

## REVIEW ARTICLE

# Review article: Emergency medical services transfer of severe traumatic brain injured patients to a neuroscience centre: A systematic review

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## Abstract

Patients with severe traumatic brain injuries require urgent medical attention at a hospital. We evaluated whether transporting adult patients with a severe traumatic brain injury (TBI) to a Neuroscience Centre is associated with reduced mortality. We reviewed studies published between 2010 and 2023 on severe TBI in adults (>18 years) using Medline, CINAHL, Google Scholar and Cochrane databases. We focused on mortality rates and the impact of transferring patients to a Neuroscience Centre, delays to neurosurgery and EMS triage accuracy. This review analysed seven studies consisting of 53 365 patients. When patients were directly transported to a Neuroscience Centre, no improvement in survivability was demonstrated. Subsequently, transferring patients from a local hospital to a Neuroscience Centre was significantly associated with reduced mortality in one study (adjusted odds ratio: 0.79, 95% confidence interval: 0.64–0.96), and 24-h (relative risk [RR]: 0.31, 0.11–0.83) and 30-day (RR: 0.66, 0.46–0.96) mortality in another. Patients directly transported to a Neuroscience Centre were more unwell than those taken to a local hospital. Subsequent transfers

increased time to CT scanning and neurosurgery in several studies, although these were not statistically significant. Additionally, EMS could accurately triage. None of the included studies demonstrated statistically significant findings indicating that direct transportation to a Neuroscience Centre increased survivability for patients with severe traumatic brain injuries. Subsequent transfers from a non-Neuroscience Centre to a Neuroscience Centre reduced mortality rates at 24 h and 30 days. Further research is required to understand the differences between direct transport and subsequent transfers to Neuroscience Centres.

**Key words:** EMS, Mortality, Neuroscience Centre, TBI, Transfer.

## Introduction

Severe traumatic brain injury (TBI) is a leading cause of morbidity and mortality worldwide, with more than 2.2 million occurring in the United States alone in 2020.<sup>1</sup> TBIs occur in all age groups and areas of the world, making TBI a significant global public health concern.<sup>2</sup> In addition, severe TBI presents a huge cost to public health. In a single year,

## Key findings

- Subsequently transferring severe TBI patients from a local hospital to a Neuroscience Centre was found to significantly reduce mortality rates (aOR: 0.79, 95% CI: 0.64–0.96).
- Subsequently transferring patients with severe TBI reduced 24-h (RR: 0.31, 0.11–0.83) and 30-day (RR: 0.66, 0.46–0.96) mortality.

it is estimated that the associated costs exceeded \$60 billion in the US<sup>1</sup> and \$37 billion across Europe.<sup>1,3</sup>

Internationally, severe TBIs are typically defined as any patient with an anatomically-based injury score (AIS), to the head of 3 or more (AIS head  $\geq 3$ ).<sup>3</sup> As a result of limited equipment available to EMS, severe TBI in the prehospital setting is instead defined as any patient with a new traumatic head injury and a GCS  $\leq 8$ .<sup>4–6</sup>

EMS play a crucial role in the treatment of patients with severe TBI. Once they have been thoroughly triaged and assessed, EMS must begin treating the patient as early as possible. In particular, they must focus on preventing secondary brain insults, namely, hypoxia, hyper/hypocarbica and hypotension.<sup>7</sup> Avoiding these is pertinent to reducing patient mortality and improving their Glasgow Outcome Score (GOS).<sup>7</sup> As EMS are typically the first medical professionals to interact with the patient, they are expected to start managing these secondary insults, most of which should be provided while simultaneously transporting. In addition, following destination policies can reduce

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the time to a CT scan, surgery and definitive care.<sup>8</sup>

It is strongly suggested that severe TBI patients be urgently transported to specialised hospitals.<sup>9,10</sup> Depending on the country, these can be called Level 1, Level 2 and/or Higher-Level Trauma Centres. These hospitals with specialised services capable of managing severe TBI patients are commonly termed Neuroscience Centres.

Research indicates that individuals with severe TBI should receive treatment at a Neuroscience Centre, as they can benefit from specialised care.<sup>1,11</sup> However, this is not always possible as EMS personnel may face challenges such as harsh weather conditions, geographical barriers, or insufficient training that may hinder their ability to treat secondary brain injuries effectively. In such situations, it may be necessary to receive treatment at a nearby hospital and then be subsequently transferred to a Neuroscience Centre for further care.<sup>11</sup> The impact of these decisions has not been analysed, so we performed a systematic review to understand the effect of transporting adult ( $\geq 18$  years) severe TBI patients to a Neuroscience Centre.

## Methodology

### Protocol and registration

This systematic review followed the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) guidelines.<sup>12</sup> The review was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on 27 April 2023 (CRD42023424247).

### Information sources and search strategy

A systematic literature search was conducted on 25 January 2023. All searches were performed by the lead author using the terms listed below and the following parameters: articles published between 2010 and 2023, in English, with a full-text version available. Medline, CINAHL and Cochrane databases were searched using the following search terms: *Hospital or trauma cent\* or neuroscience or neurosurgical*

*or emergency department AND EMS or prehospital or emergency medical services or paramedic or medical service or ambulance AND Traumatic brain injury or head injury or brain injury or TBI or traumatic intracranial haemorrhage AND Transport or transfer.* Google Scholar was searched at the same time using the following search terms: *emergency department, hospital, trauma centre, neuroscience, neurosurgical, traumatic brain injury, TBI, transport, transfer, indirect, direct, mortality, ambulance, EMS, paramedic, emergency medical service and prehospital.* Once the final review articles had been selected, a citation search of their reference lists was completed.

### Eligibility criteria

Clinical trials and observational studies comparing outcomes of severe TBI patients who were either transported to a Neuroscience Centre or to a hospital without neurosurgical capabilities were included. Studies were excluded if: the full text was unavailable, they were not in English, they reported only on patients  $< 18$  years old, or they did not report on mortality as an outcome. Severe TBI was defined as any patient with a prehospital or in-hospital GCS of  $\leq 8$  in combination with a new head injury.<sup>13</sup>

### Study selection

All publications were screened for eligibility by reviewing the title and abstract. This was independently completed by three investigators (BJ, VT and GH) with Rayyan software.<sup>14</sup> All included and undecided studies were reviewed by the four investigators (BJ, VT, GH and BD) until a unanimous decision was made.

### Data extraction

Using a standard data collection table, the lead author extracted all data. For accuracy, a second author (VT), checked all input data. Disagreements were resolved primarily through discussion between the reviewers, if unsuccessful, a third reviewer (BD or GH) resolved the dispute. Included studies had the following information recorded: (i) study characteristics: authors, study

location, year of study, the study design, the study period, sample size, the inclusion, and exclusion criteria; (ii) patient characteristics: age and gender; (iii) outcome: mortality rates of those treated at a Neuroscience Centre (or similar) and those treated at a hospital without neurosurgical capabilities; and (iv) study limitations and conclusions, shown in Tables 1 and 2.

### Assessment of study quality and risk of bias

Bias assessment was completed using a standardised critical appraisal instrument from the JBI Manual for evidence synthesis (checklist for Randomised Controlled Trials and Checklist for Quasi-Experimental Studies).<sup>15</sup> All eligible studies were assessed for bias by two authors (BJ and VT). Studies had a low risk for bias if all checklist criteria were met, had moderate risk of bias if they failed a single criterion and high risk for bias if they failed multiple criteria. These results are found in Tables 3 and 4.

### Data synthesis and statistical analysis

The results are reported in narrative format and in a table. All included studies underwent data extraction and synthesis. The risk of bias was considered in the interpretation of the review findings.

## Results

### Study selection

In total, 602 articles were retrieved, this was made up of 588 articles from four databases and 14 articles from citation lists. The 588 articles were reduced by 184 to 404 articles after applying the automation tools. During the screening process, 54 duplicates were removed and a further 297 did not meet the eligibility criteria, leaving 53 for full-text assessment. After reviewing the full-text versions of the remaining 53 articles, 7 articles met all the criteria and were included in the systematic review (Fig. 1). All 14 articles found through citation searching failed to meet the inclusion criteria.

TABLE 1. Study and patient characteristics

First author (Year)	Location	Design	Time period	Total sample size	Inclusion criteria	Exclusion criteria	Patient demographic	
							Intervention	Control
Grevfors <i>et al.</i> (2021)	Sweden	Retrospective observational cohort study	6 years	457	>14 years, confirmed TBI, prehospital charts available and treated at the neurosurgery department at KUH.	Admitted >6 h post-injury, admitted to KUH >24 h post-admission to any hospital or admission from another country.	Direct-to-TC: <i>n</i> = 320 (70%); Median age, 47; Male, 231 (72%)	Transfer-to-TC: <i>n</i> = 137 (30%); Median age, 56; Male, 103 (75%)
Hsiao <i>et al.</i> (2010)	Taiwan	Retrospective observational	6 years	254	≥18 years old, severe TBI (GCS 3–8).	Death prior to admission, GCS >8 after drugs or alcohol excluded, multiple traumas, penetrating brain injury.	Direct-to-TC: <i>n</i> = 87; Median age, 55; Male, 64 (74%)	Transfer-to-TC: <i>n</i> = 167; Median age, 48; Male, 115 (69%)
Joosse <i>et al.</i> (2011)	Netherlands	Retrospective observational	4 years	80	Severe TBI (AIS Head ≥3) and neurosurgical intervention within 6 h of level 1 TC admission.	Admitted for observation and subsequently deteriorated leading to surgery.	Direct-to-TC: <i>n</i> = 56; Male, 40 (71%); Median age, 46	Transfer to TC: <i>n</i> = 24; Male, 16 (67%); Median age, 53
Lecky <i>et al.</i> (2017)	England	RCT feasibility study	19 months	293	Significant TBI (GCS <13/14), sign of head injury, stable ABC.	<16 years, obvious life-threatening airway, breathing or circulatory problem, more than 1 h from an NSC, transported by another service.	Direct-to-NSC: <i>n</i> = 169; Median age, 44.6; Male, 118 (69.8%)	NSAH with selective transfer to NSC: <i>n</i> = 124; Median age, 48.8; Male, 82 (66.1%)
Nishijima <i>et al.</i> (2020)	USA	Prospective observational	1 year	350	≥55 years old with a TBI (closed head injury with LOC and/or amnesia, GCS ≤ 14) or traumatic ICH on CT.	Penetrating head trauma, prisoners, pregnant women, no reliable follow-up, no consent.	TC (level 1 or 2): <i>n</i> = 257 (73%)	Non-TC: <i>n</i> = 93 (27%) Patient characteristics not further defined

(Continues)

TABLE 1. Continued

First author (Year)	Location	Design	Time period	Total sample size	Inclusion criteria	Exclusion criteria	Patient demographic	
							Intervention	Control
Sugarman <i>et al.</i> (2012)	USA	Retrospective trauma registry review	2 years	51 300	≥18 years old, severe TBI (AIS Head ≥3) treated at a level 1 or 2 trauma centre.	ISS < 16, GCS motor score of 6, aged ≤17	Direct-to-TC: <i>n</i> = 31 195; Mean age, 50.4; Male, 22 752 (72.9%)	Transfer to TC: <i>n</i> = 20 105; Mean age, 59.7; Male, 13 295 (66.1)
Waalwijk <i>et al.</i> (2023)	Netherlands	Prospective observational	2 years	631	Transported to a trauma centre.	Non-trauma patients, ISS < 16, directly transferred to a higher-level TC, burns patients	TG: <i>n</i> = 233; Median age, 57.9; Female, 109 (33.9%)	NTG: <i>n</i> = 398; Median age, 69.5 Female, 327 (44%)

AIS, abbreviated injury score; GOS-E, Glasgow outcome scale; ICH, Intracranial haemorrhage; KUH, Karolinska University Hospital; LOC, loss of consciousness; MTC, major trauma centre; NSAH, non-specialist acute hospital; NTG, non-transfer group; SNC, specialist neuroscience centre; TBI, traumatic brain injury; TC, trauma centre; TG, transfer group; TU, trauma unit.

### Study characteristics

The seven reviewed studies had a combined total of 53 365 patients (Table 1). Two were undertaken in the US,<sup>1,11</sup> two in the Netherlands,<sup>8,16</sup> one in England,<sup>17</sup> one in Sweden<sup>18</sup> and the last in Taiwan.<sup>19</sup> Two were prospective observational studies, four were retrospective observational studies and the last was a feasibility study for a randomised control trial (RCT). The earliest was completed in 2010,<sup>19</sup> the most recent in 2023.<sup>16</sup> Study periods ranged from 1 to 6 years. They each assessed mortality as an outcome, but non-measured mortality over a consistent period (Table 2). Mortality ranged from death at any time during the study period to mortality within 6 months. This was recorded within both the control and intervention groups of all studies except for one, which lacked a control group.<sup>1</sup>

### Patient characteristics

As shown in Table 1, most studies looked at adult patients (≥18 years), with one study looking at older adults (≥65 years)<sup>1</sup> and another study

including patients under 16.<sup>16</sup> The study including paediatric cases enrolled 1065 patients and did not separate the outcomes between adults (≥18, *n* = 1037) from paediatrics (<18; *n* = 28).<sup>16</sup> As the paediatric population represented less than 3% of all patients, the paper was included. Across the studies, the median age ranged from 48 to 69.5 years. Sex was recorded in all studies, with males overrepresented in each study (56–75%). Injury severity score (ISS) was inconsistently reported among the reviewed studies. Four studies found higher ISS in patients transported directly to Neuroscience Centres compared to non-Neuroscience Centres.<sup>8,11,16,18</sup> Two studies found the control and intervention groups to have a similar ISS and/or GCS,<sup>17,19</sup> the last had no comparator group.<sup>1</sup>

### Mortality

In four studies, increased rates of mortality were observed when severe TBI patients were directly taken to a Neuroscience Centre, but this did not reach statistical significance.<sup>11,17–19</sup> Conversely, one study

reported a non-significant reduction in mortality in patients directly transported to a Neuroscience Centre with both 30-day survival and long-term GOS improving.<sup>8</sup> Although seeming clinically relevant, with a low sample size (*n* = 80), the results were not statistically significant.<sup>8</sup> One study did not detail the results of patients taken to a non-Neuroscience Centre; nor did they report any benefit to transporting older adult patients directly to a Neuroscience Centre.<sup>1</sup> A further study only reported on the outcomes of patients taken directly to a non-Neuroscience Centre and then subsequently transferred on if they had been undertriaged.<sup>16</sup> Undertriage was defined as any patient with severe injuries taken to a non-Neuroscience Centre.<sup>16</sup> It was reported that severe TBI patients subsequently transferred to a Neuroscience Centre had improved outcomes, with a relative risk (RR) of 24-h mortality of 0.31 (95% confidence interval [CI]: 0.11–0.83) and 0.66 (95% CI: 0.46–0.96) for 30-day mortality.<sup>16</sup>

Similar results were found in another study (adjusted odds ratio [aOR]: 0.79, 95% CI: 0.64–0.96).<sup>11</sup>

TABLE 2. Outcome measures

First author (Year)	Mortality		Author conclusion
	Intervention (transport to Neuroscience Centre)	Comparator (transport to a non-Neuroscience Centre)	
Grevfors <i>et al.</i> (2021)	30-day mortality, $n = 37$ (12%)	30-day mortality, 13 (9.5%)	Transferred patients had significant delays to CT and neurosurgery when compared to direct-to-TC patients, though this had an insignificant impact on mortality and long-term functional outcomes. For most patients, EMS were able to triage TBI patients and transport them to the correct hospital.
Hsiao <i>et al.</i> (2010)	Mortality (unspecified), $n = 55$ (63.2%)	Mortality (unspecified), $n = 86$ (51.5%) OR (95% CI): 0.51 (0.24–1.10)	Transfer was not significantly correlated with mortality. High mortality rates amongst both groups were noted in the region of study. Basic EMS scope of practice in this area was hypothesised as a possible cause of high mortality as hypotension, hypertension and hyperglycaemia were found to have a statistical difference in mortality. No time frame was given for mortality; patients either died at some time while in hospital or were discharged.
Joosse <i>et al.</i> (2011)	30-day mortality, $n = 15$ (27%)	30-day mortality, $n = 8$ (33%)	No significant difference in mortality or long-term outcomes between the two groups. Secondary transferred patients received neurosurgery roughly 2.5 h later than the directly transferred group. 14/24 patients had neurological deterioration during the transfer.
Lecky <i>et al.</i> (2017)	30-day mortality, $n = 159$ (9.4%)	30-day mortality $n = 113$ (8.8%)	The impact of directly transporting or transferring TBI patients to an SNC has an insignificant impact on their mortality; these results were not statistically significant. False positives for TBI were 4:1. 12/25 deaths were from TBI, remainder were from medical conditions/elderly frailty. Poor protocol adherence (62%) and low numbers of enrolled patients with TBI prevented the full trial from commencing.
Nishijima <i>et al.</i> (2020)	3-month mortality, $n = 51$ (19.5%) 6-month mortality, $n = 55$ (21.2%)	Not reported	This study had no comparator group. Patients with TBI or traumatic ICH had no improved functional outcomes with initial triage to a TC. No difference in GOS-E at 6 months in those transported to a level 1 <i>versus</i> level 2 TC. Most deaths were due to non-TBI factors.
Sugarman <i>et al.</i> (2012)	Mortality (in-hospital), $n = 10$ 125 (32.5%)	Mortality (in-hospital), $n = 5546$ (27.6%) aOR (95% CI): 0.79 (0.64–0.96)*	Significantly reduced likelihood of mortality in transferred patients. 37% of all severe TBI patients were not initially seen at a Level 1 TC. Transferred patients arrived at the level 1 or 2 TC almost 7 h later than directly transferred patients. After removing deaths within 24 h, transferred patients had reduced mortality rates.

(Continues)

TABLE 2. Continued

First author (Year)	Mortality		Author conclusion
	Intervention (transport to Neuroscience Centre)	Comparator (transport to a non-Neuroscience Centre)	
Waalwijk <i>et al.</i> (2023)	Relative risk (95% CI) 24-h mortality, 0.31 (0.11–0.83)† 30-day mortality, 0.66 (0.46–0.96)†	24-h mortality, $n = 27$ (all deaths, not isolated to TBI) 30-day mortality, $n = 115$ (all deaths, not isolated to TBI)	A significant reduction in the likelihood of mortality was observed in transferred patients. Inter-hospital transfer to a higher-level hospital only benefited patients with TBI. Inter-hospital transfer of severely injured patients was safe and could improve survivability.

\* $P < 0.05$ . †Twenty-four mortality (including death in ED). 95% CI, 95% confidence interval; AIS, abbreviated injury score; aOR, adjusted odds ratio; GOS-E, Glasgow outcome scale; ICH, intracranial haemorrhage; LOC, loss of consciousness; MTC, major trauma centre; NSAH, non-specialist acute hospital; NTG, non-transfer group; OR, odds ratio; SNC, specialist neuroscience centre; TBI, traumatic brain injury; TC, trauma centre; TG, transfer group; TU, trauma unit.

TABLE 3. JBI critical appraisal checklist for analytical cross-sectional studies

Author	Outcome	Question no. Time to mortality	Question								Risk of bias		
			1	2	3	4	5	6	7	8			
Grevfors <i>et al.</i>	Mortality	In-hospital	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low	
Hsiao <i>et al.</i>	Mortality	In-hospital	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low	
Joosse <i>et al.</i>	Mortality	30 days	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	High	
Nishijima <i>et al.</i>	Mortality	3 months	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Moderate	
Sugarman <i>et al.</i>	Mortality	6 months											
		<6 h	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low	
		6–24 h											
		1–14 days											
Waalwijk <i>et al.</i>	Mortality	≥14 days											
		24 h	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Low
		30 days											

Question:  
 1: Were the criteria for inclusion in the sample clearly defined?  
 2: Were the study subjects and the setting described in detail?  
 3: Were the study subjects and the setting described in detail?  
 4: Were objective, standard criteria used for measurement of the condition?  
 5: Were confounding factors identified?  
 6: Were strategies to deal with confounding factors stated?  
 7: Were the outcomes measured in a valid and reliable way?  
 8: Was appropriate statistical analysis used?

Reviewer:  
 1: Ben Jones  
 2: Verity Todd  
 Rating system:  
 All 'Yes' = Low risk of bias  
 A single 'No' = Moderate risk of bias  
 Greater than one 'No' = High risk of bias

### Time to definitive care

Patients requiring subsequent transfer to a Neuroscience Centre often

experienced prolonged delays of up to 7 h to receiving definitive care when compared to those directly

transported to the Neuroscience Centre (485.03 min *vs* 83.71 min).<sup>11</sup> Similar results were found in four other

TABLE 4. JBI critical appraisal checklist for assessment for risk of bias for randomised controlled trials

Domain	1	2	3	4	5	6	7	8	9	10	11	12	13	Risk of bias
Question no.	1	2	3	4	5	6	7	8	9	10	11	12	13	
Author:	Outcome:	Time to mortality	Yes	No	Yes	No	Yes	Yes	Unclear	No	Yes	N/A	N/A	High
Lecky <i>et al.</i>	Mortality: 30 days													
Question:														
	1: Was true randomisation used for the assignment of participants to treatment groups?													
	2: Was allocation to groups concealed?													
	3: Were treatment groups similar at the baseline?													
	4: Were participants blind to treatment assignment?													
	5: Were those delivering the treatment blind to treatment assignment?													
	6: Were treatment groups treated identically other than the intervention of interest?													
	7: Were outcome assessors blind to treatment assignment?													
	8: Were outcomes measured in the same way for treatment groups?													
	9: Were outcomes measured in a reliable way?													
	10: Was follow-up complete and if not, were differences between groups in terms of their follow-up adequately described and analysed?													
	11: Were participants analysed in the groups to which they were randomised?													
	12: Was appropriate statistical analysis used?													
	13: Was the trial design appropriate and were any deviations from the standard RCT design (individual randomisation, parallel groups) accounted for in the conduct and analysis of the trial?													

Reviewers:

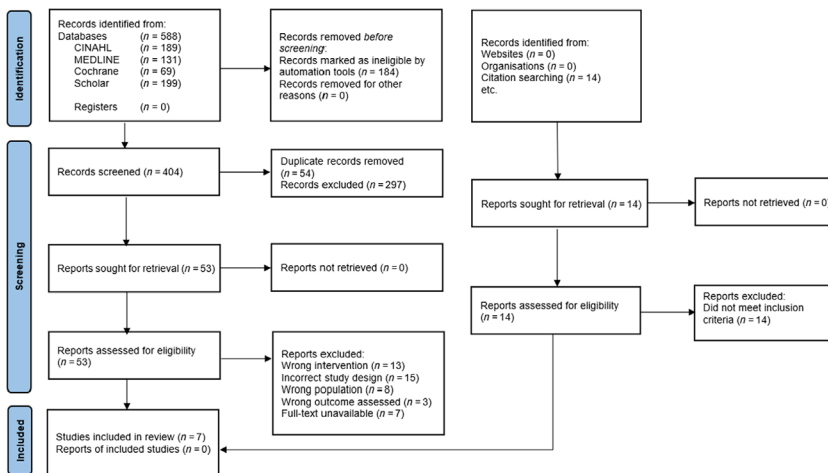
Ben Jones, Verity Todd

Risk of bias rating system:

All 'Yes' = Low risk of bias

A single 'No' = Moderate risk of bias

Greater than one 'No' = High risk of bias



**Figure 1.** PRISMA flow diagram. PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analysis.

studies, with subsequent transfer delaying time to definitive care by between 153 min and 4 h.<sup>8,16,18,19</sup> One study did not report on delays<sup>1</sup> and the last found the time difference between the control and intervention groups receiving definitive care was minimal.<sup>17</sup>

### Impact of subsequent transfers

With many studies reporting prolonged delays from subsequent transfers to a Neuroscience Centre, several looked at the impact this had on patients. In one, subsequently transferred patients had lower GOS scores, indicating worse long-term outcomes, as well as increased mortality rates when compared to the direct-to-Neuroscience Centre group.<sup>8</sup> Poorer outcomes were attributed to the neurosurgical intervention delay, but these were not statistically significant because of the small sample size ( $n = 80$ ).<sup>8</sup> Subsequent transfers also increased the costs associated with managing each patient, with additional EMS costs and diagnostic tests at the receiving hospital accounting for much of this.<sup>8</sup> Another study compared the percentage of patients with a GCS <8 who were either taken directly to a Neuroscience Centre or subsequently transferred to one. Their GCS scores were measured at both the accident site and when they arrived at the Neuroscience Centre.

In the group directly transferred to the Neuroscience Centre 52% of patients had a prehospital GCS score <8 at the site of injury which increased to 54% upon arriving at the Neuroscience Centre. On the other hand, only 11% of patients who required subsequent transfer had a prehospital GCS score <8 at the site of injury and this increased to 33% upon arrival at the Neuroscience Centre.<sup>18</sup>

## Discussion

### Summary of evidence

This systematic literature review was undertaken to identify if an association existed between adult severe TBI patients who were transferred to a Neuroscience Centre and mortality. After analysing the seven included studies, direct transport to a Neuroscience Centre did not reduce mortality, but some patients did benefit from being subsequently transferred to a Neuroscience Centre.

### Strengths and limitations

This systematic review was conducted in accordance with the PRISMA guidelines.<sup>12</sup> All included studies were assessed for methodological bias using the JBI critical appraisal checklist.<sup>15</sup> Four observational studies<sup>11,16,18,19</sup> were considered to have a low risk of bias and one observational study<sup>1</sup> was

considered to have a moderate risk of bias. The last two studies were considered to have a high risk of bias,<sup>8,17</sup> one of which was the feasibility study (Tables 3 and 4).

The reviewed studies typically focused on mortality as their primary outcome, but the methods of measuring this varied greatly, ranging from <6 h post-injury to <6-month post injury. As the data sets were unavailable, we could not analyse mortality consistently between studies. Some studies showed higher mortality rates; however, these studies often measured mortality over a longer time period. For example, one study measured mortality at any stage during the patients' hospital admission and had mortality rates of 32.5%,<sup>11</sup> whereas others measured mortality over 30 days and had rates as low as 12%.<sup>18</sup> Several studies note much of the mortality was attributed to illness, existing medical conditions, elderly frailty or non-head injuries,<sup>1,17</sup> with some finding more than 50% of patients died from non-TBI related illness or injury.<sup>1</sup> This potentially clouded the impact that transport to a Neuroscience Centre had. We recommend establishing a standard time frame for recording mortality to improve study comparability. This should be long enough to capture all individuals dying from severe TBI, but short enough to minimise the risk of patients surviving the injury yet dying from pre-existing conditions.

Several limitations were identified across the seven studies. Small sample sizes were commonly described, with only a single study having more than 1000 patients, causing some studies to be underpowered.<sup>8,17,19</sup> A lack of consistency in the participants was also observed. Some studies looked at the general population, whereas another looked at the geriatric population only. In addition, those transported directly to a Neuroscience Centre typically had higher ISS scores.<sup>8</sup> This heterogeneity made drawing conclusions challenging. A further limitation was the number of observational studies, which increased the possibility of unmeasured confounders being missed during analyses.<sup>1,8,16,19</sup> The only interventional study reviewed was a

feasibility study for a larger planned RCT. As the present study lacked sufficient power through low recruitment, poor adherence to the protocol, and loss of follow up, the larger trial was never completed.<sup>17</sup> A well-constructed RCT would be pivotal to understanding what, if any, differences exist between severe TBI patients that are directly transported *versus* subsequently transferred to a Neuroscience Centre. A final limitation is the difference in EMS scopes of practice. One service was restricted in the interventions EMS can perform, rarely performing airway interventions or providing intravenous fluid to correct hypotension, a common adverse finding in the mortality group.<sup>19</sup>

### Clinical implications

No studies in this literature review demonstrated a reduction in mortality rates when patients were transported directly to a Neuroscience Centre, even after removing patients who died early in the ED or in the ambulance.<sup>11,19</sup> However, some confounders were listed as potential causes for this. The most likely confounder is heterogeneity between the intervention and control groups, with those transported directly to the Neuroscience Centre often having a higher ISS and a lower GCS compared to those who were subsequently transferred, potentially negatively skewing the mortality in the cohort directly transported to a Neuroscience Centre.<sup>8,18</sup> Although this created heterogeneity, it also demonstrates that EMS can recognise severe TBI and are able to follow trauma policies.

Among subsequently transferred patients, two studies found that the transfer was associated with reduced mortality.<sup>11,16</sup> The need for transfer was not because of EMS mistriage but was instead because of subsequent deterioration once at the non-Neuroscience Centre.<sup>11</sup> Interestingly, one study found only 30.2% of deteriorating patients were subsequently transferred to a Neuroscience Centre, indicating not all severe TBI patients require management at a Neuroscience Centre.<sup>16</sup> This finding was comparable to another study, which,

despite delays of several hours, found a wait-and-see approach to neurosurgery was safe and did not prove detrimental to severe TBI patients.<sup>18</sup> However, it is necessary to conduct more research to determine which patients, and which specific types of severe TBI, would benefit from either direct transfer to a Neuroscience Centre or early transfer to one.

Accurate triage is crucial to ensure severe TBI patients are transported to the correct hospital. This also helps to prevent Neuroscience Centres from being overwhelmed with unnecessary patients. One study reported a false positive over-triage ratio of 4:1 for severe TBI and 13:1 for neurosurgery.<sup>17</sup> It is important to note that the high rate of over-triage observed in the study can be attributed to the methodology used, as severe TBI was defined as anyone with a new head injury and a GCS <14. This definition of severe TBI is not commonly used in prehospital settings globally. However, the authors of the study chose this definition to capture all severe TBI, as some head-injured patients with a high GCS deteriorate once in hospital.

Delays caused by subsequent transfers were reported to negatively impact patient care, particularly in patients requiring urgent neurosurgical intervention.<sup>8</sup> The direct-to-Neuroscience Centre group had a reduced time to surgery when compared to the subsequently transferred group (151 min *vs* 304 min) ( $P < 0.001$ ).<sup>8</sup> Additionally, the subsequent transfer group often deteriorated during transport, leading to additional CT scanning, further delaying surgical intervention. However, despite these deteriorations, the GOS scores between the transfer and direct groups did not meet statistical significance ( $P = 0.866$ ).<sup>8</sup>

### Conclusion

There were no studies included in this review with statistically significant findings indicating that direct transportation to a Neuroscience Centre increased survivability for patients with a severe TBI. Subsequently, transferring patients from a local hospital to a Neuroscience Centre was found to significantly reduce mortality

rates based on a study that included over 90% of all reviewed patients (aOR: 0.79, 95% CI: 0.64–0.96).<sup>11</sup> It also reduced 24-h (RR: 0.31, 0.11–0.83) and 30-day (RR: 0.66, 0.46–0.96) mortality in another.<sup>16</sup> There appears to be a subset of patients that benefit from urgent neurosurgical intervention and in this group, direct transport to a Neuroscience Centre does improve rates of mortality, although the exact population was not identifiable.<sup>8</sup> Critically unwell patients can be accurately recognised and transported directly to a Neuroscience Centre by EMS staff. A skewing towards transporting more severely injured patients to Neuroscience Centres exists, and this may mask any potential survival benefit of direct transportation to a Neuroscience Centre. Further research is needed to discern potential differences in direct transport *versus* subsequent transfer to a Neuroscience Centre for patients with severe TBI.

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### Data availability statement

The data that supports the findings of this study are available in the Supporting Information of this article.

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