical Services”, “ambulance”, “outcome”, “endpoint”.  
51  
52 Consideration was given to international variations of spelling. Other online  
53  
54 resources, including [www.clinicaltrials.gov](http://www.clinicaltrials.gov), Web of Science and Google Scholar  
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56 were also searched for articles not found in the database search. An example of the  
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3 search strategy is given in Supplementary Material 1. The last search was performed  
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5 on 25<sup>th</sup> February 2017.  
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### 10 **Study Selection**

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12 All titles and abstracts were screened, duplicates removed and full texts were  
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14 obtained for studies of interest. Eligible studies were identified from reading full texts.  
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16 Reference lists in appropriate reviews and studies of interest were examined for  
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18 further potentially eligible studies.  
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### 23 **Data Extraction**

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25 Data were extracted from all eligible studies. Study-related data included: the type of  
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27 intervention investigated; study population under investigation, eligibility criteria;  
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29 country of origin; first author and year of publication. Patient-related data included:  
30  
31 number of patients, injury details (injury severity and mechanism); demographic  
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33 details (age, gender); primary and secondary outcomes. Reported outcomes were  
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35 extracted *verbatim*. The time scale of the outcomes were also recorded (short term,  
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37 long term, intermediate, or indeterminate). “Short term” outcomes were defined as  
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39 those that occurred within 30 days of admission, and “long term” outcomes were  
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41 those that occurred after 6 months, with “intermediate” including all those in  
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43 between. Time scale was “indeterminate” if no specific timing was mentioned (for  
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45 example “length of hospital stay” or “survival to discharge”).  
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## 54 **Patient and Public Involvement (PPI) exercise**

### 55 **Selection of participants**

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3 Our trauma research unit sponsors an Accident, Burns and Critical Care Patient and  
4 Public Involvement (PPI) group in order to facilitate discussions between study  
5 investigators and previous patients and their relatives. This group is invited to regular  
6 meetings with research staff throughout the year. Some of the patients and relatives  
7 in this group joined after being invited following a hospital stay, or participation in a  
8 trauma, burns or critical care study. Further members of the group were recruited  
9 following similar invitations placed in volunteer newsletters distributed at the NHS  
10 Trust. This PPI group was invited to participate in our focus group to discuss trauma  
11 outcomes in prehospital clinical trials. This group was considered to be  
12 approximately representative of those affected by trauma, including relatives, as well  
13 as those who had suffered trauma in the past.  
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### 31 ***Nominal Group Technique***

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33 For this exercise, basic Nominal Group Technique was used in 5 stages: (1)  
34 Introduction and explanation; (2) Silent reflection; (3) Sharing of ideas with the group;  
35 (4) Group discussion; and (5) Ranking of items in a voting process. Firstly, we  
36 presented the findings of our systematic review to the group in a concise manner,  
37 explaining the meaning and relevance of outcome measures that have been  
38 reported. These outcomes were divided into categories according to type of outcome  
39 measure. Then, participants were given sheets of paper and asked to write down  
40 their own views without discussing with the rest of the group. They were asked to (i)  
41 put the categories of outcome measures in rank-order of personal importance (with  
42 number 1 being the most important); (ii) highlight any outcome measures that were  
43 particularly important, or considered completely irrelevant; and (iii) write down what  
44 they considered most important to them in terms of outcomes following prehospital  
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3 trauma trials (free text). Each participant was then asked to share their ideas with the  
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5 rest of the group in turn, and this was followed by a group discussion. At the end of  
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7 this discussion, the group were asked to vote on the rankings of the trauma outcome  
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9 categories. The whole exercise was completed in 1 hour, and consensus statements  
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11 for each outcome measure were recorded by the authors. The age and gender were  
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13 recorded for all participants.  
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## 20 **Data analysis**

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22 Systematic review findings are presented in summative form, with no meta-analysis  
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24 (no comparison was made between outcomes for any intervention). For the PPI  
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26 exercise, median assigned rank was calculated for each outcome measure. These  
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28 are presented in order of median rank, with interquartile range. The free text  
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30 comments are summarised in themes.  
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## 40 **Results**

### 41 **Systematic search results**

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43 Figure 1 shows the PRISMA diagram for study selection. The initial search yielded  
44  
45 998 studies of which 803 were non-duplicates. After screening titles and abstracts  
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47 the full texts of 100 studies were examined, identifying 27 articles as eligible having  
48  
49 met all inclusion criteria [8-34].  
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### 58 **Study characteristics**

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3 The 27 included studies were published between 1985 and 2015 and were all RCTs;  
4  
5 20 were from the United States with the remaining seven from Canada [8, 26],  
6  
7 Australia [10, 18, 19], Germany [20] and the United Kingdom [30]. With a total of 20  
8  
9 different individual first authors. There was a diverse range of sub-groups  
10  
11 investigated within the wider major trauma population, but most (17/27 (62%))  
12  
13 investigated patients with either traumatic brain injury or haemorrhagic shock.  
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### 19 **Patient characteristics**

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22 There were 9,537 patients. All included studies reported no statistically significant  
23  
24 difference in the basic demographic details (age, sex, mechanism and severity of  
25  
26 injury) of patients between either interventions or controls. Table 1 summarises the  
27  
28 patient demographics for all included studies according to the intervention arm of  
29  
30 each study.  
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### 36 **Study interventions**

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38 All studies compared a specific intervention to a standardised control. Four of the  
39  
40 studies investigated two interventions versus a control [15, 16, 21, 33], one tested  
41  
42 three interventions [32]; and one tested five against controls [34]. The most  
43  
44 commonly investigated intervention was hypertonic saline/dextran (n = 11); six  
45  
46 studies investigated the use of hypertonic saline ; four studies investigated a variant  
47  
48 of the anti-shock garment [11, 12, 17, 23] and two studies investigated the impact of  
49  
50 physician-led care compared to paramedic-led care [9, 19]. However, no other single  
51  
52 intervention was investigated by more than one study.  
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### 59 **Outcomes reported**

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3 Table 2 details the outcomes reported by all included studies, as reported *verbatim*;  
4  
5 seven (26%) exclusively reported short term outcomes, two (7%) reported  
6  
7 exclusively long term outcomes, and seven (26%) studies exclusively reported  
8  
9 outcomes of an indeterminate length. The remaining 11 studies (41%) reported  
10  
11 outcomes that were assessed over a range of timescales.  
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### 17 **Primary Outcomes**

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19 All 27 papers stated at least one primary outcome in their methodology, with eight  
20  
21 reporting multiple primary outcomes; overall 32 different and unique outcomes were  
22  
23 reported. The most frequently reported individual primary outcome was Extended  
24  
25 Glasgow Outcome Score (6 month) in four studies [10, 15, 18, 21], with the  
26  
27 remainder of all other outcomes being shared by only 3 or fewer studies. Outcomes  
28  
29 relating to mortality and survival were the most commonly reported primary  
30  
31 outcomes (n = 16), but there were 15 permutations according to timescale, cause  
32  
33 and stay in hospital; “survival to discharge” was the most common variation in three  
34  
35 [13, 31, 32]. Table 3 illustrates the type of primary outcomes, categorised by the  
36  
37 nature of the intervention. It is notable that 10/17 studies that investigated fluid  
38  
39 resuscitation strategies in hypotensive major trauma patients reported a variant of  
40  
41 mortality as their primary outcome. Similarly, in trials where the intervention was fluid  
42  
43 administration for the treatment of traumatic brain injury, half of the primary  
44  
45 outcomes reported are a quality of life assessment. No study reported both short and  
46  
47 longer term primary outcomes and of the six that did report a long term primary  
48  
49 outcome, only three (50%) reported a short term secondary outcome.  
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### 58 **Secondary Outcomes**

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3 Thirteen studies reported at least one secondary outcome, most commonly related  
4 to either physiological parameters (n = 13) or complications (n = 13), with fluid/blood  
5 requirement in the first 24 hours being the most frequently reported individual  
6  
7  
8 secondary outcome (n = 3), with the remainder of secondary outcomes only being  
9  
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11 shared by 2 studies or none at all. None of the included studies reported a long term  
12  
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14 secondary outcome.  
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### 19 **Patient and Public Involvement exercise**

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22 There were 10 members of the PPI group, with a mean age of 59, and six (60%)  
23  
24 were female. The outcome measures were divided into nine categories according to  
25  
26 the systematic review findings : quality of life; length of stay; mortality/survival;  
27  
28 physiological parameters; fluid/blood product requirements; complications; health  
29  
30 economics; safety and feasibility; and intervention success. The consensus ranks of  
31  
32 the nine outcome categories are shown in Figure 2 with the median and interquartile  
33  
34 range of ranks assigned by individual members of the group in stages 2 and 3 of the  
35  
36 Nominal Group Technique exercise.  
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41 The consensus statements for each outcome category are summarised in  
42  
43 table 4. The PPI group agreed that quality of life outcome measures were the most  
44  
45 important overall. Where mortality/survival outcome measures are reported, quality  
46  
47 of life outcomes should also be reported in order to make the former be meaningful.  
48  
49 Although the group agreed that health economics was important for society, when  
50  
51 asked about the importance to themselves and their family, they found this aspect of  
52  
53 lesser importance. Participants did not express views on any particular outcome  
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55 measures not already reported by the included studies.  
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## Discussion

The main findings from the current study are that there are a wide range of outcome measures reported by clinical trials of trauma patients in the prehospital setting, with mortality/survival being the most common, and that trauma survivors consider this outcome measure important. Quality of life outcome measures were also considered very high in importance amongst our PPI group, who also agreed that such outcomes should be reported in addition to mortality/survival. It is notable that outcome measures related to complications were considered of high importance by trauma survivors, but these were only reported as secondary outcome measures in the studies that we found, with no study reporting these as primary outcome measures (Table 2). A large proportion of included studies reported physiological parameters and length of stay outcomes, which were not considered as important by the PPI group.

Our systematic review found that there is heterogeneity in the selection of both primary and secondary outcomes, and also the time points at which these outcomes are assessed. No single outcome measure was shared by more than four studies, and no single secondary outcome was shared by more than three studies. Even mortality and survival were reported in multiple different permutations according to timescale, cause, and relating to time spent in hospital. This heterogeneity is present even within groups of studies that investigated similar interventions, suggesting that there is limited consensus on the types of outcomes to report for any given intervention, and that perhaps a more consistent approach is warranted. Similar heterogeneity and variation of outcome reporting has been described in studies of cardiac arrest [35] and surgery [36]. There have been published calls for further

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3 research towards the development of comprehensive outcome measures, developed  
4 within an internationally recognised framework, following the work undertaken in  
5 other areas of research (stroke, brain injury, multiple sclerosis) where a core set of  
6 health outcome measures already exist [37]. The use of a framework (such as the  
7 International Classification of Function Disability and Health [38]) for the  
8 development of a core set of health-related outcome measures may be crucial in  
9 developing consensus in this area. The Core Outcome Measures in Effectiveness  
10 Trials (COMET) initiative has been established to find agreement in 'core outcome  
11 sets' (COS), which are considered the minimum to be measured and reported for  
12 any given condition. It is important during the development of COS to strengthen  
13 patient and public engagement in research [39]. Our findings may contribute to such  
14 efforts by adding information from patients and public in order to facilitate such a  
15 process. If future trial investigators are to agree on 'standard' outcome measures to  
16 report for prehospital studies of trauma patients, it would be prudent to consider  
17 patient reported outcomes. PROMS are already being collected for elective surgery  
18 [40], and such an approach would ensure that the most relevant PROMS were  
19 reported for prehospital clinical trials in trauma, and comparable to those PROMS  
20 recorded by bodies such as TARN.  
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47 Only 11% of studies reported both a short and long term outcome. Our study  
48 suggests there is a lack of a consensus regarding core outcomes and timescales  
49 within this patient population. This is notable because our PPI group agreed that  
50 they would prefer both short term and long term outcomes reported in such trials, in  
51 particular, the combination of mortality outcomes and longer term quality of life  
52 outcomes. Prehospital clinical trials that include trauma patients represent a logistic  
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3 challenge, and are difficult to plan and undertake, which may explain the relatively  
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5 low number of studies identified by our search. Because of this limitation, it is  
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7 important to answer as many research questions as possible for any give trial in  
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9 such a setting – including both the shorter and longer term clinical outcomes relevant  
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11 to patients.  
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17 A revised Utstein template published in 2008 aimed to provided consensus in the  
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19 way data is reported following major trauma by precisely defining certain variables;  
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21 one such core data variable was survival status, the template proposing a binary  
22  
23 outcome of “dead or alive” assessed at the 30 day time point [41]. Yet, despite this  
24  
25 recommendation, “survival to discharge” is still the most widely reported mortality  
26  
27 and survival-based outcome report in prehospital RCTs of major trauma patients.  
28  
29 Since TARN records 30-day survival data for all major trauma patients, studies  
30  
31 based in England and Wales should be encouraged to include this readily available  
32  
33 information in outcome reporting. The use of mortality and survival as outcome  
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35 measures are advantageous since they are easy to assess, and this may partly  
36  
37 account for the frequency of their use. There is, however, debate as to how sensitive  
38  
39 a measure mortality is [42] and, as such, consideration should be given to its use.  
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41 We recommend that in all circumstances where mortality is listed as a primary  
42  
43 outcome, an additional quality of life assessment tool be reported, so that “survival”  
44  
45 has a meaningful value to those patients within the study, and can be transferable to  
46  
47 clinical practice in a way that is patient-centered. There have been other calls for the  
48  
49 use of quality of life outcomes other than mortality [43-45], yet implementation of this  
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51 practice has been slow and their use is not without risk of bias [46]. Our study serves  
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53 to illustrate that such an aim might be regarded as patient-centred.  
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6 If we agree that the reporting of quality of life outcomes is patient-centred and  
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8 important for translatability to clinical practice, the measurement of such outcomes  
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10 should be of high quality, and with a low drop-out rate of trial participants. One  
11  
12 difficulty with obtaining these data may be that patients become lost to follow up, or  
13  
14 occasionally cannot be contacted months and years after their hospital treatment  
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16 [47]. Data may therefore be vulnerable to bias towards those who are more able to  
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18 respond, or make a visit to the research facility or hospital. Or, conversely, patients  
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20 who are still within long term rehabilitation facilities may be more easily contacted,  
21  
22 biasing the data towards worse functional outcomes. In either circumstance, quality  
23  
24 of life data may be less complete, and perhaps less reliable, than those regarding  
25  
26 survival. Ongoing research in the UK aims to develop electronic capture of PROMs  
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28 (ePROMs) in trauma patients [48]. An electronic interface may improve PROM data  
29  
30 capture in patients who are able to engage with such a programme, but may  
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32 exclude patients who do not have access to, or are unable to use a computer.  
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### 40 **Limitations**

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42 Our search of the literature excluded paediatric patients, and the PPI group were all  
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44 adults, and only discussed adult trauma, so the findings may not necessarily be  
45  
46 translatable to the paediatric population. The PPI group was relatively small, and  
47  
48 although they all had first-hand experience of trauma and hospital treatment, their  
49  
50 opinions may have been biased by some factors in their participation: they all  
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52 survived their injuries, and had successful treatments that rendered them mobile,  
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54 stable, and willing to participate in such a group. Our PPI group was older and had a  
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56 higher percentage of female members than the average trauma population from our  
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3 systematic review. However, we consider it likely that their opinions are  
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5 representative of the wider community of those affected by trauma, such as patient  
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7 relatives as well as trauma patients alone. The methods used in the current study  
8  
9 are limited in scope, and do not present a comprehensive investigation of the issues  
10  
11 presented. However, our findings highlight the broader issues of lack of consensus,  
12  
13 and some limitations in patient-centred approach to prehospital research. Further  
14  
15 attention may be warranted for specific types of research, and for specific patient  
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17 populations.  
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### 23 ***Future Direction***

24  
25 The current study highlights an inconsistency in outcome reporting in prehospital  
26  
27 RCTs of major trauma patients, and the variability in patient-centred outcome  
28  
29 measures. This variability includes a sparsity of studies that report both short and  
30  
31 longer term outcomes, or a combination of survival and quality of life data – both of  
32  
33 which were considered important and appropriate by our PPI group. It may be  
34  
35 important for both clinicians and patients that future research looks to specify  
36  
37 minimum variations of outcomes and strong, robust assessment methods without  
38  
39 limiting assessments [49, 50]. Research should involve stakeholders including  
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41 patients, their relatives, those that fund healthcare, make health policy, clinicians and  
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43 scientific investigators. Designers of prehospital RCTs that include major trauma  
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45 patients may benefit from a “core” set of outcome measures, using standardised and  
46  
47 precisely defined outcome measures on which to base the reporting of their findings,  
48  
49 in a manner that is in keeping with initiatives such as COMET [39]. This approach  
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51 may ensure consistency and comparability of outcome reporting, and support future  
52  
53 synthesis of data. Moreover, it will help to ensure the creation of a strong evidence  
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3 base upon which the development of healthcare policy and the evaluation of novel  
4 interventions can be based. The focussed approach to establishing standardised  
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6 outcomes that is proposed here has already been demonstrated in other areas of  
7  
8 clinical research, such as in cardiac arrest trials [51]. Investigators of prehospital  
9  
10 major trauma may wish to build on the progress in other areas of research and seek  
11  
12 consensus on the outcomes reported in prehospital trauma research, including a  
13  
14 patient-centred approach.  
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23  
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25  
26 assistance in the data collection and focus group exercise.  
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3 **FIGURE LEGENDS**  
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7 **Fig 1. PRISMA diagram of search results**  
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11 **Fig 2. Outcome categories shown in rank order according to the Patient and**  
12 **Public Involvement group consensus, with median individual ranks also**  
13 **illustrated (interquartile ranges are shown as horizontal bars around the median)**  
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