Helsingin yliopiston digitaalinen arkiste



Impact of Trauma System Structure on Injury Outcomes: A Systematic Review and Meta-Analysis

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Abstract

Background The effectiveness of trauma systems in decreasing injury mortality and morbidity has been well demonstrated. However, little is known about which components contribute to their effectiveness. We aimed to systematically review the evidence of the impact of trauma system components on clinically important injury outcomes.

Methods We searched MEDLINE, EMBASE, Cochrane CENTRAL, and BIOSIS/Web of Knowledge, gray literature and trauma association Web sites to identify studies evaluating the association between at least one trauma system component and injury outcome. We calculated pooled effect estimates using inverse-variance random-effects models. We evaluated quality of evidence using GRADE criteria.

Results We screened 15,974 records, retaining 41 studies for qualitative synthesis and 19 for meta-analysis. Two recommended trauma system components were associated with reduced odds of mortality: inclusive design (odds ratio [OR] = 0.72 [0.65-0.80]) and helicopter transport (OR = 0.70 [0.55-0.88]). Pre-Hospital Advanced Trauma Life Support was associated with a significant reduction in hospital days (mean difference [MD] = 5.7 [4.4-7.0]) but a nonsignificant reduction in mortality (OR = 0.78 [0.44-1.39]). Population density of surgeons was associated with a significant reduction density of surgeons was associated with a significant reduction in mortality (OR = 0.58 [-0.22 to 1.39]). Trauma system maturity was associated with a significant reduction in mortality (OR = 0.76 [0.68-0.85]). Quality of evidence was low or very low for mortality and healthcare utilization.

Conclusions This review offers low-quality evidence for the effectiveness of an inclusive design and trauma system maturity and very-low-quality evidence for helicopter transport in reducing injury mortality. Further research should evaluate other recommended components of trauma systems and non-fatal outcomes and explore the impact of system component interactions.

The International Injury Care Improvement Initiative (IICII) is a global effort of over 60 injury care experts, harnessing national capabilities in injury control from 30 countries in pursuit of our mission to reduce the global burden of injuries.

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Introduction

Injury is the leading cause of death under 40 years of age, the leading cause of loss of active life years, and is second only to cardiovascular diseases in terms of healthcare costs

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in high-income countries [1]. Low- to middle-income countries carry more than 90% of the fatal injury burden [2]. Important reductions in injury mortality, disability, and costs have been achieved in many healthcare jurisdictions with the introduction of trauma systems [3, 4].

There are multiple specific definitions of a trauma system, but broadly, it is an organized, regional, multidisciplinary response to injury [5, 6]. Many injury organizations, including the World Health Organization (WHO) [7] and the American College of Surgeons (ACS) [8], provide consensus-based recommendations on the structure of trauma systems. Consequently, system components such as pre-hospital triage and transport protocols, accreditation and designation and benchmarking activities as well as their level of integration vary significantly across trauma systems [9]. The effectiveness of trauma systems has now been well established; they have been estimated to lead to a 15% reduction in the odds of mortality [10] and have been associated with reductions in disability and costs [11]. However, there is still a major knowledge gap on which components of a trauma system contribute to their effectiveness. Given the multitude of recommended trauma system components and the fact that they are largely based on expert consensus, there is an urgent need to build an evidence base to guide budget-constrained policy-makers, particularly in low- and middle-income countries.

Our aim was to systematically review evidence of the impact of trauma system components on clinically important injury outcomes including mortality, function, disability, quality of life, and resource utilization.

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Materials and methods

We conducted a systematic review in accordance with Cochrane guidelines [12]. The review is presented using the structure suggested in *Preferred reporting items for systematic review and meta-analysis (PRISMA) 2015* [13]. Our systematic review protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on June 20, 2016 (#42016041336) and published in Systematic Reviews [14].

Eligibility criteria

Study designs

We considered randomized and non-randomized controlled trials (RCTs) including cluster RCT, interrupted time series studies, controlled before–after studies, and prospective or retrospective observational studies. We also included studies based on qualitative methods (e.g., preventable death determined by expert consensus).

Participants

We included studies based on injury populations at large as well as studies evaluating population-based injury outcomes. No restrictions were placed on age, injury type, or injury severity. Studies based exclusively on combat injuries, isolated fractures following low falls, burns, bites, foreign bodies or late effects of injuries were excluded.

Interventions

We included studies evaluating the effectiveness of trauma system components, i.e., organizational-level structural

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interventions (single or multiple) targeting tertiary injury prevention (optimal treatment following injury). Interventions were classified using an adaptation of WHO and ACS categories, i.e., oversight, pre-hospital care, definitive care, rehabilitation, and evaluation [7, 8].

Comparators

Studies comparing a single or multiple organizational-level structural intervention to either (1) usual trauma system structure or (2) an alternative organizational structure were eligible. In order to be as inclusive as possible, and given the variation in definitions of trauma systems, we included studies based on authors' definition of a trauma system. No restrictions were based on the country or the regulatory nature of the trauma system (e.g., mandatory, non-mandatory, or volunteer). Studies comparing healthcare jurisdictions with a trauma system to those without organized trauma care were not included as evidence of the global effectiveness of trauma systems has already been reviewed [10].

Outcome measures

Primary endpoints of interest were clinically important outcomes, established by the study steering committee, including mortality, function, disability, and quality of life. Secondary outcomes were adverse events, healthcare utilization, and costs. No restrictions were imposed on the follow-up of patients for the evaluation of injury outcomes.

Information sources

The search strategy was designed to minimize publication bias, including geographical bias. We systematically searched MEDLINE, EMBASE, Cochrane CENTRAL, and BIOSIS/Web of Knowledge databases from their inception up to March 2, 2017. Unpublished clinical studies were searched using ClinicalTrials and the ISRCTN registry. We consulted thesis repositories to identify additional studies, including Thesis portal Canada, EtHOS, DART-Europe E-Theses Portal, and ProQuest Dissertations & Theses Global. We also searched the Web sites of key healthcare organizations (WHO, public health agencies) and injury organizations including the American College of Surgeons, the Trauma Association of Canada, the International Association for Trauma Surgery and Intensive Care, the Australasian Trauma Society and the Trauma Audit Research Network. We then screened references of included articles and abstracts of major injury conferences including the International Surgical Week, World Congress of Surgery, American Association for the Surgery of Trauma congress, European Congress of Trauma and Emergency Surgery, Western Trauma Association congress, World Trauma Congress, Eastern Society for the Surgery of Trauma Congress, Trauma Association of Canada annual meeting, and Australasian Trauma Society Congress.

Search strategy

We developed a rigorous systematic search strategy with a health sciences information specialist who has systematic review experience (MS) using published guidelines of The Cochrane Collaboration (see Online resource 1 for the MEDLINE search strategy via PubMed) [15]. The strategy was developed using keywords and MeSH (MEDLINE) or EMTREE (EMBASE). To be as inclusive as possible, we limited the search strategy to terms covering the concept of \ll trauma system \gg . Keywords were elaborated by co-investigators and collaborators with methodological and clinical expertise. This search strategy was then adapted to the other databases.

Study records

Data management

Citations were managed using EndNote software (version X7.0.1, New York City: Thomson Reuters, 2011). Duplicates were identified and eliminated using electronic and manual screening. No multiple publications based on the same data were identified.

Selection process

Pairs of reviewers (LM, PAT, TVP) independently evaluated citations for potential inclusion by screening titles and abstracts and assessed full publications to determine eligibility for final inclusion. To ensure high agreement on study eligibility, three samples of 500 citations were independently and consecutively assessed by each reviewer. Between each assessment, results were discussed to reach a consensus on the interpretation of inclusion criteria. Any further disagreement on study eligibility was resolved by consensus and a third reviewer (HC) adjudicated when necessary.

Data collection

A standard electronic data abstraction form was developed and piloted on a representative sample of five studies. Two reviewers (LM and PAT) with methodological and content expertise independently extracted information on study setting and design, study population, interventions, outcomes, measures of association with standard errors, and risk adjustment. If information relating to the above-mentioned elements was missing, study authors were contacted by email (up to three attempts) for further clarifications. Abstracts from conference proceedings were included if they provided information on all of the above.

Risk of bias in individual studies

Risk of bias was evaluated using a study-specific adaptation of the ROBINS-I tool [16]. This tool evaluates baseline and time-varying confounding, co-interventions, selection bias, classification bias (intervention), missing data, and bias in outcome measurement. Two reviewers (LM and PAT) independently evaluated the risk of bias and rated studies. Disagreement was resolved using arbitration by a third reviewer (HC).

Assessment of heterogeneity

Statistical heterogeneity was measured using I^2 statistics and was interpreted as low from 0 to 40%, moderate from 30 to 60%, substantial from 50 to 90%, and considerable from 75 to 100% as recommended in the Cochrane handbook [12].

Data synthesis

If two or more studies had evaluated the same intervention and the same outcome, we calculated pooled effect estimates and their 95% confidence intervals (CI) using inverse-variance random-effects models (DerSimonian and Laird) [17] adapted to the scale of measurement. We used Review Manager (RevMan), version 5.3 Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

Subgroup and sensitivity analyses

Due to lack of data and the small number of studies that assessed the same outcome for a given component, we could not perform planned subgroup analyses (age group, injury severity, injury type, length of follow-up, and World Bank country economic classifications). However, when the number of studies available for analyses was sufficient (≥ 2) , we conducted sensitivity analyses excluding studies of low methodological quality.

Publication bias

We generated funnel plots adapted to the scale of measurement to evaluate the risk of publication bias.

Quality of evidence

Two subject-content experts (LM and GOR) independently evaluated quality of evidence for each intervention-outcome evaluation included in meta-analysis using the *Grading of Recommendations Assessment, Development and Evaluation* (GRADE) working group methodology [18].

Results

Study identification and selection

The search strategy retrieved 24,758 citations, and a total of 15,974 titles were screened after removing duplicates (Fig. 1). One hundred and thirty-four full texts were assessed, of which 33 were deemed eligible. One conference abstract was included [19], and an additional seven articles were found through gray literature and hand searching of the references of included studies. In total, 41 studies were selected for the systematic review, of which 19 were included in the meta-analysis.

Study characteristics

All studies included were written in English, but study cohorts originated from thirteen different countries, six of which were situated in Europe, three in North America, three in Asia, and one in Oceania (Online resource 2). Three studies [20, 21] were conducted in low- or middleincome countries [22], and five (12%) studies compared cohorts from two different countries [20, 23-26]. Most studies (88%) used a prospective or retrospective observational design, but there were three controlled beforeafter studies [27-29], one interrupted time series [30], and one cluster randomized controlled trial [31]. Data collection spanned from 1990 [32] to 2013 [33] and included between 35 [34] and 857,534 [35] patients from 1 [32] to >600 [26] trauma centers. Mean age of patients ranged from 26 [36] to 57 [37] years (excluding three studies restricted to pediatric trauma) [28, 38, 39]. Mean ISS (when provided) varied between 10 [34] and 29 [24]. Five studies used states [33, 40] or counties [19, 41, 42] as their unit of analysis.

Risk of bias

Eighty percent (n = 32) of the studies had a moderate or serious risk of bias in relation to confounding (32, 80%) and classification of interventions (35, 88%) (Online resource 3). In the domains associated with the selection of study participants and deviations from intended



interventions, 26 (65%) and 24 (60%) studies had low or moderate risk of bias, respectively. Information on missing data was often not reported (40%), and among those studies with missing data, it was rarely handled appropriately (i.e., imputation methods which account for the uncertainty of missing data, 15%). Finally, 40 (100%) studies had a moderate or low risk of bias for the measurement of outcome and 38 (95%) for selective reporting of results.

Visual inspection of funnel plots suggested no significant bias for odds ratios (OR) (16 studies; Online resource 4, left side) but a possible publication bias in favor of studies that reported a positive intervention effect for mean differences (four studies; Online resource 4, right panel). Studies with higher standard errors were slightly more likely to report a positive intervention effect on either scale, suggesting a small-study effect.

Impact of trauma system components

Overall, 84 assessments of the association between trauma system components and outcomes were reported (Table 1). Mortality alone represented 66% of all assessments, whereas healthcare utilization and function and disability represented 21 and 7%, respectively. The impact of trauma system components on quality of life, costs, and adverse events was each assessed twice or less. The most common

Table 1	Number of evaluations	of the effectiveness	of recommended	trauma system	components ^a	according to clinical	lly important outcomes
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Trauma system component subcomponent ^a	Outcomes (number of studies)					
	Mortality	Function and disability	Quality of life	Adverse events	Healthcare utilization	Costs
Oversight						
Disaster planning						
Lead agency	1 [43]					
Trauma services medical director						
Trauma system advisory committee						
Trauma system plan	1 [43]					
Pre-hospital care						
Communication between EMS and hospitals						
Emergency services medical director						
EMS treatment protocols	6 [21, 27, 32, 61]	3 [27]			3 [27, 32]	
EMS transport system	3 [29, 62]					
Pre-hospital major trauma definition	1 [43]					
Triage and transport protocols	3 [26, 31, 43]	1 [31]	1 [31]		2 [28]	
Definitive care						
Communication between transferring hospitals	1 [43]					
Facility designation through an accreditation agency	1 [43]					
Inclusive design	6 [35, 43, 63–66]				1 [<mark>66</mark>]	1 [64]
Interfacility transfer agreements/protocols	2 [43]					
Relative location of trauma centers	7 [19, 30, 33, 37, 40, 67, 68]					
Other	2 [25, 34]				2 [25]	
Rehabilitation						
Human resources						
Educational preparation						
Workforce resources	4 [33, 41, 42]					
Evaluation						
Benchmarking	1 [69]			1 [69]	3 [<mark>69</mark>]	
Data collection-trauma registries						
Injury surveillance						
Integration of evaluation throughout the care continuum						
Interdisciplinary review committee						
Research						
Other						
System maturity	5 [4, 11, 39, 70, 71]	1 [11]		1 [4]	4 [4, 71]	
Multiple non-specified	2 [23, 24]				2 [72]	
Multiple specified	9 [20, 36, 38, 43, 73–75]	1 [38]		1 [20]	1 [38]	

^aTrauma system components recommended by the American College of Surgeons [8] and the World Health Organization [7]

system components evaluated were in pre-hospital care and definitive care (23 evaluations each). We identified 11 evaluations of trauma system maturity and 16 evaluations of specified or non-specified multiple interventions. Almost half (11 out of 24) of the recommended trauma system components were not evaluated for any outcome. No interventions related to rehabilitation were reported for any outcome.

Interventions

Pre-Hospital Advanced Trauma Life Support (PH-ATLS) was associated with a decrease in mortality in two studies but an increase in another, leading to a nonsignificant OR with considerable heterogeneity (Fig. 2). In contrast, PH-ATLS was associated with a significant decrease in hospital LOS (Fig. 3). Similarly, the overall effect of

helicopter transport suggested a significant decrease in mortality (Fig. 2). The impact of triage and transport protocols on mortality was inconclusive [31, 43]. All studies evaluating the impact of an inclusive trauma system design reported a reduction in mortality, leading to a significant OR characterized by high precision and low heterogeneity. Likewise, all studies but one [11] that assessed the association between trauma system maturity and mortality reported a statistically significant OR with a narrow IC and moderate heterogeneity. Finally, increased population density of surgeons was associated with a statistically significant decrease in mortality in both studies included in the analysis. In a fixed-effects model, the overall mean difference was significant (MD -0.22 [95% CI: -0.28 to -0.16]), but the association did not remain statistically significant in a random-effects model due to considerable heterogeneity (Fig. 3).

Among the 26 quantitative assessments reported in studies not included in meta-analyses, 13 (65%) were statistically significant and all but one [24] suggested that the trauma system intervention was associated with a reduction in mortality (Online resource 5). In addition to lead agency, designation of trauma centers, and inclusiveness of trauma systems, all interventions related to the relative location of trauma centers were associated with a statistically significant reduction in mortality.

Quality of evidence

Among associations that were statistically significant in meta-analyses, GRADE quality of evidence was low for an inclusive design and system maturity (mortality), very low for helicopter transport (mortality), and very low for PH-ATLS (healthcare utilization; Table 2). Elsewhere, quality of evidence was low for the density of surgeons (mortality) and very low for PH-ATLS and pre-hospital triage criteria (mortality).

Sensitivity analyses

The number of studies was sufficient to conduct sensitivity analysis on risk of bias for inclusive design and maturity of trauma systems. Restricting analyses to studies of high methodological quality did not lead to any significant change in pooled estimates (Online resource 6).

Discussion

The results of this systematic review suggest that overall, the configuration of trauma systems influences clinically important injury outcomes. Meta-analyses offer low-quality evidence of the effectiveness of an inclusive design and trauma system maturity and very-low-quality evidence for helicopter transport. Effect sizes were similar across trauma system components, suggesting a reduction of around 30% in the odds of mortality. There is weaker evidence that population density of surgeons is associated with a reduction in mortality. Results also suggest that the relative location of trauma centers is an important factor, but included studies were too heterogeneous to perform a meta-analysis.

Our results offer evidence that trauma systems organized to get the right patient to the appropriate acute care facility in a timely manner offer effective injury control. First, all studies in our review on trauma system inclusiveness (five studies) and the relative location of trauma centers (six studies) reported significant associations with mortality. However, these results should be interpreted in light of studies demonstrating the negative correlation between patient volume and mortality [44], suggesting that the balance between inclusiveness and sufficient volume is not yet well understood. Second, we did not find evidence that PH-ATLS, implying longer on-scene times, is associated with reduced mortality. This is in line with another systematic review [45] on the effectiveness of PH-ATLS training and the controlled before-after trial of Stiell et al. [27], which showed no survival benefit following the introduction of an PH-ATLS program and even observed higher mortality post-implantation in patients with severe traumatic brain injury. Furthermore, a comparison of the pre-hospital trauma systems in Germany and the Netherlands showed lower mortality in a system based on fast and continuous pre-hospital treatment to reduce on-scene time [26]. Third, our review provides evidence that helicopter transport within trauma systems reduces injury mortality. However, this evidence should be interpreted with caution as it was of very low quality, in line with previous reviews that have offered inconsistent evidence of the effectiveness and cost-effectiveness of rotary-wing transport [46-50]. We did not identify sufficient evidence to conclude on the effectiveness of pre-hospital triage. Studies on pre-hospital triage mostly evaluate the sensitivity and specificity of triage tools for identifying patients with major trauma, defined using measures of injury severity or need for highlevel care (e.g., surgery, ICU admission) [51]. Our metaanalysis was based on only two low-powered studies, in line with another review that identified no studies meeting their inclusion criteria [52]. We concur with the authors of this review, who conclude that there is an important evidence gap on the effectiveness of pre-hospital triage for improving clinically important injury outcomes [52].

We identified two population-based studies offering evidence that high population density of (neuro)surgeons is associated with lower mortality. Our pooled estimate was statistically significant in a fixed-effects model but not in



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the random-effects model due to heterogeneity. Previous research has suggested that surgical workforce is an important factor globally and for specific diagnoses, particularly in low- and middle-income countries [53–57]. In addition, US counties with 24-hour coverage of general, orthopedic, and neurosurgeons have been reported to have lower motor vehicle collision mortality than those without continuous coverage [58].

Globally, trauma systems or designated trauma centers have been estimated to reduce the odds of mortality by 15% when compared to non-designated hospitals or health systems with no formal trauma system in North America [10]. Similarly, regionalized trauma systems have been associated with a 16% reduction in mortality odds compared to healthcare jurisdictions with no trauma system [59]. However, our results on trauma system maturity support the hypothesis that trauma systems are not fully effective until up to 10 years after their implementation [4, 60] and suggest that these estimates of mortality reduction are probably underestimated. Finally, interventions related to benchmarking were not associated with any outcome but all evaluations were conducted in a single study.

Strengths and limitations

This systematic review represents an important step toward identifying the components of trauma systems that drive optimal patient outcomes. Our review was based on the highest methodological standards and was informed by experts involved at all levels and in all phases of the continuum of trauma care from 30 high-, middle-, and lowincome countries. Our review does have limitations which restrict our ability to draw firm conclusions. First, the methodological quality of included studies was generally poor, and the quality of evidence for interventions included in meta-analysis was low or very low. This is partly due to the fact that most studies were observational and failed to adjust for important confounders. However, as our review was based on interventions implemented on a system level, we avoided the common problem of bias by indication encountered in studies evaluating interventions applied at a patient level. Second, we did not obtain data on all clinically important outcomes. The data available on adverse events, function, disability, and quality of life were scarce and could not be used for meta-analysis. Quality of evidence evaluations was therefore restricted to mortality. Third, we could only conduct meta-analysis for six of 24 recommended trauma system components. For 11 components, no studies were identified and for seven, available

Table 2 Qua	dity of evidence evaluation fo	r trauma system compor	nents according to the GRA	ADE system [18]				
No. of studies	Quality assessment					Summary of find	ings	
	Design	Quality	Consistency	Directness	Other modifying factors	No. of patients	Effect (95% CI)	Quality of the evidence
Pre-hospital ad	lvanced trauma life support							
Mortality (3)	Observational	Very serious limitations	Important inconsistency	Some uncertainty	None	11,607	$OR = 0.78 \ (0.44; 1.39)$	Very low
LOS (2)	Observational; controlled trial	Serious limitations	Consistent	Some uncertainty	None	3549	$MD = -5.7 \ (-7.02; \ -4.38)$	Very low
Helicopter tran.	sport							
Mortality (2)	Observational	Very serious limitations	Consistent	Some uncertainty	None	3327	$OR = 0.70 \ (0.55; \ 0.88)$	Very low
Pre-hospital tri	age protocols							
Mortality (2)	RCT; Observational	Serious limitations	No important inconsistency	Some uncertainty	None	91,268	$OR = 0.88 \ (0.45; 1.70)$	Very low
Inclusiveness								
Mortality (5)	Observational	Serious limitations	Consistent	Some uncertainty	Evidence of a dose- response gradient	938,018	$OR = 0.72 \ (0.65; \ 0.80)$	Low
Density of surg.	eons							
Mortality (2)	Observational	Serious limitations	Consistent	Some uncertainty	Evidence of a dose- response gradient	6366 counties	$MD = -0.58 \ (-1.39; \ 0.22)$	Low
Maturity								
Mortality	Observational	Serious limitations	Consistent	Some uncertainty	Evidence of a dose- response gradient	162,198	$OR = 0.76 \ (0.68; \ 0.85)$	Low
CI confidence i	interval, GRADE grading of recon	nmendations assessment, de	velopment, and evaluation, Ol	R odds ratio, MD me	an difference, LOS leng	gth of stay, RCT r	andomized controlled trial	

data did not allow meta-analysis. Fourth, we cannot make recommendations according to GRADE criteria as they require data to evaluate trade-offs between benefits and harms, net benefits and costs [18]. Fifth, very little evidence was generated for low- or middle countries. Information on trauma system component effectiveness is even more crucial in such resource-constrained environments, and many of these countries are in the process of implementing trauma systems [7]. Finally, trauma systems are complex interventions, involving interplay between components of care. As such, 13 out of 20 studies evaluated multiple specified or non-specified components (e.g., system maturity) for which it was not possible to isolate the effect of individual components. Even for evaluations of single interventions, changes in outcome may be due to a connected facet of system resourcing (e.g., helicopter service may be accompanied by better pre-hospital triage or earlier physician intervention). Furthermore, in addition to system-level structures, significant intersystem variation in trauma system outcomes may be explained by injury prevention policies and/or processes of care.

Conclusions

Injury care is a perfect example of decision-making in conditions of uncertainty and ambiguity, underlying the need for standardized practice guidelines and protocols based on the best available evidence. This review represents a step toward improving our understanding of which components of trauma system structure favor optimal injury outcomes to help policy-makers make informed decisions as to where resources should be focused. Results offer evidence that components focused on getting the right patients to the appropriate facility rapidly are associated with reduced injury mortality and that trauma systems are not fully effective until several years after their implementation. More research is needed on the effectiveness of other recommended components of trauma systems and their impact on non-fatal outcomes using both qualitative and quantitative study designs. Future research should also aim to improve our understanding of the interplay between different components of trauma systems using complex intervention evaluation methodology and care pathway analysis.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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