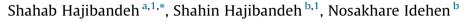
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# Injury

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# Meta-analysis of the effect of tertiary survey on missed injury rate in trauma patients



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#### ARTICLE INFO ABSTRACT Article history Background: Missed injuries are considered as an important issue in trauma patients and can lead to Accepted 22 September 2015 significant morbidity and even mortality. It has been shown that the standard primary and secondary surveys, recommended by the Advanced Trauma Life Support (ATLS) guidelines, are associated with Keywords: missed injuries. It has been suggested that tertiary survey can minimise the number and effect of missed Trauma injuries. The present paper aimed to identify comparative evidence about the effect of tertiary survey on Tertiary survey missed injury rate in trauma patients. Missed injury Methods: In accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement standards, we performed a systematic review. Electronic databases MEDLINE. EMBASE, CINAHL and the Cochrane Central Register of Controlled Trials (CENTRAL) were searched to identify randomised and non-randomised studies evaluating effect of tertiary survey on missed injury rate in trauma patients. The Newcastle-Ottawa scale was used to assess the methodological quality and risk of bias of the selected studies. Random-effects models were applied to calculate pooled outcome data. Results: Four prospective and three retrospective cohort studies, enrolling a total of 12,581 trauma patients, were selected for analysis. Pooled odds ratio (OR) analysis of 5727 patients showed that detection of missed injuries was better in trauma patients who had tertiary survey compared to patients who did not have tertiary survey [OR = 2.65, (95% CI:1.40–5.01), P = 0.003]. A moderate level of heterogeneity among the studies existed ( $l^2 = 68\%$ , P = 0.008). Also, analysis of 6.854 patients showed that fewer injuries were missed in trauma patients who had tertiary survey compared to patients who did not have tertiary survey [OR = 0.63, (95% CI: 0.44-0.90), P = 0.01]. *Conclusions:* The best available evidence demonstrates a constant trend in favour of tertiary survey in terms of missed injury reduction, and supports its use in management of trauma patients. Further studies are required to clarify the most cost-effective and systematic way of addressing missed injuries in the first 24 h. We recommend use of "missed injury detection rate" and "missed injury rate" as two different outcomes in future studies in order to address the issue of heterogeneity in definition of missed injury in the current literature.

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# Introduction

Missed injuries are considered as an important issue in trauma patients and can lead to significant morbidity and even mortality [1–5]. The reported incidence of missed injuries in literature is

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http://dx.doi.org/10.1016/j.injury.2015.09.019 0020-1383/© 2015 Elsevier Ltd. All rights reserved. variable, ranging from approximately 1% to 40% [6]. Great complexity of trauma management, together with factors such as altered level of consciousness (due to central nervous system injury, intoxication, or sedation), a distracting injury, or need for emergency surgery, can lead to undetected injuries [7].

According to the Advanced Trauma Life Support (ATLS) guidelines, the primary survey is designed to recognise and treat immediate life-threatening injuries, and the secondary survey, which is a head-to-toe examination, is designed to diagnose all other important injuries [8]. It has been shown that the standard primary and secondary surveys are associated with missed injuries [2,4,5,9–16].







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Tertiary survey (TS) refers to a comprehensive general physical re-examination and review of all investigations, including diagnostic imaging and blood results, within 24 h and again when the patient is conscious, cooperative and mobilised [17]. Since the advent of tertiary survey in 1990 [10] different authors have assessed tertiary survey in trauma patients. It has been suggested that tertiary survey can minimise the number and effect of missed injuries [7]. A systematic review of the literature showed that tertiary survey can detect up to 43% of injuries missed by primary and secondary surveys [18]. Ten studies were included in this review, of which eight studies lacked control groups. New studies have been published since this review which makes a new review worthwhile and may allow meta-analysis of outcomes for evidence synthesis.

The present paper is a systematic review of the current literature that aimed to identify comparative evidence about the effect of tertiary survey on missed injury rate in trauma patients. A critical discussion of results was attempted to determine the strengths and limitations of available data, evaluate the quality of the available evidence and identify areas for future research.

# Methods

This systematic review was performed according to an agreed predefined protocol. We reported this systematic review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement standards.

#### Criteria for considering studies for this review

# Types of studies

Randomised controlled trials (RCTs) and observational studies that investigated tertiary trauma survey as an intervention.

#### Types of participants

Blunt or penetrating trauma patients admitted to hospital for at least 24 h.

# Types of interventions

Intervention of interest

- Tertiary survey which is defined as a comprehensive general physical re-examination and review of all investigations, including diagnostic imaging and blood results, within 24 h and again when the patient is conscious, cooperative and mobilised. Comparison
- The standard primary and secondary surveys by emergency department, intensive care unit (ICU) and surgical teams.

# Types of outcome measures

# Primary outcome

• Missed injury detection rate: injuries that are not identified by primary and secondary surveys but are diagnosed by tertiary survey.

#### Secondary outcomes

- Missed injury rate: injuries that are not identified by tertiary survey.
- Clinically significant missed injury detection rate.

- Clinically significant missed injury rate.
- Mortality.

Clinically significant injuries were defined as injuries that are associated with high morbidity and mortality, or require additional procedures and alterations of therapy.

# Search methods for identification of studies

# Electronic searches

Two review authors (SH, NI) independently searched the following electronic databases: MEDLINE, EMBASE, CINAHL and the Cochrane Central Register of Controlled Trials (CENTRAL). The last search was run on 1 June 2014. The details of the search strategy are appended in Appendix 1. We adapted the search strategy to thesaurus headings, search operators and limits in each of the above databases. In addition, the following trial databases were searched for details of ongoing and unpublished studies:

World Health Organization International Clinical Trials Registry http://apps.who.int/trialsearch/. ClinicalTrials.gov http://clinicaltrials.gov/. ISRCTN Register http://www.isrctn.com/.

# Searching other resources

We searched the bibliographic lists of relevant articles and reviews for further potentially eligible trials.

#### Data collection and analysis

# Selection of studies

Two review authors (SH, NI), independently assessed the title and abstract of articles identified from the literature searches. The full-texts of relevant reports were retrieved and those articles that met the eligibility criteria of our review were selected. We resolved any discrepancies in study selection by discussion between the review authors. A third review author (SH) was consulted in the event of disagreement.

#### Data extraction and management

We created an electronic data extraction spreadsheet in line with Cochrane's data collection form for intervention reviews. We pilot-tested the spreadsheet in randomly selected articles and adjusted it accordingly. Our data extraction spreadsheet included:

- Study-related data (first author, year of publication, country of origin of the corresponding author, journal in which the study was published, study design, study size, clinical condition of the study participants, type of intervention).
- Baseline demographic and clinical information of the included populations.
- Primary and secondary outcome data.

Two review authors (SH, NI) independently collected and recorded data in the data extraction spreadsheet and we resolved disagreements by discussion. If no agreement could be reached, a third review author (SH) was consulted.

# Assessment of risk of bias in included studies

The methodological quality and risk of bias of the included articles were assessed by two independent reviewers (SH and NI), using the Newcastle-Ottawa scale [19]. This scale uses a star system with a maximum of nine stars to evaluate a study in three domains: the selection of the study groups, the comparability of the groups, and the ascertainment of outcome of interest. We judged studies that received a score of nine stars to be of low risk of bias, studies that scored seven or eight stars to be of medium risk, and those that scored six or less to be of high risk of bias. Disagreements were resolved by discussion between the two reviewers. If no agreement could be reached, a third review author (SH) acted as an adjudicator.

#### Measures of treatment effect

The primary and secondary outcomes in this study (missed injuries and mortality) were dichotomous variables; therefore, we calculated the odds ratio (OR), which is the odds of an adverse event in the TS group compared to the non-TS group, as the summary measure. For missed injury detection rate an OR of more than one would favour the tertiary survey. For missed injury rate and mortality rate an OR of less than one would favour the tertiary survey.

# Unit of analysis

We used the individual patient as the unit of analysis in our review.

#### Assessment of heterogeneity

We assessed heterogeneity among the studies using the chisquared ( $\chi^2$ , or Chi [2]) test. We quantified inconsistency by calculating I<sup>2</sup> and interpreted it using the following guide:

• 0–25%: may represent low level of heterogeneity.

- 25–75%: may represent moderate level of heterogeneity.
- 75–100%: may represent high level of heterogeneity.

# Assessment of reporting biases

We assessed reporting bias visually by evaluating the symmetry of funnel plots and formally by using the Egger regression reporting bias.

# Data synthesis

We used Review Manager 5.3 software for data synthesis (RevMan 2014) [20]. The extracted data were entered into Review Manager by an independent reviewer (SH) and checked by a second independent reviewer (SH). We used random-effects modelling for analysis and constructed a forest plot with 95% confidence intervals (CIs).

# Sensitivity analysis

We performed additional analyses to assess the robustness of our results and to explore potential sources of heterogeneity. First, we tested the effect of removing one study at a time on the pooled OR. Second, we repeated the primary analysis using a fixed-effects model. Third, the treatment effects were examined according to study design (retrospective or prospective cohort) and type of population (adult or paediatric). We deemed an  $\alpha$  level <0.05 as statistically significant.

# Results

# Results of the search

Searches of electronic databases identified 3949 articles, of which seven studies [21–27] were eligible for this review. These included four prospective [21,23,26,27] and three retrospective [22,24,25] cohort studies. Five studies [21,23,25–27] included adult multitrauma patients, one study [22] included paediatric trauma patients and one study [24] included trauma patients

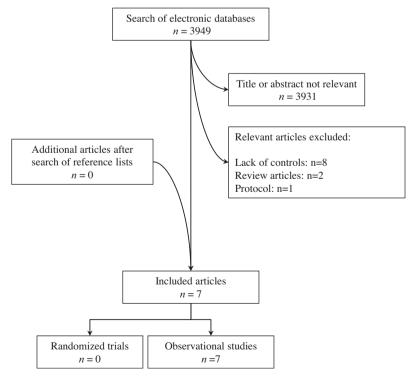


Fig. 1. Literature search flow chart.

Table 1	
Baseline characteristics of include	d studies.

	Keijzers et al. [21]	Resler et al. [22]	Giannakopoulos et al. [23]	Postma et al. [24]	Keijzers et al. [25]	Ursic et al. [26]	Biffl et al. [27]
Year	2014	2014	2012	2012	2011	2009	2003
Country	Australia	USA	Netherland	Netherland	Australia	Australia	USA
Journal	World Journal of Surgery	Journal of Trauma	Injury	Injury	World Journal of Surgery	Injury	Journal of trauma
		Nursing					
Design	Prospective cohort	Retrospective cohort	Prospective cohort	Retrospective cohort	Retrospective cohort	Prospective cohort	Prospective cohort
Population	Adult multitrauma	Pediatric	Adult	Trauma	Adult	Adult multitrauma	Adult multitrauma
	patients	trauma patients	multitrauma patients	patients involved in	multitrauma patients	patients	patients
C	407	27.40	100	plane crash	252	1007	C054
Sample size	487 No. 76	2749 NB	186	66 NB	252 No. 75	1987 Nam TC annual 42 4	6854
Age (Mean)	Non-TS group:40.4; TS group:41.1	NR	38	NR	Non-TS group: 34.8; TS group 36.7	Non-TS group 43.4; TS group: 44.4	Non-TS group: 45.3; TS group: 44.5
Sex (male)	Non-TS group:72%; TS group: 79%	NR	71.40%	NR	Non-TS group:79%; TS group:78%	Non-TS group: 69.4%; TS group: 68.9%	Non-TS group: 63%; TS group: 64%
ISS score	Non-TS group: 9; TS group: 10; (Median)	NR	6; (Median)	10; (Mean)	Non-TS group: 10.4; TS group: 23.0; (Mean)	Non-TS group: 9; TS group: 10; (Median)	Non-TS group: 10.7; TS group: 10.7; (Mean
ISS score > 15	Non-TS group: 24%; TS group: 26%	NR	NR	19.70%	Non-TS group: 18%; TS group: 73%	Non-TS group: 26.3%; TS group: 31.7%	NR
Mechanism of injury	Mainly blunt	NR	Mainly blunt (96%)	NR	Mainly blunt	Mainly blunt; (Non-TS group: 94.3%; TS group: 94.4%)	Mainly blunt (90%)
Intervention	Tertiary survey	Tertiary survey	Tertiary survey	Tertiary survey	Tertiary survey	Tertiary survey	Tertiary survey
Outcome	Missed injury	Missed injury	Missed injury	Missed	Missed injury	Missed injury detection	Missed injury rate
	detection rate; Mortality rate	detection rate	detection rate	injury detection rate	detection rate	rate; Mortality rate	
Risk of bias <sup>a</sup>	Low	Moderate	Moderate	High	Moderate	Moderate	Moderate

NR: Not reported; TS: tertiary survey; ISS: Injury Severity Score.

<sup>a</sup> Assessed by Newcastle-Ottawa scale.

involved in plane crash. The literature search flow chart and baseline characteristics of the included studies are demonstrated in Fig. 1 and Table 1, respectively.

#### Description of included studies

Keijzers 2014 [21] was a prospective cohort study that investigated effect of formalised tertiary survey intervention on missed injury rate in multitrauma patients. This study included patients aged  $\geq 16$  who were admitted for at least 24 h and met any of the following criteria: (1) injuries in two or more body regions; (2) a high impact mechanism; (3) chest or abdominal injuries; or (4) diagnosed with a fractured neck of femur (aged <65). The tertiary survey intervention in this study involved: the provision of tertiary survey forms to trauma admitting wards; repeated education for all levels of medical and nursing staff working on these wards on the use of the tertiary survey form; and a directive from the surgical departmental head for tertiary survey form completion as part of routine care within 24 h of admission [21].

Resler 2014 [22] was a retrospective cohort study that investigated effect of tertiary survey conducted by acute care trained paediatric nurse practitioners (ACPNPs), in collaboration with clinical nurse specialist and trauma medical director, on missed injury rate in paediatric trauma patients. The tertiary survey in this study involved examinations in the morning after admission, prior to mobilization, or when the child regains consciousness, in addition to daily ongoing examinations [22].

Giannakopoulos 2012 [23] was a prospective cohort study that investigated effect of tertiary survey on missed injury rate in a large cohort of adult trauma patients. The tertiary survey in this study involved a complete physical examination including revision of radiological and laboratory exams, performed since admission. It was performed by a surgical resident on the day after admission or whenever the patient regained consciousness [23].

Postma 2012 [24] was a retrospective cohort study that investigated effect of tertiary survey on missed injury rate in trauma patients involved in plane crash. The details of tertiary survey intervention were not reported in this study [24].

Keijzers 2011 [25] was a retrospective cohort study that investigated effect of tertiary survey on missed injury rate in multitrauma patients aged  $\geq 16$  who were admitted for at least 24 h and met any of the following criteria: (1) injuries in two or more body regions; (2) a high impact mechanism; (3) chest or abdominal injuries; or (4) diagnosed with a fractured neck of femur (aged <65). The tertiary survey in this study was defined as re-examination, laboratory tests, and diagnostic imaging within 24 h of admission [25].

Ursic 2009 [26] was a prospective cohort study that investigated effect of tertiary survey on missed injury rate in trauma patients who aged >15 and had one of the following criteria: obvious fracture of two or more long bones; suspected spinal cord injury; crush injury or amputation; penetrating injury to head, neck, chest, abdomen, groin, or back; abdominal distension or rigidity; facial and/or airway burns; burns  $\geq$ 20%; or suspected torso and major head injury [26].

Biffl 2003 [27] was a prospective cohort study that investigated effect of tertiary survey on missed injury rate in multitrauma patients. In this study, the tertiary survey involved a complete head-to-toe examination with additional radiographic or other investigations as necessary on all patients admitted to the trauma intensive care unit (TICU) within 24 h of admission and before discharge from the TICU [27].

Table 2

Results of methodological quality assessment by Newcastle-Ottawa scale.

Author	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts	Total score
Keijzers 2014 [21]	*	*	*	*	**	*	*	*	9
Resler 2014 [22]	*	*	*	*		*	*	*	7
Giannakopoulos 2012 [23]	*	*	*	*	*	*	*	*	8
Postma 2012 [24]		*	*	*		*	*	*	6
Keijzers 2011 [25]	*	*	*	*	*	*	*	*	8
Ursic 2009 [26]	*	*	*	*	*	*	*	*	8
Biffl 2003 [27]	*	*	*	*	*	*	*	*	8

## Risk of bias in included studies

The risk of bias was low in one study, moderate in five studies and high in one study. The results of methodological quality assessment are demonstrated in Table 2.

# **Effects of interventions**

# Missed injury detection rate

Missed injury detection rate was reported by 6 studies [21–26]. All the studies defined a missed injury as an injury that was not detected by primary and secondary surveys but was detected by tertiary survey.

There was a statistically significant difference in missed injury detection rate between TS group and non-TS group in five of the included studies. Keijzers et al. (2011) [25] reported that more missed injuries were detected in TS group compared to non-TS group (9.8% vs 1.5%, P = 0.01). This was consistent with findings of Resler et al. [22] that showed missed injury detection rate of 2.6% in TS group compared to 0.34% in non-TS group (P < 0.0001). Moreover, Giannakopoulos et al. [23] and Postma et al. [24] showed greater missed injury detection rate in TS group (30.96% and 18.60%, respectively) compared to non-TS group (23.5% and 0%, respectively). A higher missed injury detection rate in TS group was also reported by Ursic et al. [26] (6.16% vs 3.57%, P = 0.0099). Unlike the other studies, Keijzers et al. [21] (2014) did not find a significant difference in missed injury detection rate between two groups (3.8% vs 4.8%, P = 0.7773).

Pooled OR analysis of 5727 patients showed that detection of missed injuries was better in trauma patients who had tertiary survey compared to patients who did not have tertiary survey [OR = 2.65, (95% CI: 1.40–5.01), P = 0.003]. A moderate level of heterogeneity among the studies existed ( $I^2 = 68\%$ , P = 0.008), and the likelihood of publication bias was low (P = 0.22392) (Fig. 2a).

# Missed injury rate

Missed injury rate was reported by one study [27]. Biffl et al. [27] defined a missed injury as an injury that was missed by tertiary survey. This study showed that fewer injuries were missed in TS group compared to non-TS group (1.51% vs 2.37%, P = 0.0123).

Analysis of 6854 patients showed that fewer injuries were missed in trauma patients who had tertiary survey compared to patients who did not have tertiary survey [OR = 0.63, (95% CI: 0.44–0.90), P = 0.01]. The heterogeneity assessment was not applicable for this outcome as we analysed data from only one study (Fig. 2b).

# Clinically significant missed injury detection rate

None of the included studies reported clinically significant missed injury detection rate as an outcome.

# Clinically significant missed injury rate

None of the included studies reported clinically significant missed injury rate as an outcome.

The anatomical distributions of missed injuries in the included studies are shown by Table 3.

#### Mortality

Mortality rate was reported by two studies. Keijzers et al. (2014) [21] reported no significant difference in overall mortality rate between TS and non-TS groups (1.2% vs 2.6%, P = 0.4359). Consistent with this, there was no significant difference in overall mortality rate between two groups in Ursic et al. [26] (4.1% vs 5.4%, P = 0.171).

Pooled OR analysis of 2,474 patients showed no significant difference in overall mortality rate between two groups [OR = 0.71, (95% CI: 0.48–1.06), P = 0.10]. Heterogeneity across the studies was not evident ( $I^2 = 0\%$ , P = 0.52) (Fig. 2c).

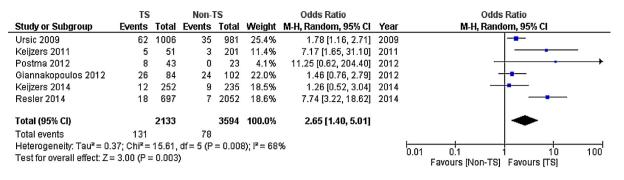
#### Sensitivity analyses

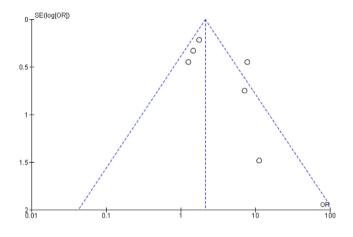
The outcomes of OR analyses remained statistically significant in favour of tertiary survey when one study at a time was excluded from the analyses. Moreover, there were no changes in outcomes when fixed-effects or random-effects models were applied. Statistical models calculating risk rather than ORs did not change the results. In addition, the direction of the effect size remained unchanged when retrospective studies and prospective studies were analysed separately (Table 4).

Our sensitivity analyses identified Resler et al. [22] and Keijzers et al. (2011) [25] as the sources of heterogeneity in the primary analysis. Removing Resler et al. [22] from the analysis reduced the  $l^2$  from 68% to 33%. When Resler et al. [22] and Keijzers et al. (2011) [25] were removed from the analysis, the  $l^2$  was reduced from 68% to 0% (Table 4 and Supplementary Fig. 1).

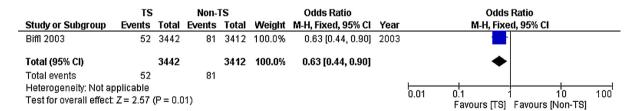
#### Discussion

We conducted a systematic review and meta-analysis of the literature to evaluate the effect of tertiary survey on missed injury rate in trauma patients. Our pooled analysis of data from four prospective and three retrospective cohort studies, enrolling a total of 12,581 trauma patients, showed that more injuries were detected and fewer injuries were missed by tertiary survey





(a)



(b)

	TS		Non-1	S		Odds Ratio			Odds	Ratio	
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	Year		M-H, Fixe	ed, 95% Cl	
Ursic 2009	41	1006	53	981	89.4%	0.74 [0.49, 1.13]	2009		-	-	
Keijzers 2014	3	252	6	235	10.6%	0.46 [0.11, 1.86]	2014		-	<u> </u>	
Total (95% CI)		1258		1216	100.0%	0.71 [0.48, 1.06]			•	-	
Total events	44		59								
Heterogeneity: Chi <sup>2</sup> = 0.42, df = 1 (P = 0.52); i <sup>2</sup> = 0%								100			
Test for overall effect:	Z=1.66	(P = 0.1	0)					0.01 0. <sup>2</sup> Fa	avours [TS]	1 10 Favours [Non-TS]	100

(C)

Fig. 2. Forest plots of comparison of (a) Missed injury detection rate (includes corresponding funnel plot), (b) Missed injury rate, and (c) Mortality rate. The solid squares denote the odds ratios (ORs), the horizontal lines represent the 95% confidence intervals (CIs), and the diamond denotes the pooled OR. M-H, Mantel Haenszel test.

compared to standard primary and secondary surveys. There was a moderate level of heterogeneity among the included studies which was noted to be mainly due to two retrospective studies according to our sensitivity analyses. The effect sizes were indicative of a benefit for the tertiary survey, and the direction of effect by the tertiary survey remained consistent throughout our sensitivity analyses.

Resler et al. [22] was a significant contributor to overall heterogeneity in our study. Unlike the other studies, this study included paediatric patients. There was a significant difference in

# Table 3

Anatomical distribution of missed injuries in included studies.

	Keijzers et al. (2014) [21]	Resler et al. [22]	Giannakopoulos et al. [23]	Postma et al. [24]	Keijzers et al. (2011) [25]	Ursic et al. [26]	Biffl et al. [27]
Head	2%	NR	4%	-	-	NR	9%
Face	5%	NR	2%	-	-	NR	-
Neck	-	NR	2%	-	-	NR	-
Thorax	2%	NR	8%	-	-	NR	2%
Abdomen	5%	NR	2%	17%	-	NR	17%
Spine	-	NR	4%	8%	-	NR	27%
Pelvis	-	NR	3%	-	-	NR	3%
Upper and lower extremities	84%	NR	75%	75%	100%	NR	39%
Others	2%	NR	-	-	-	NR	3%

NR: not reported.

#### Table 4

Results of sensitivity analysis.

Description of analysis	Number of studies	Number of patients	OR (95% CI)	P-value	$I^2$
Resler 2014 removed	5	2978	1.85 [1.17, 2.95]	0.009	33%
Keijzers 2014 removed	5	5240	3.22 [1.51, 6.85]	0.007	72%
Giannakopoulos 2012 removed	5	5541	3.28 [1.43, 7.49]	0.005	72%
Postma 2012 removed	5	5661	2.49 [1.30, 4.76]	0.006	72%
Keijzers 2011 removed	5	5475	2.32 [1.21, 4.45]	0.01	69%
Ursic 2009 removed	5	3740	3.23 [1.30, 8.07]	0.01	72%
Resler 2014 and Keijzers 2011 removed	4	2726	1.65 [1.19, 2.29]	0.003	0%
Fixed-effects model	6	5727	2.13 [1.59, 2.86]	< 0.00001	68%
Calculating Risk ratio instead of OR	6	8727	2.47 [1.34, 4.53] <sup>a</sup>	0.004	72%
Prospective studies	3	2660	1.61 [1.16, 2.24]	0.005	0%
Retrospective studies	3	3067	7.78 [3.75, 16.13]	< 0.00001	0%
Adult trauma patients	5	2978	1.85 [1.17, 2.95]	0.009	33%

OR: odds ratio; CI: confidence interval.

<sup>a</sup> Risk ratio calculated instead of OR.

the number of patients between two groups in this study. Moreover, the baseline characteristics of the included patients and their comparability were not reported in this study. Therefore, a high risk of selection bias cannot be excluded in this study. Nevertheless, removing this study from our analysis did not affect the outcome.

In Keijzers et al. (2011) [25], which was another contributor to the overall heterogeneity in our study, the average Injury severity score (ISS) was significantly different between the TS group and non-TS group. High ISS in trauma patients has been shown to be associated with increased missed injury rate. Therefore, the higher missed injury detection rate in the TS group in this study could be due to higher incidence of missed injuries in this group rather than better detection by tertiary survey.

The very low level of heterogeneity in analysis of the other five studies can be explained by homogenous patients' demographics, baseline ISS and mechanism of injury among these studies. This makes our conclusion about the effect size by tertiary survey relatively robust based on the best evidence that was available for analysis.

Missed injury has been defined heterogeneously in the literature. Lack of a consistent definition for missed injury makes it difficult and even impossible to directly compare the results of different studies especially in systematic reviews and metaanalyses, where synthesis of an outcome is important. Keijzers et al. [18] attempted to define three types of missed injuries: Type I which includes injuries missed at initial assessment; Type II which includes injuries missed at initial assessment and tertiary survey; and Type III which includes injuries missed at in spite of being well-defined and specific, this classification focuses mainly on injuries missed by each survey. However, most studies reported missed injuries as injuries that are missed by one survey and are detected by next level survey. Therefore, we believe the recommended definitions by Keijzers et al. [18] may not address the issue of heterogeneity in definition of missed injury in the current literature. We proposed two different outcome definitions for missed injury: missed injury detection rate (injuries that are not identified by primary and secondary surveys but are diagnosed in tertiary survey), and missed injury rate (injuries that are not identified by tertiary survey). These definitions allowed us to synthesis two different outcomes that can be used in future studies, in particular systematic reviews or meta-analyses.

Our findings are consistent with other authors. Keijzers et al. [18] showed that tertiary survey improved missed injury detection rate and reduced missed injury rate in trauma patients, although they did not provide any comparative evidence. There are still some outcomes that have not been addressed adequately by authors with regard to tertiary survey in trauma. These include clinically significant missed injury detection rate; clinically significant missed injury rate; and mortality.

Missed injuries may be minor and self-limiting injuries that only require conservative management. Therefore, considering the higher priorities than identifying minor injuries in management of trauma patients within the first 24 h, clinically significant missed injuries should be distinguished from minor injuries. It has been shown that approximately 15–22.3% of missed injuries are clinically significant [28]. Although our results demonstrated that tertiary survey is associated with better detection of missed injuries, the effect of tertiary survey on clinically significant missed injuries remains unknown.

Trauma patients with altered level of consciousness are more likely to have missed injuries, which may be detected when the patient gains consciousness and is able to voice complaints [7]. This highlights the need for comprehensive physical re-examination and review of all investigations again when the patient is conscious and cooperative. However, to what extent tertiary survey can affect the clinically significant missed injury rates in this group of patients is not known.

Tertiary survey has been implemented in many major trauma units. However, implementation of tertiary survey in management of trauma patients has not been formalised or mandated by international guidelines such as ATLS [8]. The decision to implement a formalised tertiary survey protocol depends on the available evidence about its clinical effectiveness and cost-effectiveness. Tertiary survey implementation requires more medical and nursing staff; moreover, it may lead to over-investigation and over-diagnosis of minor self-limiting injuries.

There are many factors that may act to prohibit high quality trials in trauma patients, and even if they are overcome and the highest quality research is performed, results may not necessarily translate into clinical practice [29]. Equipoise is a key concern and appears to be a substantial barrier to randomised trials in trauma patients [29]. Considering the fact that tertiary survey has been incorporated into trauma protocols in many trauma centres and that evidence from observational studies supports its use in trauma patients, conducting an RCT may not be ethical or practical at this stage.

The present study has some limitations. The best available evidence is from retrospective and prospective cohort studies that are inevitably subject to selection bias. Most of the included studies were of moderate methodological quality, which may bias the results in favour of either intervention in study. There were a limited number of eligible studies for this review. This did not allow us to provide adequately robust comparative evidence. The available data did not allow us to perform subgroup analyses based on parameters such as ISS. Finally, the tertiary survey protocol was not identical among all studies. This can potentially bias our results regarding the treatment effect.

# Conclusions

The best available evidence demonstrates a constant trend in favour of tertiary survey in terms of missed injury reduction, and supports its use in management of trauma patients. There is good evidence from observational studies that many injuries are missed in the first 24 h and many of these are clinically significant. The most cost-effective and systematic way of addressing this is not clear. Further studies looking at different approaches including the tertiary survey is warranted. We recommend use of "missed injury detection rate" and "missed injury rate" as two different outcomes in future studies in order to address the issue of heterogeneity in definition of missed injury in the current literature.

# Author contributions

Conception and design: SH, SH. Literature search and study selection: SH, NI, SH. Data collection: SH, NI, SH. Analysis and interpretation: SH, SH. Writing the article: SH, SH. Critical revision of the article: SH, SH, NI. Final approval of the article: SH, SH, NI. Statistical analysis: SH, SH.

# **Conflict of interest**

None declared.

#### **Ethical approval**

Not required.

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# Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.injury.2015.09. 019.

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