National Clinical Guideline Centre

DRAFT FOR CONSULTATION

Trauma: Service delivery

Major trauma services: service delivery for major trauma

Service delivery guidance

Appendices K – P

August 2015

Draft for consultation

Commissioned by the National Institute for Health and Care Excellence

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Disclaimer
Those responsible and accountable for commissioning trauma services should take this guideline fully into account. However, this guideline does not override the need for, and importance of, using professional judgement to make decisions appropriate to the circumstances

Funding
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1 # Appendices

Appendix K: Excluded economic studies

Table 1: Studies excluded from the economic review

Reference	Reason for exclusion
MUKHERJEE 2010[68]	A USA cohort study (n=152) evaluated physiologic criteria and eliminating blunt mechanism of injury on the impact of over triage (and therefore paediatric trauma team activation) and costs in children. Linear regression was used to adjust for confounders. Applicability of costing to the UK context was questionable due to the use of charges to cost. Applicability of the comparators and effect found was also questioned given the differences between the USA paediatrics service and that found in the UK. This study was assessed as insufficiently applicable to inform recommendations regarding pre-hospital triage pre-alert or tiered team activation.

Appendix L: Delay to intervention reviews

L.1 Delay to neurosurgery

L.1.1 Introduction

Head injury is a commonly seen trauma in the emergency department. The mechanical forces applied to the head during trauma can produce excoriation or laceration to the skin, skull fracture, and brain injury, for instance epidural, subdural and intracerebral haematoma.

Traumatic brain injury (TBI) is a major cause of death and disability in the United Kingdom. Mortality and morbidity are high for people with TBI and it also imposes substantial impact on quality of life. A patient's outcome depends heavily on the extent and nature of the primary damage and on the effectiveness of therapy designed to prevent or limit secondary brain damage. Secondary brain injury progresses over hours and days from physiological insults such as ischaemia, reperfusion and hypoxia to areas of the brain. Indeed, haematoma expansion typically occurs in the first 24 hours, especially in the first 4 hours. Preventing secondary injury by prompt resuscitation and early specific management can reduce both morbidity and mortality following TBI.

Neurosurgical therapy aims to minimise the secondary brain damage after a severe head injury and primarily this means control of a patient's intracranial pressure (ICP). Restoration of cerebral perfusion and reduction of ICP by surgical enlargement of the intracranial space is the primary goal of decompressive craniectomy (DC). DC is an important method for the management of severe TBI, especially when patients develop refractory intracranial hypertension for which conservative treatments are ineffective. Commonly it is performed under the guidance of ICP monitoring, and is used to reduce ICP after lack of effectiveness of conservative treatment.

However adherence to this criterion might result in a reduction in the benefits of DC because patients have already suffered from low cerebral perfusion and cerebral anoxia for an extended period. Instead pre-emptive or primary DC can be performed early, often within the first few hours after injury. It has been held that patients operated on within 4 hours of injury have a significantly better chance of survival than those operated on after 4 hours.

Brain trauma as a time-sensitive injury is promulgated by the golden hour, the time when provision of appropriate resuscitation and definitive care could save those who would otherwise die. Delays in diagnosis and treatment may result in irreversible secondary injury and increasing morbidity and mortality. Known complications of delay to a specialist centre are poorly managed systemic hypotension, hypoxemia from an unsecured airway, and intracranial hypertension. Invariably a significant period of this vital time is spent in suboptimal monitoring conditions.

L.1.2 Review question: What is the optimal timing of neurosurgery?

For full details see review protocol in Appendix A.

Table 2: PICO characteristics of review question

Population	Children, young people and adults with a head injury after a traumatic incident
Intervention and comparison	Neurosurgery or arrival to specialist neurosurgical services at different time points, as identified by the literature, to a maximum of 24 hours. Indirect versus direct transfer to neurosurgical services
Outcomes	Critical: • Mortality

	• Health-related quality of life • Length of hospital stay • Number of procedures • Glasgow Outcomes Scale (GOS) • Subdural hygroma • Epidural haematoma • Hypotension • Septic shock • Hydrocephalus • Other adverse events Data to be collected: • Survival analysis data • Important follow-up time points (4 hours, 24 hours, 7 days, 1 month, 1 year)
Study design	RCTs or systematic reviews of RCTs; cohort studies that use multivariate analysis to adjust for key confounders (injury severity, age, depth of shock, degree of head injury) or were matched at baseline for these if no RCTs retrieved**Stratification from outset** • Pre-hospital intubation **Subgroups if between-study heterogeneity exists** • Age (children and adults): child (0-15 years); young people (16-17 years); adults (18-65 years; >65 years) **Within-study confounders to consider (if cohorts used)** • Age, injury severity, depth of shock

L.1.3 Clinical evidence

Two sets of interventions and comparisons were included in this protocol. The former directly compared time from injury to neurosurgery or admission to a specialist neurosurgical centre. The latter compared the effect of direct transfer to a specialist centre to indirect transfer via a local hospital.

Two retrospective cohort studies,[30,101] were included for the neurosurgery or arrival to specialist neurosurgical services at different time points comparison; summarised in Table 3 below. Two retrospective cohort studies,[67,95] one retrospective case control study,[62] and one cluster randomised controlled trial[57] were included in the indirect versus direct transfer to neurosurgical services comparison; summarised in Table 4 below. Evidence from the studies is summarised in the clinical evidence summaries (Tables 2-8). See also the study selection flow chart in Appendix B, study evidence tables in Appendix E, forest plots in Appendix D, GRADE tables in Appendix G and excluded studies list in Appendix H. Three further studies met the inclusion criteria but were excluded because they only reported a p values for the outcome of interest.[27,53,88]

Table 3: Summary of studies included in the neurosurgery or arrival to specialist neurosurgical services at different time points comparison

Study	Intervention and comparison	Population	Outcomes	Comments
Dinh 2013[30]	Early versus late admission to a Major Trauma Centre (MTC) with specialist neurosurgical services	n=983 Conducted in Australia Major trauma admissions (15 years and older) with	**Incremental mortality** • In-hospital mortality with each incremental	Retrospective review of patient records Patients followed up until discharge from

Study	Intervention and comparison	Population	Outcomes	Comments
	Arrival time periods compared: • Within 30 minutes versus after 30 minutes • Within 60 minutes versus after 60 minutes • Within 90 minutes versus after 90 minutes • Within 120 minutes versus after 120 minutes The patient arrival time was defined as the number of minutes from recorded incident time to triage time.	severe head injury (head abbreviated injury score ≥ 3) due to blunt trauma 39% of patients intubated pre-hospital Exclusions: • Patients transferred from other health facilities or with injuries occurring more than 24 hours prior to hospital presentation • Patients who self-presented or did not arrive by ambulance • Patients with no vital signs on arrival	increase in patient arrival time in minutes **Mortality** • Arrival within 30 minutes • Arrival within 60 minutes • Arrival within 60 minutes (GCS >8) • Arrival within 60 minutes (GCS 3-8) • Arrival within 90 minutes • Arrival within 120 minutes **Good recovery**[a] • Arrival within 60 minutes	MTC Cox proportional hazards model adjusted for: • Patient arrival time • Age • Systolic blood pressure • Glasgow Coma Scale (GCS) • Injury Severity Score (ISS) • Airway intubation • Intracerebral haemorrhage • Craniotomy within 24 hours
Tien 2011 [101]	Multivariable analysis of the effect of pre-hospital delay on the outcomes of patients with head injury Rapid craniotomy was performed to completely evacuate the clot, control bleeding if possible, and resect necrotic brain tissue	n=149 Conducted in Canada Patients who underwent craniotomy for acute subdural hematoma after blunt force trauma Prehospital airway: 52% Exclusions: • All patients who were referred from other centres • Patients who also had severe injuries of either their thoracic, abdominal or pelvic areas (Abbreviated Injury Scale scores ≥3)	In-hospital mortality per minute of time spent in the prehospital setting after the traumatic incident	Retrospective cohort study Urban level 1 trauma centre Study does not stratify by, or correct for, pre-hospital intubation. Multivariate logistic regression. The covariates were: • Gender • Age • ISS • GCS • CT findings of subarachnoid haemorrhage • CT findings of herniation (basal cistern compression)

(a) Survival to hospital discharge without transfer for on-going rehabilitation or nursing home care

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2 **Table 4: Summary of studies included in the indirect versus direct transfer to neurosurgical**
3 **services comparison**

Study	Intervention and comparison	Population	Outcomes	Comments
Lecky 2015[57]	Transfer from scene to the closest non-specialist centre versus direct transfer to a specialist neuroscience centre Not all patients in the intervention arm were transferred onto a specialist neuroscience centre	n=293 Conducted in UK Young people and adults with signs of isolated TBI (GCS <13/14) and stable ABC, whose closest hospital was not a specialist neuroscience centre Median (IQR) GCS was 12 (8-13) in both groups	• 30 day mortality	Cluster RCT (74 clusters across two ambulance services) Compliance from paramedics in taking patients to their randomised hospital was 62% (90% in the control arm)
Lin 2012[62]	Indirect transfer versus direct transfer Mean time from injury to neurosurgical intervention was 334 minutes versus 179 minutes	n=60 Conducted in Israel Trauma patients over 2 years of age, sustaining an intracranial injury (ICI), who had neurosurgical intervention at a level 1 trauma centre Exclusion: people with a non-head abbreviated injury score (AIS) exceeding 2	• In-hospital mortality • ICU length of stay	Retrospective case control study Confounding: • Groups matched for age and GCS on admission. • Haematoma width was wider in the direct transfer group
Moen 2008[67]	Indirect transfer versus direct transfer Median time from injury to neurosurgery was 5.5 hours versus 3.6 hours	n=146 Conducted in Norway Patients with severe head injury and a GCS <9 Exclusions: Patients admitted more than 24 hours after injury or those with unknown time of injury.	• Mortality at 6 months	Retrospective cohort study Logistic regression analysis used to correct for variations in age and injury severity between groups.

Study	Intervention and comparison	Population	Outcomes	Comments
Sugerman 2012[95]	Indirect transfer versus direct transfer Mean (median) time from injury to specialist neurosurgery hospital was 485 (122) minutes versus 84 (37) minutes.	n=51300 Conducted in USA Adults with severe TBI (head AIS over 2) Exclusions: • ISS less than 16 • GCS motor score of 6 • Non-head AIS score over 2 • Patients with missing transfer status or death on arrival	• In-hospital mortality	Retrospective cohort study (data American College of Surgeons National Trauma Database National Population Sample) Multivariate model used to correct for key confounders.

Neurosurgery or arrival to specialist neurosurgical services at different time points

Table 5: Clinical evidence summary: incremental mortality (not all patients had craniotomy)

Outcome	Number of studies (number of participants)	Imprecision	GRADE rating	Relative effect (95% CI)	Control event rate (per 1000)	Control event rate for continuous outcomes
In-hospital mortality with each incremental increase in patient arrival time in minutes	1 (n=983)	No serious imprecision	Very low	HR 1.002 (1.001 to 1.004)	Not available: adjusted mortality not reported	-

Table 6: Clinical evidence summary: incremental mortality (all patients had craniotomy)

Outcome	Number of studies (number of participants)	Imprecision	GRADE rating	Relative effect (95% CI)	Control event rate (per 1000)	Control event rate for continuous outcomes
In-hospital mortality (after craniotomy) per minute of prehospital time	1 (n=149)	No serious imprecision	Very low	OR 1.03 (1.004 to 1.06)	Not available: adjusted mortality not reported	-

Table 7: Clinical evidence summary: early (<30 minutes) versus late (>30 minutes) arrival at MTC

Outcome	Number of studies (number of participants)	Imprecision	GRADE rating	Relative effect (95% CI)	Control event rate (per 1000)	Control event rate for continuous outcomes
In-hospital mortality	1 (n=983)	Serious imprecision	Very low	HR 1.15 (0.75 to 1.76)	Not available: adjusted mortality not reported	-

Table 8: Clinical evidence summary: early (<60 minutes) versus late (>60 minutes) arrival at MTC

Outcome	Number of studies (number of participants)	Imprecision	GRADE rating	Relative effect (95% CI)	Control event rate (per 1000)	Control event rate for continuous outcomes
In-hospital mortality	1 (n=983)	Serious imprecision	Very low	HR 0.77 (0.5 to 1.19)	Not available: adjusted mortality not reported	-
In-hospital mortality (GCS >8 on arrival)	1 (n=983)	Very serious imprecision	Very low	HR 0.87 (0.46 to 1.65)	Not available: adjusted mortality not reported	-
In-hospital mortality (GCS 3-8 on arrival)	1 (983)	Very serious imprecision	Very low	HR 0.8 (0.44 to 1.45)	Not available: adjusted mortality not reported	-
Good recovery (Survival to hospital discharge without transfer for on-going rehabilitation or nursing home care)	1 (n=983)	Serious imprecision	Very low	OR 1.78 (1.14 to 2.78)	Not available: adjusted data not reported	-

Table 9: Clinical evidence summary: early (<90 minutes) versus late (>90 minutes) arrival at MTC

Outcome	Number of studies (number of participants)	Imprecision	GRADE rating	Relative effect (95% CI)	Control event rate (per 1000)	Control event rate for continuous outcomes
In-hospital mortality	1 (n=983)	No serious imprecision	Very low	HR 0.35 (0.18 to 0.68)	Not available: adjusted mortality not reported	-

Table 10: Clinical evidence summary: early (<120 minutes) versus late (>120 minutes) arrival at MTC

Outcome	Number of studies (number of participants)	Imprecision	GRADE rating	Relative effect (95% CI)	Control event rate (per 1000)	Control event rate for continuous outcomes

Outcome	Number of studies (number of participants)	Imprecision	GRADE rating	Relative effect (95% CI)	Control event rate (per 1000)	Control event rate for continuous outcomes
In-hospital mortality	1 (n=983)	No serious imprecision	Very low	HR 0.3 (0.16 to 0.56)	Not available: adjusted mortality not reported	-

Indirect versus direct transfer to a specialist neurosurgery centre

Table 11: Clinical evidence summary: indirect versus direct transfer to a specialist neurosurgery centre

Outcome	Number of studies (number of participants)	Imprecision	GRADE rating	Absolute difference or relative effect (95% CI)	Control event rate (per 1000)	Control event rate for continuous outcomes
Mortality at 30 days (RCT data)a	1 (n=272)	Very serious imprecision	Very low	6 fewer per 1000 (from 54 fewer to 89 more)	94 per 1000	-
Mortality at varying time points (observational study data)	3 (n=51506)	Serious imprecision	Very low	OR 0.77 (0.63 to 0.95)	Not available: adjusted mortality not reported	-
Length of ICU stay	1 (n=60)	Serious imprecision	Very low	MD 1.4 higher (4.78 lower to 7.58 higher)	-	13.2 days

(a) Some patients in the intervention arm were not transferred onto a specialist neuroscience centre.

1 **Appendix A- Review Protocols**

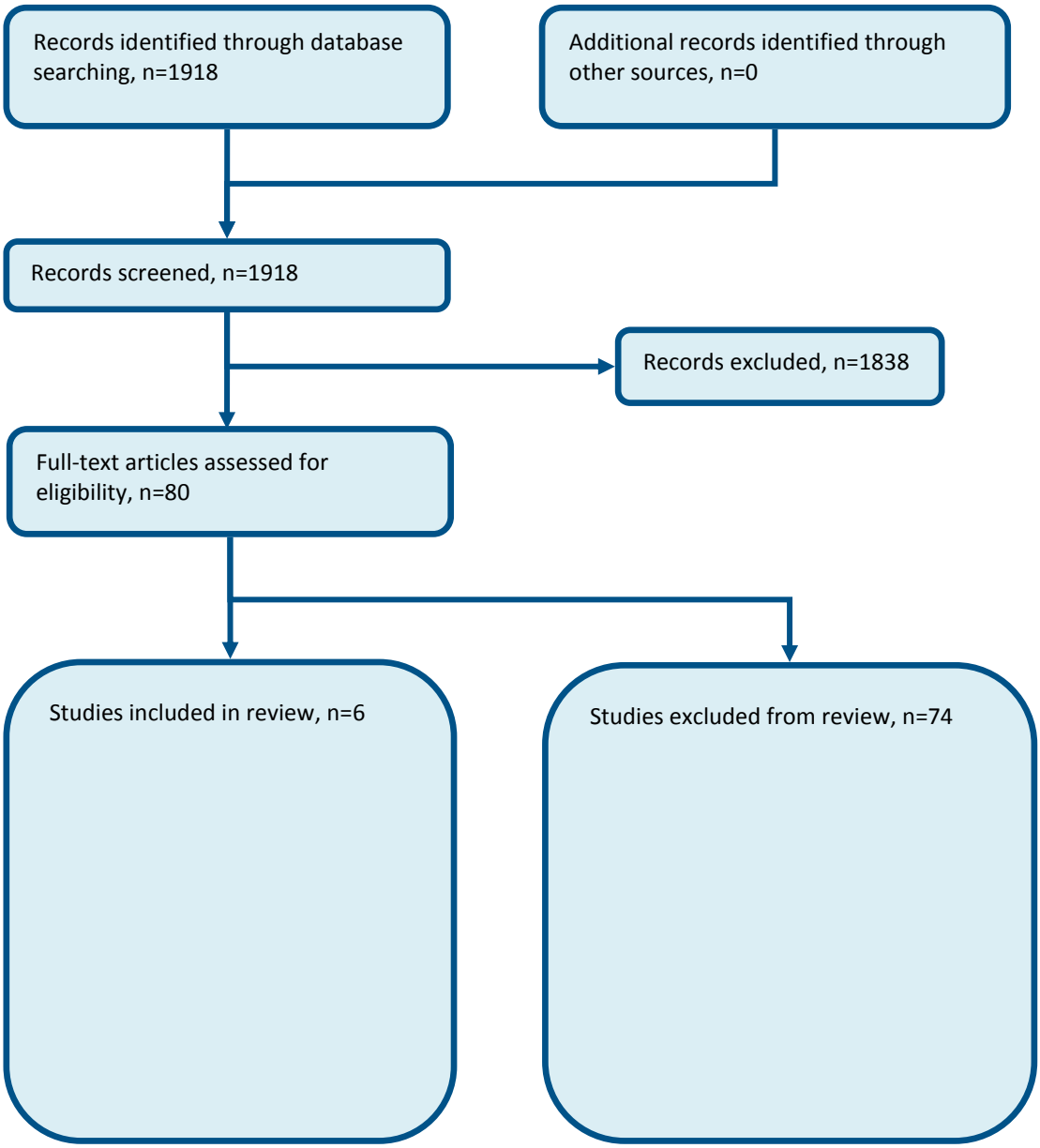
2 **Table 12: Review protocol: timing of neurosurgery**

Review question	Delay to intervention head injury
Guideline condition and its definition	Major trauma. Definition: People with life threatening condition or loss of major limb
Objectives	To see if delayed head injury intervention leads to poorer outcomes
Review population	Patients with head injury
	Adults 18 years and over Children 17 years or under Overall
Interventions and comparators: generic/class; specific/drug	Admission to specialist neurosurgical centre; Early vs. Admission to specialist neurosurgical centre; Delayed Neurosurgery; Early vs. Neurosurgery; Delayed Direct transfer to specialist neurosurgical centre vs. indirect transfer
Outcomes	CRITICAL • Quality of life • Mortality • Glasgow Outcomes Scale • Subdural hematoma • Epidural haematoma • Subdural haematoma • Hypotension • Septic shock • Hydrocephalus • Other adverse events • Length of stay • No. of procedures
Study design	RCTs or systematic reviews of RCTs; cohort studies that use multivariate analysis to adjust for key confounders (injury severity, age, depth of shock, degree of head injury) or were matched at baseline for these if no RCTs retrieved
Search strategy	Databases: Medline, Embase, the Cochrane Library Date: All years Language: Restrict to English only Study designs: RCTs or systematic reviews of RCTs; cohort studies that use multivariate analysis to adjust for key confounders (injury severity, age, depth of shock, degree of head injury) or were matched at baseline for these if no RCTs retrieved
The review strategy	Quality of life data: Collect all data for the stated QoL measure, for meta-analysis and GRADE report only overall scores Appraisal of methodological quality: The methodological quality of each study will be assessed using NICE checklists and GRADE.
Subgroup analyses if there is heterogeneity	Stratification from outset • Pre-hospital intubation Subgroups if between-study heterogeneity exists • Age (children and adults): child (0-15 years); young people (16-17 years); adults (18-65 years; > 65 years)

Review question	Delay to intervention head injury
	Within-study confounders to consider (if cohorts used) • Age, injury severity, depth of shock

Appendix B - Clinical article selection

Figure 1: Flow chart of clinical article selection for the review of timing of neurosurgery

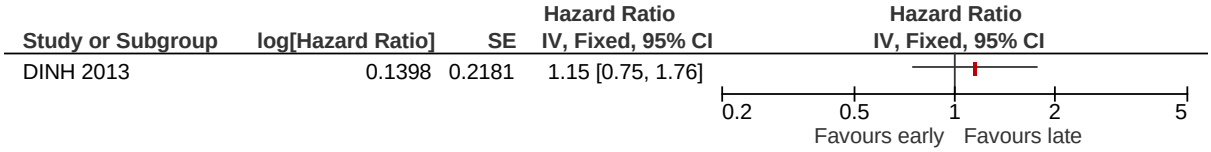


Appendix C - Forest plots for timing of neurosurgery

Neurosurgery or arrival to specialist neurosurgical services at different time points

Early (<30 minutes) versus late (>30 minutes) arrival at MTC

Figure 2: In-hospital mortality



Early (<60 minutes) versus late (>60 minutes) arrival at MTC

Figure 3: In-hospital mortality

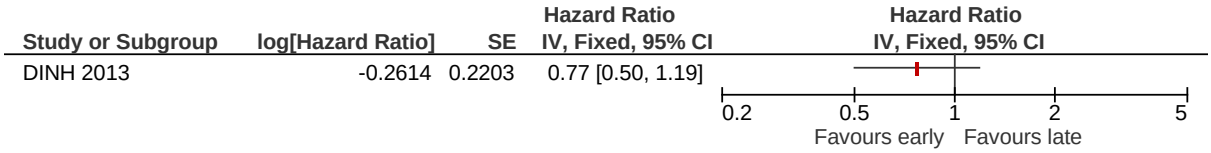


Figure 4: In-hospital mortality (GCS >8 on arrival)

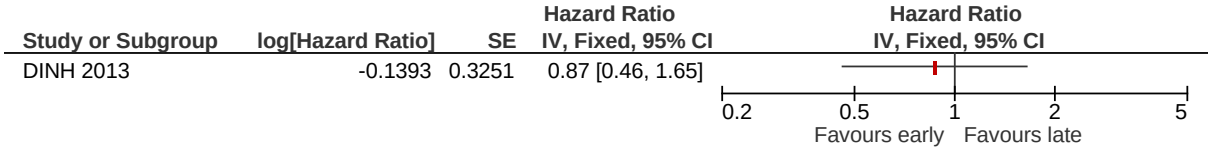


Figure 5: In-hospital mortality (GCS 3-8 on arrival)

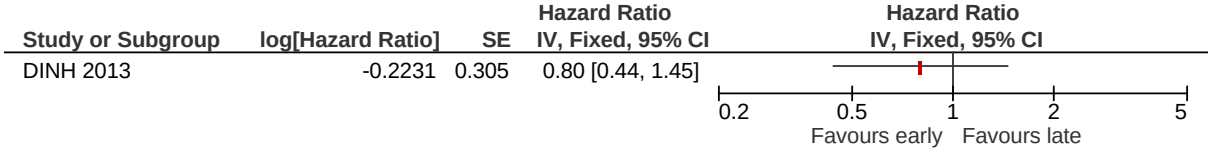
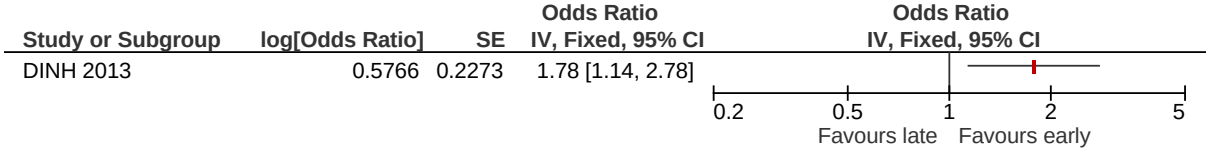


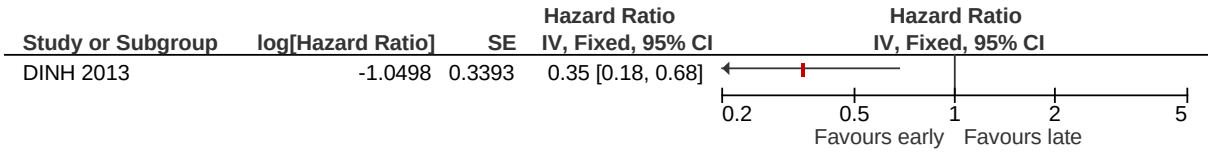
Figure 6: Good recovery*



**Survival to hospital discharge without transfer for on-going rehabilitation or nursing home care*

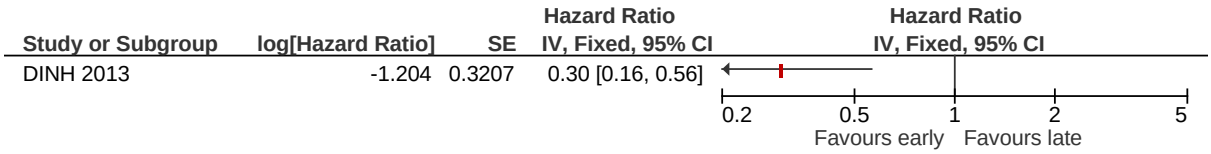
1 **Early (<90 minutes) versus late (>90 minutes) arrival at MTC**

Figure 7: In-hospital mortality



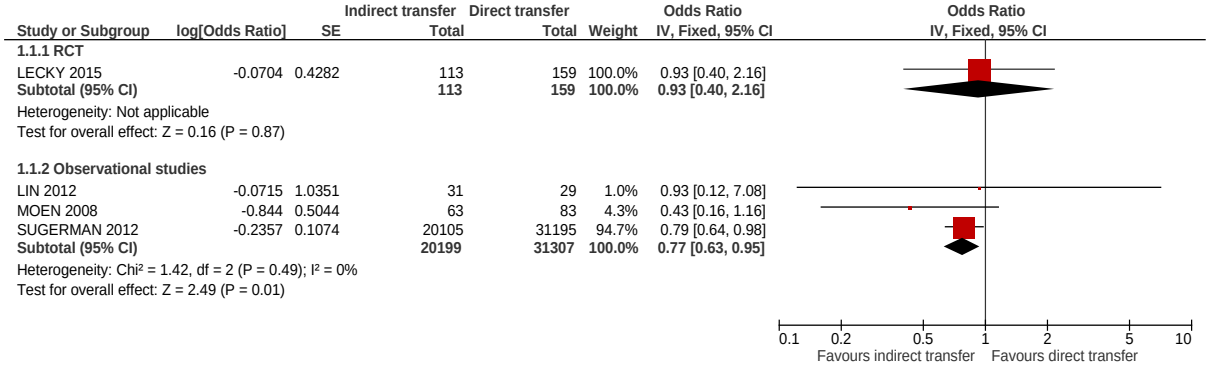
2 **Early (<120 minutes) versus late (>120 minutes) arrival at MTC**

Figure 8: In-hospital mortality



3 **Indirect versus direct transfer to a specialist neurosurgery centre**

Figure 9: Mortality (varying time points)



Lecky 2015: some patients in the intervention arm were not transferred onto a specialist neuroscience centre.

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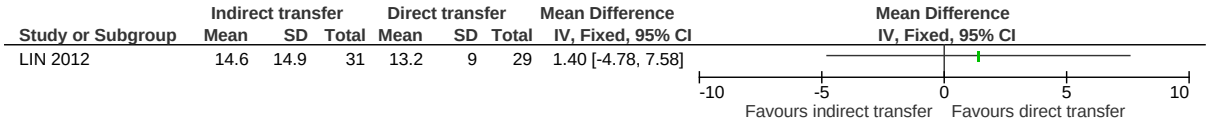
Figure 10: Length of ICU stay



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Appendix D - Clinical evidence tables

Table 13: Dinh 2013[30]

Study	Dinh 2013[30]
Study type	Retrospective cohort study
Number of studies (number of participants)	(n=983)
Countries and setting	Conducted in Australia; Setting: Major Trauma Centre
Line of therapy	1st line
Duration of study	Follow-up (post intervention): until discharge from a Major Trauma Centre
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Major trauma admissions (15 years and older) with severe head injury (head abbreviated injury score ≥ 3) due to blunt trauma
Exclusion criteria	Exclusion criteria were patients transferred from other health facilities, injuries occurring more than 24 h prior to hospital presentation, patients who self-presented or did not come by ambulance and patients with no vital signs on arrival. Patients with associated spinal injuries transferred to other spinal trauma hospitals for ongoing care were also excluded.
Recruitment/selection of patients	Data source was a hospital trauma registry (January 2000 and June 2011)
Age, gender and ethnicity	Age - Mean (SD): overall 51 (23), <60 minutes group: 50 (23), >60 minutes group: 57 (23). Gender (M:F): 707/276. Ethnicity:
Further population details	1. Age: Not applicable/Not stated/Unclear
Extra comments	Mechanism of injury: 48% falls. GCS: 14-15: 62%, 9-13: 13%, 3-8: 25%. ISS: <25: 69%, 25-50: 28%, >50: 3%. 39% of patients were intubated in the before arrival to hospital. Craniotomy performed with 24 hours of injury: 19%. Died before discharge: 15%. Multivariate analysis was utilised. The following factors were adjusted for: arrival time, age, SBP, GCS, ISS, airway intubation, ICH, craniotomy within 24 hours.
Indirectness of population	No indirectness
Interventions	(n=791) Intervention 1: Admission to MTC - Early. The patient arrival time was defined as the number of minutes from recorded incident time to triage time. Patients who arrived to the MTC within 60 minutes or less of injury time were

Study	Dinh 2013[30]
	classified "Early". Concurrent medication/care: Patients were managed using standardised severe head injury algorithms based on adult trauma life support principles. Performance indicators that were routinely assessed as part of a rigorous quality assurance programme included prehospital scene time of 20 minutes or less, definitive airways management within 10 minutes of arrival, CT scanning within 1 h of arrival and urgent craniotomies within 4 h of injury time. (n=192) Intervention 2: Admission to MTC - Delayed. The patient arrival time was defined as the number of minutes from recorded incident time to triage time. Patients who arrived to the MTC after 60 minutes of injury time were classified "Late". Concurrent medication/care: Patients were managed using standardised severe head injury algorithms based on adult trauma life support principles. Performance indicators that were routinely assessed as part of a rigorous quality assurance programme included prehospital scene time of 20 minutes or less, definitive airways management within 10 minutes of arrival, CT scanning within 1 h of arrival and urgent craniotomies within 4 h of injury time.
Funding	No funding

RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EARLY versus DELAYED

Protocol outcome 1: Mortality
- Actual outcome: In-hospital mortality at Arrival to MTC within 30 minutes; HR 1.15 (95%CI 0.75 to 1.77); Risk of bias: Very high; Indirectness of outcome: No indirectness
- Actual outcome: In-hospital mortality at Arrival to MTC within 60 minutes; HR 0.77 (95%CI 0.5 to 1.18); Risk of bias: High; Indirectness of outcome: No indirectness
- Actual outcome: In-hospital mortality at Arrival to MTC within 90 minutes; HR 0.35 (95%CI 0.18 to 0.65); Risk of bias: Very high; Indirectness of outcome: No indirectness
- Actual outcome: In-hospital mortality at Arrival to MTC within 120 minutes; HR 0.3 (95%CI 0.16 to 0.64); Risk of bias: Very high; Indirectness of outcome: No indirectness
- Actual outcome: In-hospital mortality: GCS >8 at Arrival to MTC within 60 minutes; HR 0.87 (95%CI 0.46 to 1.66); Risk of bias: High; Indirectness of outcome: No indirectness
- Actual outcome: In-hospital mortality: GCS 3-8 at Arrival to MTC within 60 minutes; HR 0.80 (95%CI 0.44 to 1.45); Risk of bias: High; Indirectness of outcome: No indirectness
- Actual outcome: In-hospital mortality with each incremental increase in patient arrival time in minutes at .; HR 1.002 (95%CI 1.001 to 1.004); Risk of bias: High; Indirectness of outcome: No indirectness

Protocol outcome 2: Glasgow Outcomes Scale

Study	Dinh 2013[30]
- Actual outcome: Survival to hospital discharge without transfer for ongoing rehabilitation or nursing home care at Arrival to MTC within 60 minutes; OR 1.78 (95%CI 1.14 to 2.79); Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life; Subdural hygroma; Epidural haematoma; Subdural haematoma; Hypotension; Septic shock; Hydrocephalus; Other adverse events; Length of stay; No. of procedures

Table 14: Head Injury Transportation Straight to Neurosurgery (HITS-NS) trial : Lecky 2015[57]

Study	Head Injury Transportation Straight to Neurosurgery (HITS-NS) trial : Lecky 2015[57]
Study type	RCT (randomised; Parallel)
Number of studies (number of participants)	(n=293)
Countries and setting	Conducted in United Kingdom; Setting: Cluster randomised controlled trial conducted across two ambulance services with 74 clusters. Ambulance stations randomised using a matched pair design.
Line of therapy	1st line
Duration of study	Follow-up (post intervention): 30 days
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Young people and adults with signs of isolated traumatic brain injury (GCS <13/14) and stable ABC, whose closest hospital was not a specialist neuroscience centre.
Exclusion criteria	.
Recruitment/selection of patients	Patients recruited over 12 months (2012-2013. Overall compliance from paramedics in terms of taking patients to their randomised hospital was 62% (90% in the control/indirect arm).
Age, gender and ethnicity	Age - Mean (SD): 46. Gender (M:F): 200/93. Ethnicity:
Further population details	1. Age: Not applicable/Not stated/Unclear
Extra comments	Median CGS was 12 in both groups.
Indirectness of population	No indirectness
Interventions	(n=124) Intervention 1: Neurosurgery - Indirect transfer. People transported from scene to the closest hospital (non-specialist). Patients were then transferred to a specialist centre if required. Concurrent medication/care: Median (IQR) time from leaving scene to hospital: 16 (8 to 25.3). 35 of 114 had TBI.

Study	Head Injury Transportation Straight to Neurosurgery (HITS-NS) trial : Lecky 2015[57]
	(n=169) Intervention 2: Neurosurgery - Direct transfer. Transported to specialist neuroscience centre. Concurrent medication/care: Median (IQR) time from leaving scene to hospital: 19 (12 to 25.5). 35 of 162 had TBI.
Funding	Academic or government funding (NIHR HTA)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INDIRECT TRANSFER versus DIRECT TRANSFER Protocol outcome 1: Mortality - Actual outcome: Mortality at 30 days; Group 1: 10/113, Group 2: 15/159; Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life; Glasgow Outcomes Scale; Subdural hygroma; Epidural haematoma; Subdural haematoma; Hypotension; Septic shock; Hydrocephalus; Other adverse events; Length of stay; No. of procedures

Table 15: Lin 2012[62]

Study	Lin 2012[62]
Study type	Non-randomised study
Number of studies (number of participants)	(n=60)
Countries and setting	Conducted in Israel; Setting: Level 1 trauma centre
Line of therapy	1st line
Duration of study	Not clear: Until discharge from hospital
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Intervention group: wounded (>2 years old), sustaining blunt ICI as diagnosed by CT scan that were evacuated to an intermediate hospital before being transferred to a level 1 trauma centre and underwent neurosurgical intervention. Control group: Similar to the intervention group except they were primarily evacuated to level 1 trauma centre. These were matched to the intervention group by random selection of 29 people who met the inclusion criteria.
Exclusion criteria	Wounded were excluded if the abbreviated injury score (AIS) of any other body region (non-head) exceeded 2.
Recruitment/selection of patients	Retrospective case control study. Recruited from 1st January 2008 to 31st May 2010.

Study	Lin 2012[62]
Age, gender and ethnicity	Age - Mean (SD): 31. Gender (M:F): 50/10. Ethnicity:
Further population details	1. Age: Not applicable/Not stated/Unclear
Extra comments	Groups matched for age (32 years vs. 29 years), GCS on admission (11 vs. 10.4). Haematoma width was wider in the direct transfer group (24mm vs. 20 mm). Mean time from injury to neurosurgical intervention was 334 minutes vs. 179 minutes).
Indirectness of population	No indirectness
Interventions	(n=31) Intervention 1: Neurosurgery - Indirect transfer. Transferred to an intermediate hospital without specialist neurosurgical services before transfer to a level 1 trauma centre with specialist neurosurgical services. (n=29) Intervention 2: Neurosurgery - Direct transfer. Transferred directly from scene to a level 1 trauma centre with specialist neurosurgical care.
Funding	No funding (It was stated that there were no conflicts of interest)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INDIRECT TRANSFER versus DIRECT TRANSFER Protocol outcome 1: Mortality - Actual outcome: In-hospital mortality at .; Group 1: 2/31, Group 2: 2/29; Risk of bias: Very high; Indirectness of outcome: No indirectness Protocol outcome 2: Length of stay - Actual outcome: ICU stay at .; Group 1: mean 14.6 days (SD 14.9); n=31, Group 2: mean 13.2 days (SD 9); n=29; Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life; Glasgow Outcomes Scale; Subdural hygroma; Epidural haematoma; Subdural haematoma; Hypotension; Septic shock; Hydrocephalus; Other adverse events; No. of procedures

Table 16: Moen 2008[67]

Study	Moen 2008[67]
Study type	Retrospective cohort study
Number of studies (number of participants)	(n=146)
Countries and setting	Conducted in Norway; Setting: Hospital (department of neurosurgery)

Study	Moen 2008[67]
Line of therapy	1st line
Duration of study	Not clear:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Patients with severe head injury and a GCS <9
Exclusion criteria	Patients admitted >24 hours after injury or those with unknown time of injury.
Recruitment/selection of patients	Consecutive patients from 1st January 1998 to 31st December 2002. Patients were retrospectively identified through patient records.
Age, gender and ethnicity	Age - Median (range): 34 (1-88). Gender (M:F): 116/30. Ethnicity:
Further population details	1. Age: Not applicable/Not stated/Unclear
Extra comments	Logistic regression analysis used to correct for variations in age and injury severity between groups. 49% of patients had surgery for a mass lesion (no significant difference between groups). . Confounders: groups were matched in terms of age (mean of 34 in each). Groups not matched in terms of injury severity. The mean ISS (range) for the direct group was 31.8 and 27 in the transfer group. 77% of the direct group had a fGCS <9 compared to 63% in the transfer group. 83% of those in the direct group with fGCS <9 were intubated compared to 38% in the transfer group.
Indirectness of population	No indirectness
Interventions	(n=83) Intervention 1: Neurosurgery - Direct transfer. Patients transported directly to the specialist neurosurgery hospital. Concurrent medication/care: 59% of patients transported in an air ambulance. Median (range) time from injury to specialist neurosurgery hospital was 1.8 hours (0.3-15.8). Median (range) time from injury to neurosurgery was 3.6 hours (1.8-17.6). (n=63) Intervention 2: Neurosurgery - Indirect transfer. Patients initially transported to a local hospital before transfer to a specialist neurosurgical centre. Concurrent medication/care: 51% of initial transport to local hospital by ground ambulance without an anaesthetist. Median (range) time from injury to specialist neurosurgery hospital was 5.5 hours (0.8-23). Median (range) time from injury to neurosurgery was 5.5 hours (2.5-19.6).
Funding	Funding not stated
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INDIRECT TRANSFER versus DIRECT TRANSFER	

Study	Moen 2008[67]
Protocol outcome 1: Mortality - Actual outcome: Mortality at 6 months; OR 0.43 (95%CI 0.16 to 1.14); Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life; Glasgow Outcomes Scale; Subdural hygroma; Epidural haematoma; Subdural haematoma; Hypotension; Septic shock; Hydrocephalus; Other adverse events; Length of stay; No. of procedures

Table 17: Sugerman 2012[95]

Study	Sugerman 2012[95]
Study type	Retrospective cohort study
Number of studies (number of participants)	(n=51300)
Countries and setting	Conducted in USA; Setting: Level I or II trauma centres (multicentre)
Line of therapy	1st line
Duration of study	Not clear: Until discharge from hospital
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	Adult (≥18 years) with severe TBI patients
Exclusion criteria	ISS < 16; GCS motor score = 6; non-head AIS score ≥ 3; head AIS < 3; patients with missing transfer status, and death on arrival
Recruitment/selection of patients	Patient data from the American College of Surgeons National Trauma Database (NTDB) National Population Sample (NSP), combining data from 2007-09
Age, gender and ethnicity	Age - Other: 18-39 years: 16110, 40-59 years: 13384, >59 years: 21806. Gender (M:F): 36047/15010. Ethnicity:
Further population details	1. Age: Not applicable/Not stated/Unclear
Extra comments	Multivariate model used to correct for key confounders.
Indirectness of population	No indirectness
Interventions	(n=20105) Intervention 1: Neurosurgery - Indirect transfer. Patients initially transported to a local hospital before transfer to a specialist neurosurgical centre. Concurrent medication/care: Mean time from injury to specialist neurosurgery hospital was 485 minutes. Median time from injury to specialist neurosurgery hospital was 122 minutes.

Study	Sugerman 2012[95]
	(n=31195) Intervention 2: Neurosurgery - Direct transfer. Patients transported directly to the specialist neurosurgery hospital. Concurrent medication/care: Mean time from injury to specialist neurosurgery hospital was 84 minutes. Median time from injury to specialist neurosurgery hospital was 37 minutes.
Funding	Other (Supported by US Centers for Disease Control and Prevention)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: INDIRECT TRANSFER versus DIRECT TRANSFER Protocol outcome 1: Mortality - Actual outcome: In-hospital mortality at .; OR 0.79 (95%CI 0.64 to 0.96); Risk of bias: Very high; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life; Glasgow Outcomes Scale; Subdural hygroma; Epidural haematoma; Subdural haematoma; Hypotension; Septic shock; Hydrocephalus; Other adverse events; Length of stay; No. of procedures

Table 18: Tien 2011[101]

Study	Tien 2011[101]
Study type	Retrospective cohort study
Number of studies (number of participants)	(n=149)
Countries and setting	Conducted in Canada; Setting: Urban level 1 trauma centre
Line of therapy	1st line
Duration of study	Follow-up (post intervention): Until discharge from hospital
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	All patients who underwent craniotomy to drain an acute subdural hematoma after blunt force trauma
Exclusion criteria	All patients who were referred from other centres, those who also had severe injuries of either their thoracic, abdominal or pelvic areas (Abbreviated Injury Scale scores ≥3), and those with admission blood alcohol concentrations of ≥10 mmol/litre. Patients who died before undergoing craniotomy or underwent craniotomy without CT imaging to avoid survivor treatment bias. To create a more homogenous sample, all patients who only underwent

Study	Tien 2011[101]
	craniotomy after a period of observation were excluded
Recruitment/selection of patients	From 1st January 1996 to 31st December 2007
Age, gender and ethnicity	Age - Mean (SD): 44.7 (19.6). Gender (M:F): 110:39. Ethnicity:
Further population details	1. Age: Not applicable/Not stated/Unclear
Extra comments	Prehospital hypotension (%) 5.0, Prehospital hypoxia (%) 4.2, Prehospital Airway (%) 52.3, Hospital mortality (%) 40. Overall mortality was 60/149. . ISS: mean (SD) 35.6 ± 9.2, GCS: median (IQR) 6 (3–9).
Indirectness of population	No indirectness
Interventions	(n=149) Intervention 1: Neurosurgery - Early. Rapid craniotomy was performed to completely evacuate the clot, control bleeding if possible, and resect necrotic brain tissue. Intracranial pressure (ICP) monitors were placed, and the bone flap was removed at surgeon's judgment. . Duration NA. Concurrent medication/care: Patients were treated according to standard ATLS R protocol.36 Patients with severe brain injury were treated with assisted ventilation to maintain oxygen saturation over 94%, and to maintain an end-tidal CO2 at 35. In general, indications for craniotomy were compliant with the Guidelines for the Surgical Management of Traumatic Brain Injury published by the Brain Trauma Foundation in March 2006. One area where there was some difference in practice was in the use of the absolute volume of subdural haemorrhage as an indication for craniotomy.
Funding	No funding (None of the authors have any conflicts of interests or financial disclosures to make)
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: EARLY [INTERVENTION 1] ONLY Protocol outcome 1: Mortality - Actual outcome: In-hospital mortality per minute of prehospital time at .; OR 1.03 (95%CI 1.004 to 1.06); Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life; Glasgow Outcomes Scale; Subdural hygroma; Epidural haematoma; Subdural haematoma; Hypotension; Septic shock; Hydrocephalus; Other adverse events; Length of stay; No. of procedures

Appendix E - GRADE tables

Neurosurgery or arrival to specialist neurosurgical services at different time points

Table 19: Clinical evidence profile: incremental mortality (not all patients had craniotomy)[c]

Quality assessment							No. of patients		Effect			
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Continuous mortality outcome	Control	Relative (95% CI)	Absolute	Quality	Importance
In-hospital mortality with each incremental increase in patient arrival time in minutes												
1	Observational studies	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	-	0%	HR 1.002 (1.001 to 1.004)	[b]	VERY LOW	CRITICAL

(a) The majority of evidence was from studies at high risk of bias
(b) Calculation of absolute effect was not possible. Adjusted mortality not reported
(c) No forest plot produced for these data

Table 20: Clinical evidence profile: incremental mortality (all patients had craniotomy)[c]

Quality assessment							No. of patients		Effect			
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Timing	Control	Relative (95% CI)	Absolute	Quality	Importance
In-hospital mortality (after craniotomy) per minute of prehospital time												
1	Observational studies	Serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	-	0%	OR 1.03 (1.004 to 1.06)	[b]	VERY LOW	CRITICAL

(a) The majority of evidence was from studies at high risk of bias
(b) Calculation of absolute effect was not possible.
(c) No forest plot produced for these data

Table 21: Clinical evidence profile: early (<30 minutes) versus late (>30 minutes) arrival at MTC

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	GR Early (<30 minutes)	Late (>30 minutes) arrival at MTC	Relative (95% CI)	Absolute		
In-hospital mortality												
1	Observational studies	Very serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	-	0%	HR 1.15 (0.75 to 1.76)	[c]	VERY LOW	CRITICAL

(a) The majority of evidence was from studies at very high risk of bias
(b) Confidence interval crossed one MID
(c) Calculation of absolute effect was not possible. Adjusted mortality not reported.

Table 22: Clinical evidence profile: early (<60 minutes) versus late (>60 minutes) arrival at MTC

Quality assessment							No. of patients		Effect		Quality	Importance
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	GR Early (<60 minutes)	Late (>60 minutes) arrival at MTC	Relative (95% CI)	Absolute		
In-hospital mortality												
1	Observational studies	Serious[a]	No serious inconsistency	No serious indirectness	Serious[b]	None	-	0%	HR 0.77 (0.5 to 1.19)	[c]	VERY LOW	CRITICAL
In-hospital mortality (GCS >8 on arrival)												
1	Observational studies	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	-	0%	HR 0.87 (0.46 to 1.65)	[c]	VERY LOW	CRITICAL
In-hospital mortality (GCS 3-8 on arrival)												
1	Observational studies	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[d]	None	-	0%	HR 0.8 (0.44 to 1.45)	[c]	VERY LOW	CRITICAL
Good recovery (assessed with: survival to hospital discharge without transfer for ongoing rehabilitation or nursing home care)												
1	Observational studies	Very serious[e]	No serious inconsistency	No serious indirectness	Serious[b]	None	-	0%	OR 1.78 (1.14 to 2.78)	[c]	VERY LOW	CRITICAL

(a) The majority of evidence was from studies at high risk of bias
(b) Confidence interval crossed one MID
(c) Calculation of absolute effect was not possible. Adjusted mortality not reported.
(d) Confidence interval crossed both MIDs
(e) The majority of evidence was from studies at very high risk of bias

Table 23: Clinical evidence profile: early (<90 minutes) versus late (>90 minutes) arrival at MTC

Quality assessment							No. of patients		Effect			
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	GR Early (<90 minutes)	Late (>90 minutes) arrival at MTC	Relative (95% CI)	Absolute	Quality	Importance
In-hospital mortality												
1	Observational studies	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	-	0%	HR 0.35 (0.18 to 0.68)	[b]	VERY LOW	CRITICAL

(a) The majority of evidence was from studies at very high risk of bias
(b) Calculation of absolute effect was not possible. Adjusted mortality not reported.

Table 24: Clinical evidence profile: early (<120 minutes) versus late (>120 minutes) arrival at MTC

Quality assessment							No. of patients		Effect			
No. of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	GR Early (<120 minutes)	Late (>120 minutes) arrival at MTC	Relative (95% CI)	Absolute	Quality	Importance
In-hospital mortality												
1	Observational studies	Very serious[a]	No serious inconsistency	No serious indirectness	No serious imprecision	None	-	0%	HR 0.3 (0.16 to 0.56)	[b]	VERY LOW	CRITICAL

(a) The majority of evidence was from studies at very high risk of bias
(b) Calculation of absolute effect was not possible. Adjusted mortality not reported.

Indirect versus direct transfer to a specialist neurosurgery centre

Table 25: Clinical evidence profile: direct versus indirect transfer

Quality assessment							No. of patients		Effect			
No. of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other**	**Indirect**	**Direct**	**Relative (95% CI)**	**Absolute**	**Quality**	**Importance**
Mortality at 30 days: RCT data[6]												
1	Randomised trials	Serious[a]	No serious inconsistency	No serious indirectness	Very serious[b]	None	10/113 (8.8%)	9.4%	OR 0.93 (0.4 to 2.16)	6 fewer per 1000 (from 54 fewer to 89 more)	VERY LOW	CRITICAL
Mortality at varying time points: observational study data												
3	Observational studies	Very serious[c]	No serious inconsistency	No serious indirectness	Serious[d]	None	-	-	OR 0.77 (0.63 to 0.95)	[e]	VERY LOW	CRITICAL
Length of ICU stay (Better indicated by lower values)												
1	Observational studies	Very serious[c]	No serious inconsistency	No serious indirectness	Serious[d]	None	31	29	-	MD 1.4 higher (4.78 lower to 7.58 higher)	VERY LOW	CRITICAL

(a) The majority of evidence was from studies at high risk of bias
(b) Confidence interval crossed both MIDs
(c) The majority of evidence was from studies at very high risk of bias
(d) Confidence interval crossed one MID
(e) Calculation of absolute effect was not possible. Adjusted mortality not reported.
(f) Some patients in the intervention arm were not transferred onto a specialist neuroscience centre.

1 **Appendix F - Excluded clinical studies**

2 **Table 26: Studies excluded from the clinical review**

Study	Exclusion reason
Akyuz 2010[1]	Incorrect intervention: post 24 hours
Albanese 2003[2]	Incorrect comparator: post 24 hours
Bell 2010[4]	No clinical outcomes linked to delay
Bulters 2009[8]	No clinical outcomes
Cadotte 2010[9]	No clinical outcomes linked to delay
Carter 2010[10]	No separate data for head injury patients
Cavusoglu 2010[11]	Case series
Chalya 2011[12]	No separate outcome data for head injury patients
Chiaretti 2002[14]	No data for intervention (arrival at specialist neurosurgical care) at different time-points
Chibbaro 2007[15]	Incorrect comparator: post 24 hours
Chowdhury 2012[16]	No clinical outcomes linked to delay
Cianchi 2012[17]	Incorrect comparator: post 24 hours
Compagnone 2007[19]	Incorrect comparator: post 24 hours
Connelly 2006[20]	Not review population
Cornwell 2003[21]	No separate data for head injury patients
Davidson 2012[23]	No data on time from injury to specialist neurology centre
Dent 1995[27]	No useful outcome data - study only reported p value in multivariable analysis
Deverill 2007[28]	Did not account for key confounders (injury severity, age, depth of shock)
Dieppe 2009[29]	No clinical outcomes
Fuller 2014[35]	Control group not admitted to a specialist neurosurgical centre or admitted post 24 hours
Gomes[36]	Incorrect population: a major trauma population was used and no separate results were presented for head injury
Gong 2014[37]	Case series
Guresir 2008[38]	No clinical outcomes linked to delay reported
Harrison 2013[39]	Control group not admitted to a specialist neurosurgical centre or admitted post 24 hours
Hartings 2014[40]	No data on delay due to triage
Hasler 2014[41]	Not review population
Hatashita 1993[42]	Did not account for key confounders (injury severity, age, depth of shock)
Hedges 2009[43]	Incorrect comparison: surgery versus conservative treatment
Henzler 2007[44]	No data on delay due to triage
Honeybul 2013[46]	Not primary research
Jagannathan 2007[48]	Incorrect intervention: post 24 hours
John 2014[49]	Not primary research
Joosse 2012[50]	Did not account for key confounders (injury severity, age, depth of shock)
Josan 2006[51]	Incorrect comparison: surgery vs. conservative treatment
Kejriwal 2009[53]	No useful outcome data - study only reported p value in multivariable analysis
Kim 2010[54]	No clinical outcomes

Kim 2011[55]	No data on pre-hospital delay
Leach 2007[56]	No clinical outcomes linked to delay reported
Lee 1998[58]	Does not account for key confounders (age, injury severity, depth of shock)
Lee 2008[59]	No data on delay due to triage
Limpastan 2013[61]	Did not account for key confounder (injury severity)
Massaro 1996[64]	Did not account for key confounder (injury severity)
Mendelow 1979[65]	Did not account for key confounder (injury severity)
Messing-junger 2003[66]	Time from trauma to neurosurgical care was not reported
Munch 2000[69]	Incorrect intervention: post 24 hours
Naval 2010[70]	Incorrect comparison: direct transport vs. transferred
O'sullivan 1990[71]	No clinical outcomes linked to delay due to triage
Plesnila 2007[74]	Not primary research
Raj 2013[78]	Does not account for key confounders (age, injury severity, depth of shock)
Reed 2002[80]	No clinical outcomes reported
Richardson 2009[81]	No separate outcome data for head injury patients
Rivas 1988[83]	Does not account for key confounders (age, injury severity, depth of shock)
Rosenfeld 2000[84]	Incorrect study design: preventable death study
Rubiano 2009[85]	Incorrect intervention: post 24 hours
Seelig 1981[88]	No useful outcome data - study only reported p value in multivariable analysis
Servadei 1988[89]	Incorrect intervention: post 24 hours
Siddiqui 2004[91]	Incorrect study design: preventable death study
Sigurta 2013[92]	No comparison of patients by delay due to triage
Splavski 1998[94]	Delay to neurosurgery not linked to clinical outcomes
Tagliaferri 2012[96]	Mixed population. No separate results presented for 57% with traumatic brain injury
Taylor 2001[98]	Incorrect interventions: surgery vs. conservative
Thomale 2010[99]	No data on delay due to triage
Tian 2008[100]	Logistic regression includes patients operated on after 24 hours
Tiesman 2007[102]	Does not account for key confounders (age, injury severity, depth of shock)
Vavilala 2014[104]	Clinical outcomes linked to transfer not timing
Wang 2007[106]	Incorrect interventions: not neurosurgery
Wang 2014[107]	No details of pre-hospital delay
Welkoborsky 2011[108]	Not in English language
Wen 2011[109]	Incorrect interventions: surgery vs. conservative
Wilberger 1990[110]	Does not account for key confounders (age, injury severity, depth of shock)
Wilberger 1991[111]	Does not account for key confounders (age, injury severity, depth of shock)
Woertgen 2006[113]	No clinical outcomes linked to delay due to triage
Yatsushige 2009[114]	Comparator groups differ in prognosis
Zafrullah arifin 2013[115]	No clinical outcomes linked to delay due to triage
Zhao 2009[116]	Does not account for key confounders (age, injury severity, shock)

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L.2 Delay to blood transfusion

L.2.1 Introduction

L.2.2 Review question: Delay to blood transfusion

For full details see review protocol in Appendix A.

Table 27: PICO characteristics of review question

Population	*Children, young people and adults who have experienced a traumatic incident.*
Intervention(s)	Blood transfusion at different time points (as identified by the literature) to a maximum of 24 hours
Comparison(s)	Comparison of above
Outcomes	Critical: • Mortality up to 12 months • Health-related quality of life • Length of hospital stay • Number of procedures • Adverse events • GOS (head injury)
Study design	RCTs or systematic reviews of RCTs; cohort studies that use multivariate analysis to adjust for key confounders (injury severity, age, depth of shock, degree of head injury) or were matched at baseline for these if no RCTs retrieved

L.2.3 Clinical evidence

No relevant studies were identified.

L.2.4 Evidence statements

Clinical

No relevant clinical studies were identified.

Economic

No relevant economic evaluations were identified.

Appendix A - Review protocols

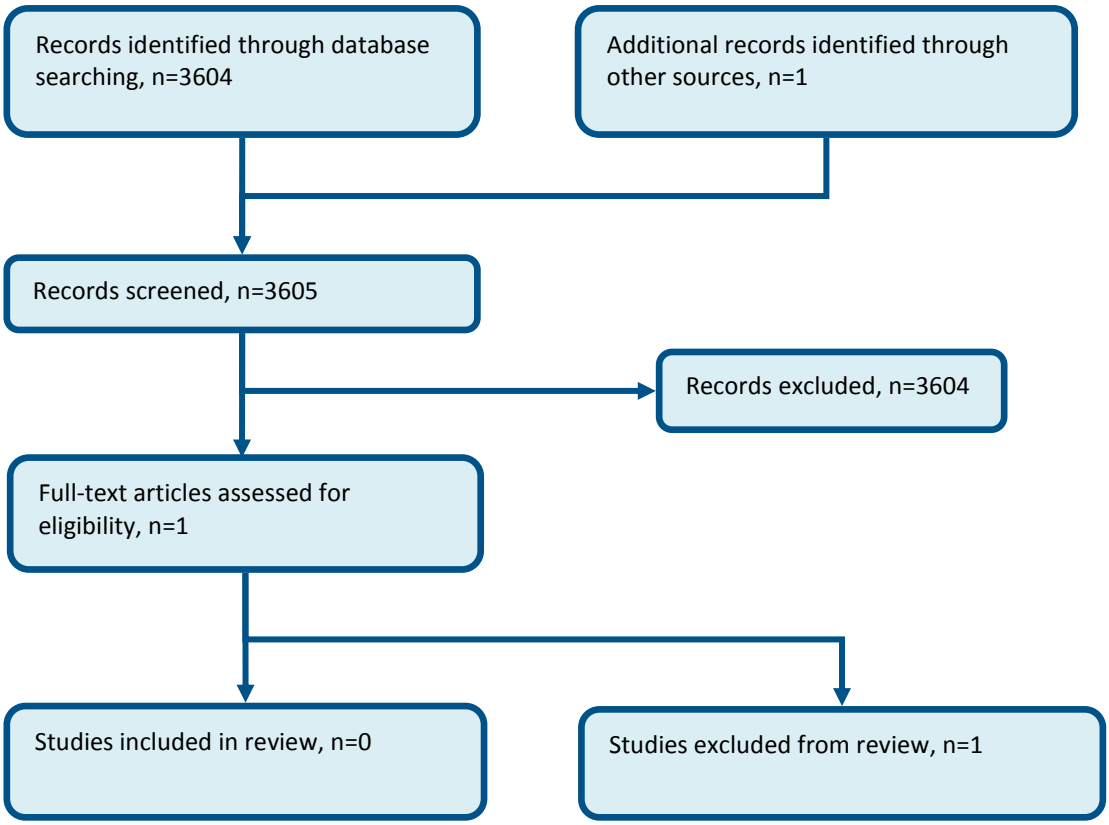
Table 28: Review protocol: Delay to blood transfusion

Review question:	**What is the optimal timing of Intubation/surgical airway**
Objective:	• To determine the differential impact on clinical outcomes of a delay to definitive treatment • How does time from injury to definitive treatment impact outcomes? • Impact of different pre-hospital competency on the relationship above • Impact of the quality of transfer on the relationship above • Impact of who receives the trauma patient in hospital on the relationship above • Impact of who receives the trauma patient in hospital on the relationship above • How may pre hospital competency, triaging decisions, quality of transfer, staffing

Review question:	What is the optimal timing of Intubation/surgical airway
	arrangements and location of services, and use of pre alert systems impact on delay>
Population	Children, young people and adults who have experienced a traumatic incident.
Intervention	Intervention at different time points (as identified by the literature) to a maximum of 24 hours
Comparison	Comparison of the above
Outcomes	Critical: • Mortality up to 12 months • Health-related quality of life • Length of hospital stay • Number of procedures • Adverse events • Amputation (for vascular compromise) • GOS (head injury) Data to be collected: • "Survival" analysis data • Important follow-up time points • 4 hours, 24 hours, 7 days, 1 month, 1 year? Population size and directness: • No limitations on sample size • Studies with indirect populations will not be considered.
Exclusion	Burns
Search strategy	Databases: Medline, Embase, the Cochrane Library Date: All years Language: Restrict to English only Study designs: RCTs or systematic reviews of RCTs; cohort studies that use multivariate analysis to adjust for key confounders (injury severity, age, depth of shock, degree of head injury) or were matched at baseline for these if no RCTs retrieved
The review strategy	Quality of life data: Collect all data for the stated QoL measure, for meta-analysis and GRADE report only overall scores Appraisal of methodological quality: The methodological quality of each study will be assessed using NICE checklists and GRADE.
Analysis	Stratification from outset MTC/TU (Where intervention was done) Presence of a given staff member (that is, a doctor) Pre-hospital intubation. Sub-groups if between-study heterogeneity exists Age (children and adults): child (0-15 years); young people (16-17 years); adults (18-65 years; >65 years) Within-study confounders to consider (if cohorts used) Age, injury severity, GCS and depth of shock,

Appendix B - Clinical article selection

Figure 11: Flow chart of clinical article selection for the review of delay to blood transfusion



Appendix C - Excluded clinical studies

Table 29: Studies excluded from the clinical review

Study	Exclusion reason
Holcomb 2015[45]	Blood and plasma transfused

L.3 Delay to surgery

L.3.1 Introduction

Sometimes vascular surgery or surgery for bleeding can be delayed for a variety of reasons including selective non-operative management or imaging. The aim of this review was to determine whether such a delay would lead to poorer patient outcomes.

L.3.2 Review question: Does delayed surgery lead to poorer outcomes?

For full details see review protocol in Appendix A.

Table 30: PICO characteristics of review question

Population	Children, young people and adults who have experienced major trauma
Objective	To determine if delayed surgery leads to poorer outcomes
Intervention	Vascular surgery (for example, fasciotomy, laparotomy, arterial shunt, debridement, intraluminal shunt, distal thrombectomy, vascular shunt) Surgery for bleeding (for example, laparotomy)
Comparison	Comparison of immediate versus delayed surgery
Outcomes	Critical: • Mortality • Quality of life • Length of stay • No of procedures • Adverse events
Study design	RCTs or systematic reviews of RCTs; cohort studies that use multivariate analysis to adjust for key confounders (injury severity, age, depth of shock, degree of head injury) or were matched at baseline for these if no RCTs retrieved

L.3.3 Clinical evidence

No RCTs relevant to this review were identified. Two retrospective cohort studies investigating the association of delayed laparotomy on patient outcomes were included in the review. [3,73] These are summarised in Table 3 below. Evidence from one study[73] is described in the summary of findings table (Table 3) and for the other study[3] described narratively in Table 4 and Table 5. See also the study selection flow chart in Appendix B, study evidence tables in Appendix E, forest plots in Appendix D, GRADE tables in Appendix G and excluded studies list in Appendix H.

Table 31: Summary of studies included in the review

Study	Intervention and comparison	Population	Outcomes	Comments
Barbosa 2013[3]	Cox proportional hazards model used to examine impact of increasing time to operation on in-hospital survival at 24 hours and 30 days of patients (n=115) that underwent laparotomy within 90 minutes of presentation and had a focused assessment with sonography for trauma (FAST) performed	Database of the PROMMTT Data Coordinating Center at the University of Texas Health Science Center at Houston was reviewed retrospectively, which enrolled patients who required the highest level activation at one of ten level 1 trauma centres and who subsequently received one or more units of red blood cells within six hours of hospital admission. Exclusion criteria included age less than 16, transfer from another hospital, pregnancy, more than 20% burn injury, inhalation injury, incarceration, cardiopulmonary resuscitation lasting more	Time to operation impact on in-hospital mortality at 24 hours and at 30 days	No comparison between groups. Cox proportional hazard model including Injury Severity Score, age, base deficit and hospital site

Study	Intervention and comparison	Population	Outcomes	Comments
		than five minutes prehospital or in the first 30 minutes after admission, and death within 30 minutes of hospital admission		
Peev 2015[73]	Early laparotomy. Performed within 120 minutes of admission to the emergency room. Median time to OR 43 (IQR 34-61) minutes. Delayed laparotomy. Selective non-operative management protocol which is an 'active' process and patients may switch to laparotomy if the haemodynamic condition or the abdominal clinical exam changes. Median time to OR 246 (172 to 419) minutes.	All patients (n=190) with abdominal stab wounds and gunshot wounds who received a laparotomy at the Massachusetts General Hospital, 2004-2012. Patients who underwent an emergency room thoracotomy or died shortly after were excluded.	Any complication, Complication grade 3,4,5 (Clavien-Dindo classification)	Statistically significant difference between the groups for blood loss, intraoperative packed red blood cells and fresh frozen plasma, CT performed and FAST performed and positive. Multivariate analysis performed to adjust for these differences.

Table 32: Clinical evidence profile: Early (less than 120 minutes) versus delayed (more than 120 minutes) laparotomy

Outcome	Number of studies (number of participants)	Imprecision	GRADE rating	Absolute difference (Laparotomy >120 m)	Early laparotomy mortality	Delayed laparotomy mortality
Any complication	1 (n=153)	Serious	Very low	OR (95% CI) = 0.39 (0.16 to 0.98), p=0.045 [a]	-[b]	[b]
Complication Grade 3,4 or 5	1 (n=153)	Very serious	Very low	OR (95% CI) = 0.68 (0.26 to 1.77), p=0.43	-[b]	[b]
Hospital length of stay > 5 days	1 (n=153)	None	Low	OR (95% CI) = 4.11 (1.76 to 9.58); p = .00011[a]	-[b]	[b]

(a) Absolute difference is not calculated as data was calculated using multivariate analysis and no raw data was provided
(b) No raw data was provided

Narrative findings

The study reports the association between increasing time to laparotomy with survival in patients with a positive FAST exam.[3] The authors examined a subset of patients from a trauma database that had a FAST performed and underwent laparotomy within the first 90 minutes after hospital admission. This time point was selected because they sought to exclude patients that underwent operation in a delayed fashion for missed injury or failure of planned non-operative management. Their examination of the distribution of T-OR for the entire database (n=1245) suggested that 90 minutes from initial presentation was a natural cut-off for this. The authors created cox proportional hazards models including Injury Severity Score (ISS), age, base deficit, hospital site, and time to operation (T-OR). They also created the same models using the time interval between performance of the FAST and the operating room (T_{FAST}-OR). In-hospital mortality at 24 hours and 30 days was studied. The authors report the hazard ratios in terms of 10-minute intervals in T-OR or T_{FAST}-OR.

Table 33: Mortality at different time points among patients with a positive FAST undergoing laparotomy in less than 90 minutes (n=115)

Time	% mortality
2 hours	3.5
6 hours	5.2
12 hours	10.4
24 hours	11.3
72 hours	12.1
30 days	20.0

Table 34: Multivariable Cox proportional hazards model demonstrating association of increased time to laparotomy with increased mortality

Time	T-OR	T_{FAST} OR
24 hours	HR for each 10 minute increase 1.50; CI 1.14-1.97; p=0.003	HR for each 10 minute increase 1.34; CI 1.03-1.72; p=0.03
30 days	HR for each 10 minute increase 1.58; CI 1.18-2.10; p=0.002	HR for each 10 minute increase 1.40; CI 1.06-1.84; p=0.02

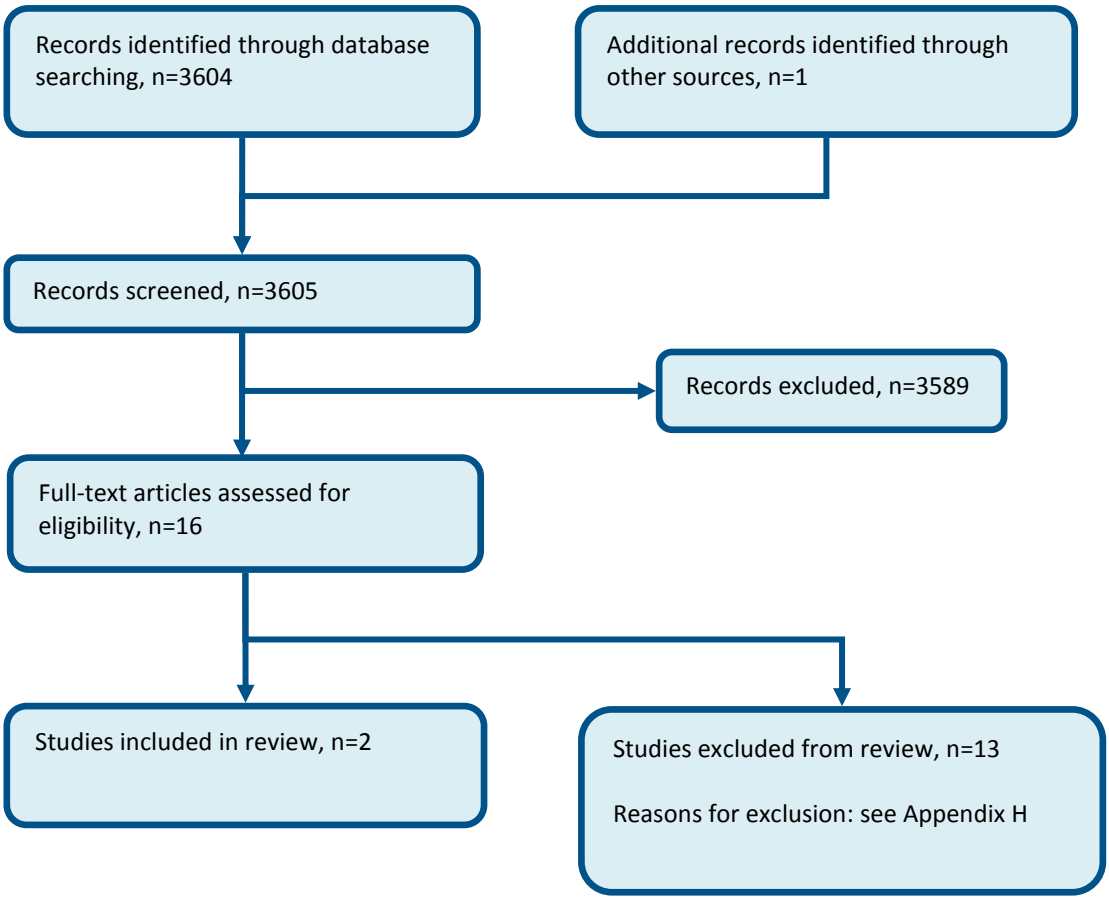
1 **Appendix A - Review protocols**

2 **Table 35: Review protocol: Delay to intervention - surgery**

Review question	Does delayed surgery lead to poorer outcomes?
Guideline condition and its definition	Major trauma. Definition: People with life threatening condition or loss of major limb
Objectives	To see if delayed surgery leads to poorer outcomes
Review population	Patients with major trauma
	Adults 18 years and over Children 17 years or under Overall
	Line of therapy not an inclusion criterion
Interventions and comparators: generic/class; specific/drug (All interventions will be compared with each other, unless otherwise stated)	Surgery; Immediate Surgery; Delayed
Outcomes	Critical: • Mortality • Quality of life • Length of stay • No of procedures • Adverse events
Study design	RCTs or systematic reviews of RCTs; cohort studies that use multivariate analysis to adjust for key confounders (injury severity, age, depth of shock, degree of head injury) or were matched at baseline for these if no RCTs retrieved
Unit of randomisation	Patient
Crossover study	Not permitted
Minimum duration of study	Not defined
Other inclusions	Matched on confounders or analysis adjusted
Subgroup analyses if there is heterogeneity	- Age (Children 0-15; Young people 16-17 years; Adults 18-65 years; Adults 65 years and over); Children may have different outcomes
Search criteria	Databases: Date limits for search: Language:

Appendix B - Clinical article selection

Figure 12: Flow chart of clinical article selection for the review of delay to intervention - surgery



Appendix C - Forest plots

Figure 13: Any complication

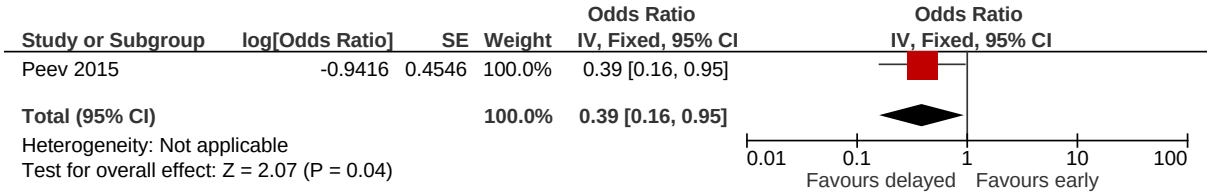


Figure 14: Complication grades 3,4 and 5

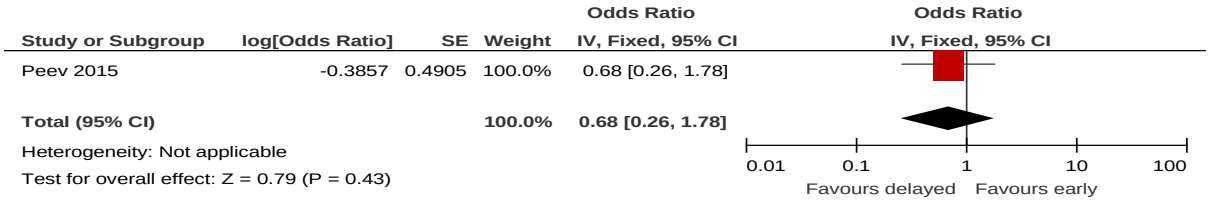
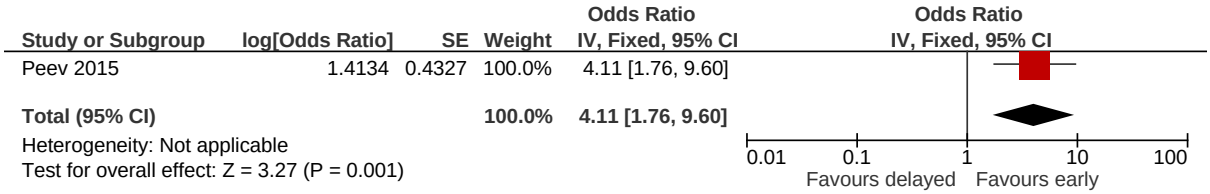


Figure 15: Hospital length of stay more than 5 days



Appendix D - Clinical evidence tables

Table 36: Barbosa 2013[3]

Study	Decreased survival with increasing time to laparotomy trial: Barbosa 2013 [3]
Study type	Retrospective cohort study
Number of studies (number of participants)	1 (n=115)
Countries and setting	Conducted in USA; Setting: Database created by PROMMTT Data Coordinating Center at the University of Texas Health Science Center at Houston for the PROMMTT study, which enrolled 1245 injured, consecutive patients who required the highest level of activation at one of ten level 1 trauma centres and who subsequently received one or more units of red blood cells within six hours of admission.
Line of therapy	1st line
Duration of study	Intervention + follow-up:
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall:
Subgroup analysis within study	Not applicable:
Inclusion criteria	Subset of patients (n=115) that had FAST performed and underwent laparotomy within first 90 minutes after hospital admission.
Exclusion criteria	age less than 16 years, transfer from another hospital, pregnancy, more than 20% burn injury, inhalation injury, incarceration, cardiopulmonary resuscitation lasting more than five minutes pre-hospital or in the first 30 minutes after admission, and death within 30 minutes of hospital admission
Recruitment/selection of patients	Subset of patients (n=115) that had FAST performed and underwent laparotomy within first 90 minutes after hospital admission. Time point was selected as authors sought to exclude patients that underwent operation in a delayed fashion for missed injury or failure of planned non-operative management. Examination of the distribution of time to operation for entire database suggested that 90 minutes from initial presentation was a natural cut-off point for this.
Age, gender and ethnicity	Age - Mean (SD): 37 years (16). Gender (M:F): 4/1. Ethnicity: not mentioned
Further population details	1. Age: Adults 18-65
Indirectness of population	No indirectness
Interventions	(n=115) Intervention: Surgery. Laparotomy. Duration 24 hours and 30 days. Concurrent medication/care: Comments: Hazard ratio of delay of intervention on in-hospital mortality was studied. No separate groups; no delay

Study	Decreased survival with increasing time to laparotomy trial: Barbosa 2013 [3]
	was intentional. n=115 overall
Funding	Academic or government funding (US Army Medical Research)
Study	Decreased survival with increasing time to laparotomy trial: Barbosa 2013 [3]
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: IMMEDIATE versus DELAYED Protocol outcome 1: Mortality at Define - Actual outcome: In-hospital mortality calculated using Cox proportional hazards model at 24 hours and 30 days; Risk of bias: Low; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at Define; No of procedures at Define; Adverse events at Define; Glasgow Outcomes Scale at Define; Length of stay at Define

Table 37: Peev 2015[73]

Study	Peev 2015[73]
Study type	Retrospective cohort study
Number of studies (number of participants)	1 (n=190)
Countries and setting	Conducted in Unknown, USA; Setting: Level 1 trauma centre
Line of therapy	1st line
Duration of study	Intervention + follow-up: Length of hospital stay
Method of assessment of guideline condition	Adequate method of assessment/diagnosis
Stratum	Overall
Subgroup analysis within study	Not applicable
Inclusion criteria	As above
Exclusion criteria	Patients who underwent an emergency room thoracotomy or died shortly after were excluded.
Age, gender and ethnicity	Age - Range of means: 29.2 to 30.5. Gender (M:F): 95% male. Ethnicity: Not reported
Further population details	1. Age: Not applicable/Not stated/Unclear
Extra comments	All patients with abdominal stab wounds and gunshot wounds who received a laparotomy at the Massachusetts General Hospital, 2004-2012.

Study	Peev 2015[73]
Indirectness of population	No indirectness
Interventions	(n=153) Intervention 1: Surgery - Immediate. Early laparotomy. Performed within 120 mina of admission to the emergency room. Established practice is to take patients with penetrating injuries immediately to the operating room if the decision is made based on clinical symptoms and signs. A CT was available within 20 minutes. Median time to OR 43 (IQR 34-61) min. Duration Not relevant. Concurrent medication/care: Not reported (n=37) Intervention 2: Surgery - Delayed. Delayed laparotomy. Selective non-operative management protocol which is an 'active' process and patients may switch to laparotomy if the haemodynamic condition or the abdominal clinical exam changes. Median time to OR 246 (172 to 419). Duration Not relevant. Concurrent medication/care: Not reported
Funding	No funding
RESULTS (NUMBERS ANALYSED) AND RISK OF BIAS FOR COMPARISON: IMMEDIATE versus DELAYED Protocol outcome 1: Length of stay at Define - Actual outcome: Length of stay > 5 days at Not applicable; OR 4.11 (95%CI 1.76 to 9.58); Risk of bias: High; Indirectness of outcome: No indirectness Protocol outcome 2: Adverse events at Define - Actual outcome: Any complication at Length of hospital stay; OR 0.39 (95%CI 0.16 to 0.98); Risk of bias: High; Indirectness of outcome: No indirectness - Actual outcome: Complication Grade 3,4,5, at Length of hospital stay; OR 0.68 (95%CI 0.26 to 1.77); Risk of bias: High; Indirectness of outcome: No indirectness	
Protocol outcomes not reported by the study	Quality of life at Define; Glasgow Outcomes Scale at Define; Mortality at Define; No of procedures at Define

Appendix E - GRADE tables

Table 38: Clinical evidence profile: Early (less than 120 minutes) versus delayed (more than 120 minutes) laparotomy

Quality assessment	No of patients	Effect	Quality	Importance

No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other	Delayed (>120 minutes)	Early laparotomy	Relative (95% CI)	Absolute		
Any complication												
1	Observational studies	No serious risk of bias	No serious inconsistency	No serious indirectness	Serious[a]	None	-	0%[b]	OR 0.39 (0.16 to 0.98)	[c]	VERY LOW	CRITICAL
Complication Grade 3,4,5 (assessed with: Clavien-Dindo)												
1	Observational studies	No serious risk of bias	No serious inconsistency	No serious indirectness	Very serious[a]	None	-	0%[b]	OR 0.68 (0.26 to 1.77)	[c]	VERY LOW	CRITICAL
Hospital length of stay > 5 days												
1	Observational studies	No serious risk of bias	No serious inconsistency	No serious indirectness	No serious imprecision	None	-	0%[b]	OR 4.11 (1.76 to 9.58)	[c]	LOW	CRITICAL
Quality of life												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL
No of procedures												
0	-	-	-	-	-	-	-	-	-	-	-	CRITICAL

(a) No explanation was provided
(b) No adjusted raw data presented
(c) Generic inverse variance

Appendix F - Excluded clinical studies

Table 39: Studies excluded from the clinical review

Study	Exclusion reason
Clarke 2002[18]	No baseline data reported early versus late
De boer 1982[26]	No details of baseline variables
Faber 2012 [34]	Fasciotomy performed after vascular surgery
Lee 1984[60]	No details of baseline variables
Lu 1993[63]	No early versus late comparison
Pommerening 2014[75]	Wrong comparison
Poole 1994[76]	Wrong comparison
Rabin 2014[77]	Groups not matched on ISS and no adjustment in analysis
Reed 2006[79]	Delayed group greater than 24 hours
Ritenour 2008[82]	Differences at baseline and no adjustment in analysis
Sheridan 1976[90]	Not all trauma patients
Simmons 2011[93]	No details of GCS or shock
Tanizaki 2014[97]	No details of baseline variables
Velmahos 1997 [105]	Fasciotomy performed after vascular surgery
Williams 1997[112]	Late fasciotomy included patients >36 hours

Appendix M: Major trauma service delivery systems model

M.1 Introduction

Chapter 6 summarises the services and skills recommended across the following NICE guidelines on different aspects of trauma care: Complex Fractures CG XXX; Fractures CG XXX; Major Trauma CG XXX; Spinal injuries assessment CG XXX; and Major Trauma Services CG XXX. To further explore the impact of the clinical recommendations on trauma services we aimed to develop a service systems model evaluating different service configurations. This appendix describes in detail the approach to the systems model.

M.2 Methods

M.2.1 Background to analytic framework and conceptual modelling

The analytic framework of the trauma service guidance evaluative process was based on the premise that all parts of a service system are interconnected to an extent. Through processes of iterative refinement we sought to simplify the service system by assessing the strength of association between different components of the system and identify which, if any, of the components could be evaluated as distinct entities using traditional NICE methodologies of systematic review. The remaining components were considered as candidate topics which could benefit from exploration through systems modelling. The stages undertaken in the conceptual modelling exercise have been defined in Chapter 6.

M.2.2 Introduction to topics considered to benefit from systems modelling

Whilst the stages of conceptual modelling activity aimed at refining the decision problems which may benefit from a systems approach, it also opened and broadened discussion on the difficulty of assessing trade-offs looking at potential service strategies to reduce costs and enhance service efficiency whilst maintaining optimal clinical outcomes through provision of timely care. Such trade-offs could be explored and framed through a multitude of questions. For example:

- What prediction tools are the most accurate at predicting a safe outcome when the patient is received by a trauma unit as opposed to a major trauma centre, or by a core trauma team as opposed to an advanced trauma team?
- What type of injury or level of severity does a trauma patient need in order to benefit more from a MTC than a trauma unit?
- What type of injury or level of severity does a trauma patient need in order to benefit more from a MTC within a certain timeframe? What is the prognosis of a person if MTC services are not provided in a certain time frame?
- What is the definition of a correct referral to an MTC, and how do you determine a true positive if you are not sure of the extent of the benefit of an MTC vs TU for a particular person?
- Who is at risk if the UK model moves towards fewer specialities available as part of the core trauma team as part of a tiered response?
- Who can safely be treated without, or with “delay”, of this speciality involvement?
- How much benefit does having these “speciality” staff available promptly have on the outcomes for given groups?
- How frequent are cases where immediate specialist input is required?

- Is this benefit sufficient to outweigh the opportunity cost of enabling prompt access (given over triage rates/false alarms etc.)?
- How can we measure the opportunity cost of "wasted" staff time/hospital disruption?
- What information needs to be recorded pre -hospital to predict what health care staff needs to be there on arrival?
- What are the ambulance tools attempting to predict?
- How does anticipated journey time and quality of transfer influence triaging and initial destination decisions?

It is clear that the answer to any one of the given questions will not be able to provide sufficient information to design a system in its entirety; rather, it simply provides information on one piece of a very complex and dynamic picture. With this in mind, the system model comparators, structure and related systematic evidence review protocols were designed to gather as much of the essential information as possible using the maps described in the above stages as a precursor to discussion. Details of the system model are reported in section M.2.3.

There are various strategies which aim to ensure that a person with traumatic injury receives the right services in a timely way. From the conceptual mapping discussion, developers felt the following scope topic areas may benefit from being explored via systems model:

- Application of triage tools
- Pre-alert
- Tiered trauma teams

It was noted that travel times, skills and expertise of pre-hospital staff, quality of transfer and staffing arrangements within hospital (on call and outreach) may influence or be influenced by the above key areas.

M.2.2.1 Application of triage tools

The first step in such strategies is accurately triaging the patient at scene, ensuring that the patient is conveyed to a provider with the most appropriate services to treat their condition.

The current assumption which underpins UK trauma triage is that people with major trauma (defined as having an ISS of 15 or greater) would benefit from services provided within a major trauma centre (MTC), and those patients with less serious trauma could be safely treated in a trauma unit. If the initial triaging decision is incorrect, the patient could incur critical delay in reaching the appropriate service to treat their condition. Alongside potential clinical harm, there will be costs of transfer of such patients to the appropriate place of treatment and additional downstream costs associated with clinical complications from delayed treatment.

However, exploring and evaluating the optimal strategy of roadside triage is not straight forward, as the majority of patients to whom the tool is applied will not have a time-critical major trauma injury and can be safely treated at a trauma unit. Whilst over-triage to an MTC does not carry safety risks to the patient concerned, inappropriate trauma team activation can cause disruption to the MTC hospital services detracting staff and diverting resources from other patients. In many geographical locations, the MTC may be far from the patient's residence and unnecessary repatriation transfer costs to their local provider would be incurred.

On the other hand, under-triage could result in direct clinical harm for the patient as well as unnecessary resource use as the patient will require a further transport to a MTC. However, the rarity of major traumatic incidents alongside the expertise available to stabilise at trauma units should be taken into account when considering the risk of under-triage and subsequent absolute harm that may be incurred. Where there is time-critical injury, it may be that such patients require prompt treatment such as airway stabilisation which could be provided at a trauma unit and delay in

receiving such treatment may lead to a greater harm than a delay in reaching a MTC for their other injuries.

Further complication in the evaluation of roadside triage is added with the consideration of the expertise available on scene. A clinical staff member who is competent in airway management may allow for patients to be safely transported for longer distances to a MTC avoiding bypass to a trauma unit – this may be sufficient to sway the triaging decision. Added to this, the experience and competency of the attending pre hospital staff member may impact on the interpretation of the triage tool and alter its accuracy, or indeed negate the need for a tool to assist the triaging decision. The expertise promptly available on scene is greatly dependent on dispatch decision making, and generally it would not be considered appropriate to send senior clinicians out to every call as the majority of trauma calls would not be considered major. With this in mind it is accepted that ambulance triage tools have a role to play but their value is uncertain.

Local service configuration inclusive of bypass policies, availability of expertise on scene, distances and time from injury to a given service, and the time critical nature of the injury become important factors within the triaging decision. Perhaps due to the plethora of criteria that inform the initial triaging decision, several ambulance triage tools exist across the UK. There remains little consensus on which adult UK ambulance triage tool performs in a superior manner, or indeed the extent local service configuration should play a role within these tools.

M.2.2.2 Pre-alert information for tiered trauma team activation

Further steps in strategies to reduce delay to timely treatment may include using information collected in the triaging activity or relaying information about treatments given during transport to the staff at the receiving hospital (also known as pre-alert activation). Such information may allow for the presence of staff receiving the patient at hospital to be tailored to patient need, avoiding unnecessary disruption through call outs of staff who are not needed. A tiered team response according to pre-alert may be a means of balancing the trade-off between over staffing patient reception and potential time delays to appropriate treatment which could be incurred with under staffing.

M.2.3 System model objectives

The systems model objectives were drawn up to identify key changes in the system the GDG wished to explore and under which constraints. The most important objective of the modelling activity was to link service changes and recommendations to the key patient outcomes of survival and quality of life, through the determination of how a service change altered the extent of delay to definitive treatment (inclusive of appropriate discharge with no intervention). In order to understand this link, it was necessary to determine the differential impact of a delay to definitive treatment on clinical outcomes, and the index conditions (subgroups) to be modelled were selected in part with this aspect in mind. Equally, we were interested in how various factors identified across the scope of the guidance may impact on this relationship. Such factors may be:

- pre-hospital competency
- transport times and quality of transfer
- who receives the trauma patient in hospital (tiered teams)

The model objectives are outlined in the below table. To note, constraints indicate what should be kept constant when exploring the service issue in the first instance. However, such constraints could be lifted or modified within a sensitivity analysis to explore the impact a change in this parameter may have on the overall service. In this way, one service model can explore many service issues and potential changes highlighted in the scope.

The population of interest, compared strategies, and specific outcomes of interest to meet the model objectives are detailed afterwards.

Table 40: Model specifications

Purpose (what the model hopes to measure)	To explore the extent of delay to definitive treatment (inclusive of appropriate discharge with no intervention). Definitive treatment may be the initial surgery, interventional radiology, admission to ICU, time of stabilisation.
Change (the key change in service configuration to be explored)	When using different pre hospital triage interventions, and using pre-hospital information in different ways to determine which staff should be immediately available on patient arrival (in other words incorporating pre-alert information and tiered trauma teams).
Target performance (what we want to achieve or avoid above all else when determining which change is optimal)	• To enable a reduction in "in-active staff time" whilst maintaining the same clinical outcomes as in current practice • To enable a reduction in resource use whilst maintaining the same clinical outcomes as in current practice • To enable a reduction in patient time spent in system whilst maintaining the same clinical outcomes as in current practice

Constraints (factors which need to be taken into account and should be kept constant in the first instance to explore the service change)	• The grades/types of staff available at any given MTC/trauma unit
	• On call rota/onsite rota arrangements – location of staff
	• Person/team on scene and intervention and time on scene [(a)]:
	  ○ The person or team on scene first may be: BASICS, pre hospital care doctor, paramedic crew, enhanced paramedic , emergency care practitioners, ambulance technician
	• Intervention on route
	  ○ In particular intubation
	• Epidemiology and demography
	  ○ Timing and location of the injury
	  – >> anticipated and real length of journey time
	  ○ Incidence of different types of traumatic injury
	  ○ Seasonal variation
	  ○ Proportion of elderly in population.
	• Prognosis of a given type of trauma
	• Effectiveness of interventions (at different time points, by different staff)
	• Interventions pre hospital in part determined by pre-hospital staff available
	• Specification of definitive treatment
	• Accuracy of triage tools /judgement may change according to situation on scene
	• Method of transport. (different quality of transfer and what you can do on route)
	• Potential miscommunication through control centres when relaying pre-alert information or dispatch teams.

Outcomes	• Time in system • Delay to definitive intervention • Survival, Quality of life

	• Costs and resource use (staff hours used for definitive management, LOS) • Number of interventions (blood tests and imaging) • Discharge without admission • Number of transfers • Number treated in MTC • Number first referred and treated only in TU

(a) Note that time on scene in part depends on the interventions undertaken and by type of patient – i.e. children less time on scene). Such factors are likely to be correlated with who the first attenders are.

M.2.3.1 Population

The population considered in the model were adults who had suspected trauma and required services at a trauma unit or MTC. It was felt that although triage of children was an important issue, without consensus on an adult tool it was unlikely a universally applied ambulance triage tool in children would be accepted. Further to which, service consideration and clinical pathways for children would differ than that for adults, and may require separate model inputs and parameters.

Sub populations

To assist evaluation of the service, key sub populations with specific traumatic injuries were identified as "index conditions". These index conditions were identified and prioritised according to the potential to:

- Illustrate service functioning for patients experiencing:
  a. a common traumatic injury
  b. a rare traumatic injury
- enable the time critical nature of acute care on health outcomes to be captured
- explore functioning of the system for injuries which require intensive resource use or the treatment thereof may impact system efficiency
- address uncertainty regarding a service delivery issue of importance to stakeholders or developers which would otherwise remain unclear.

For developers, it was important to examine subgroups for which there was less certainty in determining firstly whether the condition was time-critical, and secondly who would benefit from MTC services versus TU services. In particular the GDG were interested in exploring whether reduction in delay in haemorrhage control (which could only be definitively treated at an MTC) should take priority over time to a definitive airway management (and a potential bypass delay to a trauma unit) if the airway could be managed.

The index conditions identified were:

1. Patients with a compromised airway and require
   - intubation or surgical airway
2. Patients with blood loss and require
   - Imaging to identify blood loss (as a treatment enabler)
   - surgery for bleeding control
   - interventional radiology
   - blood transfusion
3. Patients with chest trauma and require
   - laparotomy/thoracotomy
4. Patients with vascular compromise and require

- vascular surgery

5. Patients with head injury and require
   - neurosurgery
   - neurological ICU
6. Patients with open fracture and require
   - ortho-plastic services for debridement, fixation and cover.

M.2.3.2 Comparators of interest

The model hoped to inform on the potential outcome of combining different service components within one strategy.

The service strategies assessed consisted of:

- Use of an ambulance triage tool ±
- provision of pre alert information ±
- a given level of staffing at the receiving centre (i.e. a tiered team response)

The service strategies were assessed in relation to their ability to reduce delay in receiving appropriate care. Thus, the model could implicitly compare the effectiveness and cost effectiveness of care given at different time points within this evaluation.

The detail contained within each component of the strategy are outlined in the below in Table 41. In addition to the strategies outlined in this matrix, additional variations on the strategies could be explored by sensitivity analysis (i.e. varying the time it takes for staff to arrive on site according to type of rota).

Protocols were drawn up for the application of triage tools, pre-alert, trauma team response, access to airway management, access to interventional radiology for haemorrhage control. It was anticipated that recommendations for these scope areas would be drafted from the model. In addition, protocols on access to other interventions important to people with major trauma (including neurosurgery) were made to populate the model with additional data but recommendations would not be made on these reviews (see Chapter 6 for the supporting evidence reviews).

Table 41: Service strategies under comparison

Ambulance triage tools	Pre-alert information	Tiered team response
a) Application of triage tool by itself Example clinical triage tools: • Circulation, Respiration, Abdominal Motor and Speech Scale • The trauma score • The current London 'major trauma decision tool' (the Healthcare for London Major Trauma Programme Pre- Hospital Care Group in 2010). • American College on Surgeons Committee on Trauma Field Decision Tool. • American College of Surgeons triage decision scheme • GAP (GCS, BP, age) • MGAP (mech of injury) • Other UK ambulance trust triage tools as identified by the literature or GDG members Key components of a triage tool: Physiology, mechanism of injury, obvious injury at scene. Other factors: elderly, pregnancy **b) Clinical triage tool being applied with clinical judgement of** • Advanced practitioners • Paramedic • Ambulance technician **c) No application of triage tool** • Automatic transfer to MTC • Automatic transfer to nearest hospital (TU/MTC)	Example pre-alert information: • ATMIST information (Age of patient, Time of incident, Mechanism of injury, vital Signs, and Treatment given)	Examples of staffing in team response: At reception may be an ED clinician or Triage nurse **a) Basic response:** • ED consultant, ED registrar (st4), nurse (grade 6 or 7) **b) Standard response:** • ED consultant, ED registrar (st4), 2 nurses (grade 6 or 7), anaesthetist (registrar, st4), OT surgeon (st4), general surgeon (st4), radiographer. • If paediatric patient then paediatric surgeon, paediatric anaesthetist and paediatrician. **c) Advanced response:** • Standard + extra surgical consultant + anaesthesia consultant. Extras may include orthopaedic, vascular, plastic or cardio-thoracic surgeons, obstetrics and gynaecology, urology, maxillofacial, paediatric, neurosurgery, radiologist.
	a) No application of a pre alert system (also applicable for walk ins)	**Trauma Unit** • Reception will call for a standard team response. Immediate interventions may include stabilisation and imaging (x-ray, CT and MRI variable). The standard response team will call extras as required (i.e. staff for general surgery, anaesthesia, T&O, obs and gynae, variable specialities in trauma unit) Note standard team may also ask for transfer to MTC, inclusive of patients who require neurosurgery, plastics, interventional radiology, vascular surgery; specific imaging unavailable at trauma unit **Major Trauma Centre** • ED clinician will call for a standard team response. Immediate

Ambulance triage tools	Pre-alert information	Tiered team response
		interventions may include stabilisation and imaging. • Triage nurse will call for basic trauma team, who then triages and calls a standard response, who then calls for advanced response
	b) Application of a pre alert system	**Trauma Unit** • Standard trauma team on arrival • Basic team on arrival, who upgrades, and then standard/or call and transfer • standard team on arrival with additional members called in • standard team on arrival, and transfer to MTC. **Major Trauma Centre** • Basic team + upgrade if required (to standard or advanced) + extras • standard team + upgrade if required (to advanced + extras) • Advanced team + call extras if required.
	c) Response tailored to information in pre-alert	**Trauma Unit** • Team on arrival dictated by information in pre alert • Possible advice given for direct transfer to MTC **Major Trauma Centre** • Team on arrival dictated by information in pre alert • Possible advice given for direct transfer to TU

Notes regarding links and scope of strategies assessed to other components of the system:

Direct transport to and staffing at a specialist centre (i.e. for neurosurgery or burns) was considered outside the scope of the topic addressed

The skill and competency level of staff available on scene will link to what interventions can be undertaken on scene, the quality of transfer and possibly the journey time which is acceptable. This in turn may impact on triaging decisions.

The key clinical difference between response strategies is the potential delay induced by waiting for on call specialists to attend to patient. Key opportunity cost is the inactive hours and subsequent

M.2.3.3 Time horizon, perspective, discount rates

The appropriate time horizon of analysis in part depends on the unit of analysis and prioritised outcome.

For evaluation of the trauma system itself, an annual horizon may be sufficient to evaluate service outcome measures (as this also takes into account potential for changes in seasonal demand and supply factors impacting the service). In order to evaluate the success of a service change in improving health outcomes, a more appropriate horizon is that which captures the full benefit (and possible cost) that accrues for patient over their life time.

It was anticipated that findings from any analysis would be presented using the time horizons outlined above. Associated economic analysis should follow the standard assumptions of the NICE reference case including discounting at 3.5% for costs and health effects (with a sensitivity analysis using a discount rate of 3.5% for costs and 1.5% for health benefits), use of an NHS provider perspective and results evaluated by incremental analysis.

M.2.4 Approach to systems modelling

M.2.4.1 Initial anticipated model structure

It was anticipated that a patient-level time-to-event simulation model would be the most appropriate to evaluate the service and was due to be built in simul8. This was due to:

- the patient heterogeneity within the patient population and the importance of the specific type of injuries sustained and patient characteristics in the triaging decision algorithms and also on the potential for deterioration;
- the availability of a UK individual patient level dataset to inform the model and to draw patients from, mirroring UK demography and epidemiology exactly;
- the importance of measuring time to events within the model;
- the ability to scale the model up to look at issues of limited resources or capacity if required at a later stage of development.

Initially review protocols were drafted to ensure broad consideration of data for modelling purposes; it soon became clear that evidence base was too limited to inform a systems model.

It was thought that TARN could provide the patient-level data to which a retrospective triaging decision could be applied; in addition, mortality could be obtained based on patient index group, and correct and incorrect destination of transport. This was not the case and the option of conducting the economic analysis based on TARN data was considered unfeasible. See M.2.5.1 for detail on the use of TARN data in this guidance and in the Major Trauma and Complex fracture Clinical Guidelines.

Therefore a simplified model focusing only on triaging tools was considered and this is reported in section M.2.4.2.

The following sections of the report detail on the anticipated use of data and programming of each component to inform the model objectives prior to the retrieval of data.

M.2.4.1.1 Entry into the model and assignment of key baseline characteristics

A patient would enter the model and baseline characteristics would be assigned to the patient, inclusive of those outlined in the triage tools to be assessed, the time of injury and type of injury (i.e.

whether the patient fell into one of the subgroups with an index condition). Such information would be assigned according to a random draw from a sample taken from TARN.

Where the patient fell into an index subgroup, information extracted from the clinical review control group, or from a TARN analysis, would inform the likely clinical outcome if no intervention was forthcoming. Using this information, time of expected death could be calculated and "scheduled" for that individual patient.

Assumptions according to local circumstance and geography would need to inform and label the patient with anticipated travel times to the nearest trauma unit and MTC. The distribution around such parameters could be varied within a scenario analysis to give information how triage decisions may change according to local geographical factors such as density of MTCs.

The rate of entry into the model and timing of injury in relation to time of day or season only becomes important if the model is required to explore the impact of demand and capacity, and waits are incorporated due to lack of available resources. Such information is important to include to demonstrate the potential impact of economies of scale on optimal staffing arrangements and configurations (i.e. on site for higher major trauma incidence rates versus on call for low incidence rates). Arrival rates and distributions could be tested within a scenario analysis to inform this aspect of service provision.

M.2.4.1.2 Pre-hospital triage decision and outcome

The next stage of the model involved determining the outcome of the pre-hospital triage decision. This could in theory be achieved in two ways.

Firstly, predictive and accuracy outcomes of a pre-hospital ambulance tool or decision maker found through the systematic evidence review could be applied to predict the likelihood that patient would be appropriately triaged to a MTC or trauma unit.

Secondly, if such data was not forthcoming, the tool criteria could be applied to the baseline characteristics of the patients, and thereby the decision which would have been reached had the tool been applied could be modelled. To understand whether the tool had been correctly applied, clinical members would need to indicate the preferable destination of the modelled patient given the baseline characteristics.

As a result from the application of the triage tool or clinical judgement, the patient would be routed to a MTC as a triage positive patient. This would either be the most appropriate place for the patient according to their main injury (true positive) or not as they could have been safely treated in a trauma unit (false positive). Alternatively the patient would be routed to a trauma unit as a triage negative patient. This would either be appropriate (true negative) or not as they require services only found within a MTC (false negative).

M.2.4.1.3 Time spent on scene

The need to programme, record and include time spent on scene will be dependent on the time point from which the clinical data on time to expected death was derived and whether or not it is necessary to factor in time required to stabilise, if the appropriate skills are present at the scene. In the first iteration it was assumed time spent on scene from injury would be the same for every patient and for every strategy employed, and therefore not considered further for modelling purposes.

M.2.4.1.4 Travel time to health provider

Before the patient is routed to the MTC or trauma unit, a check to see which centre is nearest would be programmed in the model. If the MTC is the closest provider of trauma services, it is assumed this is the correct location to attend in any circumstance (as an ambulance team would not travel further than the closest provider). Where a triage negative patient happens to be closer to a MTC than a TU, application of the triage tool is redundant in any case and an additional label would note this. The initial destination of the triage negative patient is then changed to an MTC.

At this point in the model, the patient should be labelled with its next destination (a MTC or TU) and the time it would take from model entry to arrive at this destination. If the expected time of arrival is later than the scheduled time of death due to injury, the modelled patient dies and exits the model with time recorded. If the expected time of death is after arrival at the destination then the patient continues to the next component of the model.

M.2.4.1.5 Requirement to stop at a trauma unit for stabilisation

Dependent on findings of the clinical guidelines and reviews, it may be apparent that an additional strategy of pit stopping and/or bypass needs to be evaluated as another component of the strategies being assessed. In such cases, outcomes of an additional strategy whereby triage positive patients further away from an MTC to TU should go via a trauma unit for stabilisation before continuing to their final destination should be evaluated. This could be programmed in at a later stage if required, noting that such action would alter the scheduled time of death for that injury.

M.2.4.1.6 Pre alert activation

Based on the outcome of the triaging decision, a pre-alert may be activated or not, according to the strategy being assessed in the model. Where pre-alert is activated, a label is attached to the patient indicating what response can be expected on arrival at their next destination without delay. To note, if the triage tool indicated that the patient was triage negative (i.e. needing the services of a trauma unit only) but due to their location they happened to be redirected to the nearest provider which was an MTC, the strategy would dictate that no pre alert nor tiered response is required. A standard response as per a trauma unit would be given. It is the outcome of triage decision, rather than the scheduled destination, that dictates the activation of the pre alert system.

M.2.4.1.7 Arrival at the destination and the clinical response received

This component of the model has the most important programming based on the initial destination, triaging decision, and pre-alert activation.

The first aspect to determine is whether the patient promptly receives the services they require. To do this we would use some “IF” programming statements outlined below.

If the patient is labelled as a true positive, they have been transported to an MTC, pre-alert has been activated, then we can assume that appropriate treatment is initiated promptly. The risk of mortality is amended in line with findings from clinical effectiveness data (either via a look up of survival rate for the time elapsed in the model or via application of a relative risk) and the time of death is rescheduled accordingly.

If the patient is labelled as a true negative, and they have been transported to an MTC or trauma unit then we can assume that appropriate treatment is initiated, and as the patient does not have a serious traumatic injury, survival can be designated in accordance with national life expectancy averages.

If the patient is labelled as a false positive, they have been transported to an MTC, pre-alert has been activated, then we can assume that appropriate treatment is initiated, and as the patient does not have a serious traumatic injury survival can be designated in accordance with national life expectancy averages. At this point it is noted that the initial destination for this patient was not appropriate only if a TU was closer than a MTC in the first instance. If the destination was inappropriate then this patient is routed to the trauma unit incurring the cost of repatriation transfer. If the MTC was the closest provider, no repatriation costs are involved.

If the patient is labelled as a false negative, they have been transported to a trauma unit and no pre-alert has been activated, then we cannot assume that appropriate treatment is given promptly. A time delay is assumed whilst the patient is admitted to the trauma unit for initial assessment and the additional travel time to reach the major trauma centre is added to the overall time delay incurred before reaching appropriate treatment. If the patient is labelled as a false negative but they have been transported to an MTC (because this was the closest facility) then the only delay encountered would be that due to the lack of pre-alert activation and of tiered response. Assumptions regarding the time taken to access on call team members (i.e. 30 minutes) would inform the additional delay incurred.

At this point the model would check to see if the newly calculated expected time of intervention occurs before the scheduled time of death. If the scheduled time of death occurred after the expected time of the appropriate intervention, then the patient is routed to that intervention and their risk and time of death is updated according to the extent of delay. If scheduled time of death occurs before the expected time of the intervention, then resources involved in the patients care up to that point in time would be recorded (i.e. transfer costs if the patient died within the travel time to the next destination) but the patient would exit the model before the risk of mortality could be updated.

Resources used in the patients care are tallied according to their clinical history labels. For example, if the patient has had a pre-alert activation and a tiered response at an MTC, then the cost of providing this response will be added to the patient's record, regardless of whether the response was appropriate or not. Likewise the cost of high dependency transfer from a trauma unit to a MTC will be added to those patients incorrectly routed to a trauma unit, or the lower cost of repatriation will be assigned to patients who inappropriately arrived at MTCs.

To note that the initial destination of an MTC for a false positive patient is only inappropriate if a TU was closer than a MTC in the first instance. If the destination was inappropriate then this patient is routed to the trauma unit incurring the cost of repatriation transfer. If the MTC was the closest provider, no repatriation costs are involved. Likewise if the initial destination for a false negative patient happens to be the MTC as this is the closest facility, no transfer costs would be involved.

M.2.4.1.8 Application of additional and longer term outcomes

If data are forthcoming, additional modification to outcomes associated with the delay of treatment could be incorporated, i.e. changes to length of stay within hospital. A cost per day could be attached with estimated time in hospital for example. Further, a quality of life could be given to a patient for the duration of their expected survival time to estimate QALYs. Due to the nature of the expected data, it is highly likely that an assumption will be needed that should a patient survive to 30 days, then they could expect to live an average life expectancy.

M.2.4.1.9 Tally of survival and costs

Results and timings from the patient's journey through the model can be recorded when they exit the model and tallied to calculate means for the whole cohort passing through the model within its run time or for a specific number of simulated patients. Specific outcomes such as number of

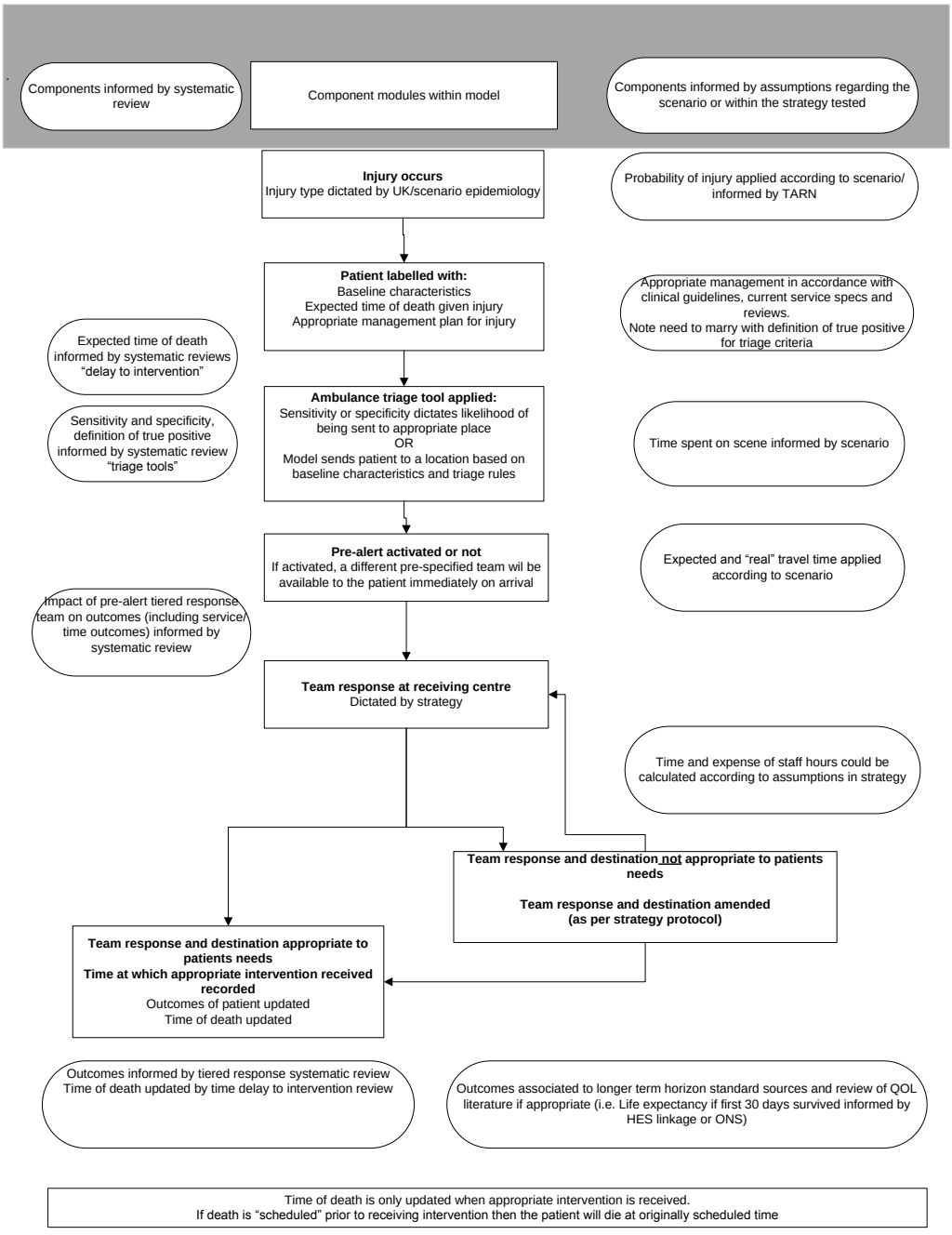
incorrectly triaged patients arriving at an appropriate destination due to local circumstance could also be recorded if desired, so that impact of local scenarios could be explored.

M.2.4.1.10 Patient diary

For validation purposes, assignment of labels, changing of labels and arrival/departure of the patient at clinical locations or activities can be time stamped and recorded in a patient log. Clinical members can select to review these entries to ensure the model is acting credibly.

The labelling process is depicted in Figure 16.

Figure 16 - Labelling process in the model



M.2.4.2 Simplified model structure

After looking for model inputs data, it became clear that these were too limited to inform a systems model and the model structure was simplified to a decision tree which focused only on the assessment of triaging tools. The structure of this model is represented in Figure 17 below. Patients were categorised according to whether they had major trauma (defined by an ISS>15) with or without airway issues, head injury or major bleeding, or no major trauma (ISS equal or less than 15). Based on the tool sensitivity, a proportion of patients with major trauma would be taken to the destination of choice as defined by the general rule applied together with the triaging tool (for example, take patients with airway issues to the nearest and all the other major trauma to a MTC).

When the patient in the model was transported to the appropriate destination, this would count as a correct triaging decision (0 values in the payoff of the model), and vice versa (1 values).

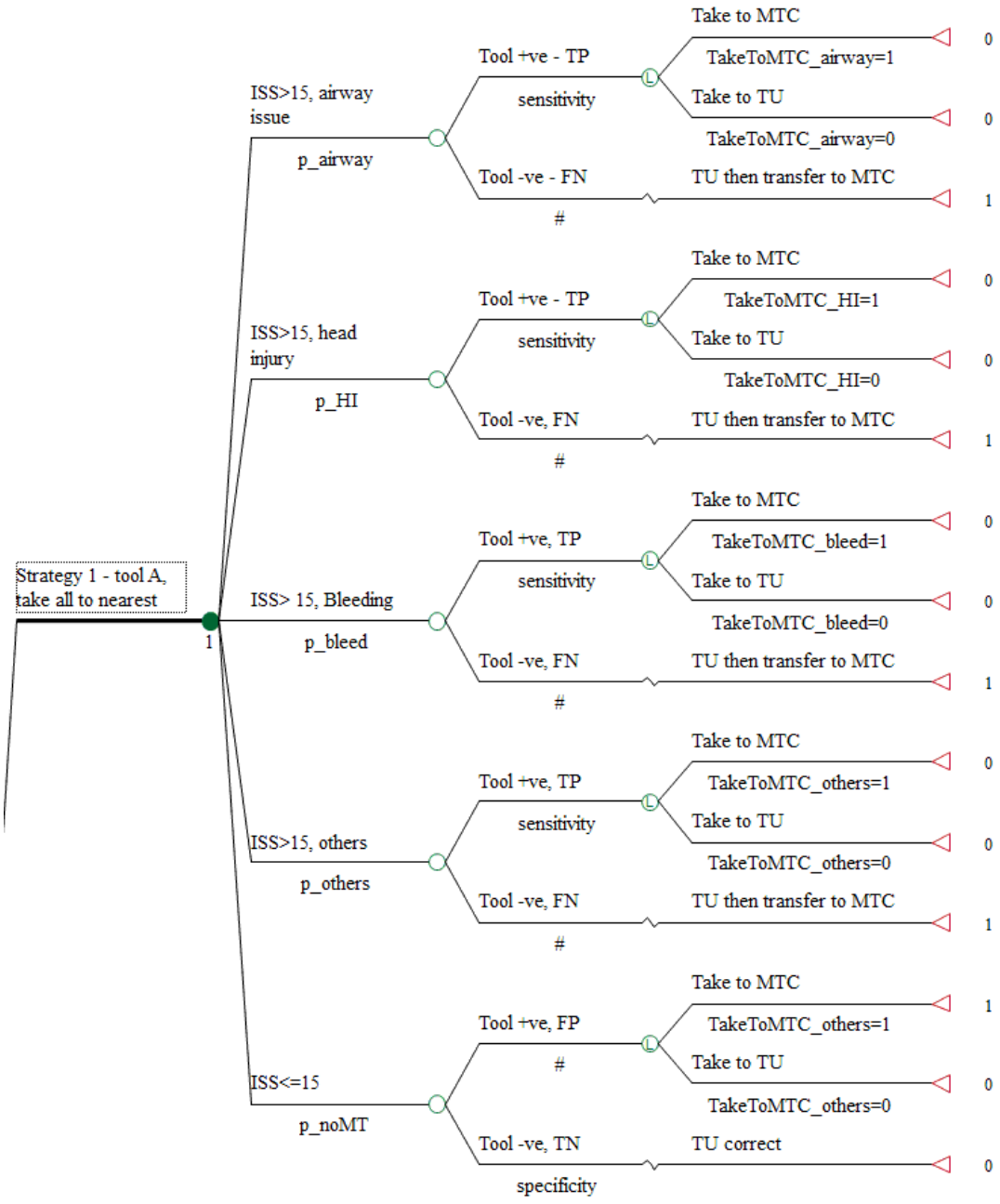


Figure 17 - Simplified decision tree on triaging tools. In this strategy a triaging tool (A) is applied to patients together with a more general rule ('take all patients to nearest hospital' in this example) which would dictate which patient groups should be taken to a MTC or trauma unit.

M.2.5 Model inputs

M.2.5.1 Summary of data identification for model inputs

Model inputs were based on clinical evidence identified in the systematic review undertaken for the guideline, supplemented by additional data sources as required. Model inputs were validated with

clinical members of the GDG. A summary of the evidence identified and the conclusions drawn from the published evidence found to parameterise by systematic review is provided in Table 42.

As can be seen, published estimates of effect size for outcomes required for the model were in the main absent or from lower quality studies. For this reason, we considered the availability of alternative sources identified through GDG knowledge and also the appropriateness, usefulness and feasibility of bespoke analysis of TARN audit data.

Use of the TARN dataset

It was thought that TARN could provide the patient-level data to which a retrospective triaging decision could be applied; in addition, mortality could be obtained based on patient index group, and correct and incorrect destination of transport.

Fields which could be identified from TARN include physiological observations (such as blood pressure, GCS score, pulse rate) and mechanism of injury (blunt/penetrating, details of the car crash). However, anatomical aspects of the injury are less clearly recorded (i.e. whether there was a suspected open fractures, chest injury, etc.). Such detail is likely to be identified from the free text fields on the incident.

There are three main methods which are commonly employed to estimate treatment effect from observational data. These are use of regression, propensity score matching, and use of instrumental variables. The conclusion of this discussion is that regression (accounting in the first instance for the key confounders specified in any related systematic review protocol undertaken for the guideline) would be the primary method of analysis, with this method being compared to the results of propensity score matching.

When discussing the use of TARN as a potential data source, developers were made aware of the following limitations:

- TARN does not include patients who died before hospital (either dead at scene or deteriorated and died en route);
- the majority of patient records within TARN are reported from MTCs due to current incentive structures, with less records available for less injured patients who were only treated at a trauma unit.

These were considered major limitations for the purpose of our model, as the mortality/time to death data would not reflect the real situation since the more severe patients (those who died en route) died before the data could be collected, and also data for the true negatives (those who were sent to a trauma unit correctly) would not be available as TARN does not report data for minor injuries.

Furthermore, primary analysis undertaken for the Major Trauma model highlighted very serious limitations in use of regression to address bias when using this data source to inform treatment effect. The analysis, its limitations and implications for methodological research are described in depth in Appendix M of the Major Trauma Guideline.

For these reasons, the option of conducting the economic analysis based on TARN data was considered unfeasible.

Table 42: Overview of the systematic reviews undertaken to populate the model

Parameter/input	Data summary	Limitations identified by the GDG	Conclusion regarding use in the model	Sources
Triage Accuracy of ambulance tools	Four studies were included in the review. Three studies reported on the sensitivity and specificity of the ASC-COT tool (one reported in adults and children). One study compared the sensitivity and specificity of UK paediatric trauma tools. Results: ACS-COT adults Very low quality evidence from 3 prospective studies with 4900 adults showed that the ACS-COT tool has a median (95% CI) sensitivity of 0.76 (0.70 to 0.82) and a corresponding specificity of 0.97 (0.96 to 0.98) for diagnosing patients with an ISS>15. ACS-COT children Very low quality evidence from a single prospective study with 238 children showed that the ACS-COT tool has a mean (95% CI) sensitivity of 0.73 (0.39 to 0.94) and a corresponding specificity of 0.96 (0.92 to 0.98) for diagnosing patients with an ISS>15. UK Triage Tools children Moderate quality evidence from a single prospective study with 701 children showed that 6 UK-based triage tools have a median (95% CI) sensitivity of 91% (0.87 to 0.95) and a corresponding specificity of 0.23 (0.19 to0.27) for diagnosing patients with an ISS>15. Studies excluded from the review: In adults, 20 studies using 7 different triage tools were found following the literature search. The majority of	Limitations of the evidence included the different skills and competencies of the professionals administering the tool compared to the UK, for example pre-hospital physicians. The GDG indicated that the criteria in each tool were not reported in the studies and this limited their ability to comment on the tool's performance. The limitations of each study are summarised in Chapter 9.	Only data on sensitivity and specificity for adult triage using the ACS-SCOT tool are available. We therefore do not have a comparator arm for adults. We are aware of upcoming work using TARN which is due to be published soon, however, we cannot use unpublished estimates in the model. In conclusion, we cannot undertake meaningful comparative analysis of triage tools in the adult population.	CHEUNG2013[13] COX2012[22] DINH2012[31] DO2014[3] OCAK2009[72]

Parameter/input	Data summary	Limitations identified by the GDG	Conclusion regarding use in the model	Sources
	these tools focused primarily on the physiological criteria associated with trauma and were excluded by the GDG as such tools are not currently used in UK practice. Moreover, as the tools primarily focused on the physiological criteria following injury they were likely to miss patients with major trauma.			
Pre-alert	No evidence identified	NA	No evidence identified	NA
Impact of delay to definitive treatment for:				
Intubation or surgical airway	**Type of evidence:** 1 RCT (Bernard 2010[5]); 5 cohort studies [6] [7] [24] [25] [86] The below refers to the RCT only. For details of the cohort studies please see related review. **Comparators** (n=160) Intervention 1: Intubation/surgical airway – Immediate was applied to all patients. After intubation patients received a single dose of pancuronium and intravenous infusion of morphine and midazolam. If intubation was not achieved at first attempt one further attempt was allowed. Duration Time at scene 35 (SD12) min. Concurrent medication/care: Not stated apart from intervention (n=152) Intervention 2: Intubation/surgical airway - Delayed. Hospital intervention: High flow supplemental oxygen by mask and assisted bag/mask ventilation if required. An oropharyngeal or nasopharyngeal airway was inserted if airway suctioning was required. A small dose of morphine was permitted. Patients underwent rapid sequence induction. . Duration Time at scene 25 (SD10) min. Concurrent medication/care: See intervention Outcomes reported: Mortality; Glasgow Outcomes Scale extended 5-8;	The GDG thought the RCT[5]) was applicable to the UK and could be used in the model. The cohorts were thought to not be applicable as they were conducted in countries with healthcare systems not comparable to the UK. Also they did not specify what technique was used and who did the intubation. The paper on thoracic injury was not relevant because of the population.	Outcomes from the RCT (mortality, craniotomy, length of stay; Glasgow Outcomes Scale) could be used in a model	[5]; [6]; [7]; [24]; [25]; [86].

Parameter/input	Data summary	Limitations identified by the GDG	Conclusion regarding use in the model	Sources
	Craniotomy within 6 hrs of ED arrival			
Imaging to identify blood loss (as an enabler of timely treatment)	No specific systematic review was planned on this topic – see Chapter 11 in Major Trauma guideline. Bespoke TARN analysis was planned.	See Chapter 11 in Major Trauma guideline.	TARN analysis was discarded	
Interventional radiology	**Comparators:** Early versus delayed interventional radiology **Type of evidence:** No RCTS; 2 retrospective cohort studies [47,87] **Outcomes reported:** In hospital mortality reported for rapid interventional radiology (< 1 hour of admission) vs. delayed interventional radiology (1-3 hours following admission) 30-day mortality reported for interventional radiology during regular working hours (median time from admission to IR = 193 mins (137 – 275)) vs. Interventional radiology during evenings and weekends (median time from admission to IR = 301 mins (211-389)	Two cohort studies are at very high risk of bias and both only reporting mortality as an outcome of delayed IR. The GDG suggested that a level I and level II trauma centre in this study were both similar to the service provided by a Major Trauma Centre in the UK. However, the proportion of patients with penetrating injuries (53.85%) in the US paper (Howell) may be too high to be relevant to UK population. As a consequence, the GDG felt that the analysis in this paper combining patients treated in level I and level II trauma centres and stratifying by mechanism of injury (blunt vs. penetrating injury) was the most relevant analysis for this review. A key limitation of both studies is that patient records did not specify the length of time between the time of injury and admission to hospital. As a consequence, the time of intervention is from admission and not from time of injury, and it is unclear whether the groups differed in the length of time spent prior to admission.	The only outcome of interest reported was mortality. No other important outcomes required for modelling objectives were reported (i.e. health related quality of life; length of hospital stay; number of procedures; adverse events). Survival analysis data were incomplete with adjusted ORs due to delays reported. Concerns regarding applicability due to epidemiological differences can be addressed in the model by applying the treatment effect for each type of	47,87

Parameter/input	Data summary	Limitations identified by the GDG	Conclusion regarding use in the model	Sources
			respective injury to the proportions of patients you would expect with that injury type in the UK.	
Blood transfusion	No evidence identified	NA	No evidence identified	NA
vascular surgery: thoracotomy	No evidence identified	NA	No evidence identified	NA
vascular surgery: laparotomy	Two retrospective cohort studies on laparotomy were identified: The study by Barbosa (2103) is a cohort study where the authors examined a subset of patients from a trauma database that had a FAST performed and underwent laparotomy within the first 90 minutes after hospital admission. The authors created cox proportional hazards models including Injury Severity Score (ISS), age, base deficit, hospital site, and time to operation (T-OR). They also created the same models using the time interval between performance of the FAST and the operating room (TFAST-OR). In-hospital mortality at 24 hours and 30 days was studied. The authors report the hazard ratios in terms of 10-minute intervals in T-OR or TFAST-OR. The study by Peev (2015) is for a single cohort of patients where they enter time to laparotomy into a multivariate cox regression to predict survival. HR data and numbers at risk provided.	Neither study compared time from injury to operation, only time from admission to operation.	Both studies could be used in the model.	[3]; [73]
Vascular surgery: fasciotomy	No evidence identified	NA	No evidence identified	NA
Neurosurgery	**Question 1: Time from injury to neurosurgery or**	**Time from injury to neurosurgery or admission**	**Time from injury to**	[30,101 57 67,95]

Parameter/input	Data summary	Limitations identified by the GDG	Conclusion regarding use in the model	Sources
Or neurological ICU	**admission to a specialist neurosurgical centre.** Type of evidence: No RCTs; 2 retrospective cohort studies,[30,101] Comparator**:** Time from injury to neurosurgery or admission to a specialist neurosurgical centre. Outcomes reported: Incremental mortality reported for arrival within 30 minutes, 60 minutes (GCS >8) (GCS 3-8),90 minutes ,120 minutes Good recovery reported for arrival within 60 minutes In-hospital mortality per minute of time spent in the prehospital setting after the traumatic incident. **Question 2: Direct transfer to a specialist neurosurgical services** Type of evidence: 1 cluster RCT;[57] 3 retrospective cohort studies[62,67,95] Comparator: Indirect transfer to a specialist neurosurgical services Outcomes reported: In-hospital, 30 day, 6 month mortality. ICU length of stay	**to a specialist neurosurgical centre.** The GDG did not consider these studies were ideal in terms of their structure for the economic model. They were in a population who were transported directly to specialist neurosurgical centres and this does not inform on care for people with head injury who were initially transported to non-specialist centres. Both studies used timings from injury to admission to a specialist neurosurgical centre and the GDG felt that delays from admission to treatment were a serious confounding factor. In addition the GDG said stated that one paper did not separate the confounding factor of pre-hospital intubation from the effects of early neurosurgery. Separating time to intubation from early neurosurgery was believed to be fundamental to finding the benefits of early specialist neurosurgical care. **Direct transfer to a specialist neurosurgical services** The GDG did not consider that any of the studies adequately separated the confounding factor of early intubation from the effects of early neurosurgery in the studies. The GDG did not think it was clear whether the mortality point estimates favouring transport to a non-specialist centre were an effect of earlier in-hospital intubation or neurosurgical care or a combination of the two.	**neurosurgery or admission to a specialist neurosurgical centre.** Outcomes of interest reported were mortality, good recovery, and length of stay. No other important outcomes required for modelling objectives reported (i.e. Health related quality of life; Number of procedures; Glasgow Outcomes Scale (GOS) and complication rates). **Direct transfer to a specialist neurosurgical services** These studies were not deemed suitable to be used in the model.	[62]
Ortho-plastic	**Type of evidence:** No RCTs. Six cohorts	See Chapter 6 in Complex Fracture guideline.	Bespoke analysis using	Complex

Parameter/input	Data summary	Limitations identified by the GDG	Conclusion regarding use in the model	Sources
services for debridement, fixation and cover of open fracture	**Comparators:** Differential timing of debridement **Outcomes reported:** Deep infection, re-operations and amputation. No studies reported mortality up to 12 months, health-related quality of life, return to normal activities, functional outcomes or length of stay. **Comparators:** Orthoplastic versus normal practice approach to debridement **Type of evidence:** No RCTs. One retrospective cohort	Only three of the debridement studies specified type of antibiotic used. The comparator timings in these studies were limited to <6hrs vs >6hrs, <8hrs vs >8hrs and a comparison of different days up to >5 days and therefore does not capture all comparators on the protocol. The study on orthoplastic approach had a high risk of bias as the two groups were patients from two different hospitals. Baseline characteristics were not reported and no attempt had been made to adjust for confounding.	TARN deemed more likely to be appropriate for modelling than published data. However TARN analysis was discarded.	Fracture guideline
Tiered team response	**Type of evidence:** 3 before-and-after cohort studies. **Comparators:** Two studies[33,103] looked at a two-tiered response with introduction of different triage tools to determine which tiered team should be activated for the in-coming patient(s). The third study[52] compares an initial period of two-tiered response with a later period following the implementation of a three-tiered response. For the three-tiered period the earlier full trauma team is split into two categories where the new 'middle' tier team does not immediately include the trauma attending and anaesthetist. **Applicability** **Information reported on:** Mortality; Hospital length of stay (days); ED length of stay (minutes) - All patients (code, alert or consultation); ED length of stay (minutes) - Code patients only	Despite USA setting, on inspection of the types of members in the tiers, the GDG felt they were similar to what they would define as different teams (with "top tier" similar to an MDT team and "lower tier" similar to an ED team). No information provided on: The impact of the full response does on the rest of the hospital – e.g. when you pull anaesthetists and surgeons away for a trauma often (anecdotally) ED waiting times (for non-trauma) increase and there might be back-log in other scheduled operations that are now delayed etc. paediatric information: anecdotal evidence from developers' experience is that when a child <10 or 11 presents a paediatrician is called (better with drug dosages and access etc). Further,	Some data which is considered applicable to populated the model, however no information retrieved on important outcomes related to meeting objectives (i.e. impact on system functioning) or quality of life. Assumptions required for costing of "down time" by staff.	33,103 52

Parameter/input	Data summary	Limitations identified by the GDG	Conclusion regarding use in the model	Sources
	Mortality (post ED presentation); Mortality (post hospital admission); Survival; Complications; Complication rate per person; ED length of stay (hours)	children tend to be prioritised amongst other activity. Other outcomes listed in protocol: Quality of life; Time to definitive care; Time to CT; Missed/delayed diagnosis of injury; Delays to transfer; Trauma team member time The lack of data paediatric response is to be expected, given the low numbers of child presentations at MTCs		

M.3 Results

The observational data identified in the various clinical reviews is insufficient to populate a model in this topic in a meaningful way (e.g.it did not cover all outcomes or sub populations required). As such, we have explored using TARN as an alternative data source to estimate impact of delay to intervention within the suite, however, there appears to be substantial unexplained confounding despite adjustment and we do not believe that the estimates from the planned analysis would be credible, and, at worse, misleading.

A simple model approach which focused only on the accuracy of triaging tools could not be developed either due to the lack of evidence on comparative accuracy of tools in the adult population.

M.4 Discussion

The feasibility of making evidence informed recommendations regarding trauma services through quantitative systems modelling was explored. However the evidence base is extremely limited in this area to fully understand the relationships between clinical activities and outcomes considered important in evaluation of the service.

Foremost, no published high quality evidence was identified regarding the accuracy of ambulance triage tools in the adult population, except those pertaining to variants of the ASCOT tool. Therefore we had no information on a comparator to this one tool and even a more simplified version of the economic model could not be developed.

Within a patient level simulation model, an alternative to modelling with published accuracy data would be to retrospectively apply the different pre-hospital decision tools to a sample of UK patients with suspected trauma. Individual patient characteristics, as recorded by TARN, could feed into a decision rule indicated by the triage tools criteria or algorithm, and a triaging decision calculated by the model. Retrospectively, clinicians could determine whether the triage decision informed by the tool was correct or not, and respective sequences of events and outcomes applied.

At the time of writing we learnt that similar work is underway to understand the value of UK ambulance triage tools. However, even if we were to use the retrospective analysis of TARN data of triage decisions, the analysis would be limited by the use of proxy clinical indicators. In particular it would be difficult to look at many of the factors of interest on the triage decision, such as the influence of local service provision, time from injury to local provider or to MTC, the use of clinical judgement (or not), which are not described within TARN for the purposes of audit.

Further, even with accuracy of triage information, the link to clinical outcomes would be tenuous given the paucity of data on the impact of delay to intervention on clinical outcomes and of data on deterioration of different time critical injuries.

We had envisioned that we would need to look toward audit data for treatment effect on clinical outcomes, given that studies looking at delay to intervention were unlikely to be forthcoming. However, primary analysis undertaken for the Major Trauma guideline to estimate treatment effect of delay to intervention for people with suspected bleeding highlighted very serious limitations in use of regression to address bias when using this data source to inform treatment effect. Alongside the methodological limitations found within this primary analysis, analysis of the TARN dataset for treatment effect to parameterise the trauma services model would further suffer from missing data regarding the pre-hospital stage (people who died before arrival to provider are not recorded) and be potentially skewed by potential under recording of the triage negative low risk patients with

suspected injury but who are correctly sent to a trauma unit. Indeed, the fact that the pre-hospital service caters for suspected (rather than confirmed) traumatic injury and also caters for a larger proportion of acute medical emergency non traumatic patients (who form the majority of the caseload) means that ambulance trust and TARN records may need to be analysed in tandem. In particular, this would be required if we are to fully understand the economies of scale, scope and capacity of services to enable efficient provision of resources in pre-hospital and emergency systems.

M.4.1 Conclusions

The original model planned for this guideline could not be conducted due to the lack of data to inform the most important parameters of the model, including the accuracy of the triaging tools currently used in practice. For this reason, the recommendations for the following scope areas (application of triage tools, pre-alert, trauma team response, access to airway management, access to interventional radiology for haemorrhage control) anticipated to be supported by the model were made using the evidence identified and the GDG expert opinion. The GDG decided not to recommend any specific tool but to make a research recommendation instead.

M.4.2 Implications for future research

Based on our experience of attempting an economic analysis based on audit data, we identified some features of an audit system which would be beneficial for similar purposes in the future:

- Accessibility and ease of processing data for bespoke analysis
- Decision relevance
- Inclusivity of all of the relevant population and settings
    - common but lower risk groups
    - across all of the patient journey (pre-hospital information/mortality)
- Capture and linkage of intervention and indication
- Ability to record or link to other databases that record
    - long term outcomes,
    - information regarding the service configuration of the providers,
    - quality of life measure (i.e. the EQ5D).
- Consideration of variables required for comparative analysis such as
    - instrumental variables (i.e. distance from injury to provider, policy change);
    - critical time points, which in turn could assist with survival analysis (time of injury, time of critical decision), censoring;
    - prognostic and diagnostic criteria which are commonly used within the field to inform clinical or service decisions.

Appendix N: Research recommendations

N.1 Audit

Research question: What is the clinical and cost effectiveness of collecting long-term outcomes in a national trauma audit system?

Why this is important: The UK has a national audit of trauma services in place for adults (Trauma Audit Research Network [TARN]) and entry to this audit is linked to best practice tariff for major trauma centres. An equivalent audit, TARNlet, has been developed for children. Data are collected on clinical observations, timing and staffing in the acute phase in patients who are treated at a major trauma centre. Data on longer-term outcomes, for example return to normal activities, after the acute phase are not collected, despite acknowledgement that outcomes are important to monitor the effectiveness of interventions.

Criteria for selecting high priority research recommendations:

PICO question	Population • Children, young people and adults with major trauma Intervention • National trauma audit Outcomes could include: • Mortality up to 12months • Health-related quality of life • Return to normal activities • Functional outcomes (e.g., Functional Independence Measure)
Importance to patients or the population	A National audit that includes the collection of longer term outcomes will improve the assessment, diagnosis and management of people with major trauma
Relevance to NICE guidance	The NICE major trauma service delivery made recommendations on the general principles relevant to audit but there was insufficient evidence to recommend the collection of longer term outcomes.
Relevance to the NHS	Preventable death rates and risk-adjusted mortality rates are standard methods of measuring and comparing trauma centre and trauma system performance. However mortality by itself is not an adequate measure of performance because it does not measure the impact of the entire trauma care pathway and says little about the long term impact of injury and associated costs.
National priorities	Department of Health initiative on regional trauma networks.
Current evidence base	The Trauma Audit & Research Network (TARN) is an established national clinical audit for trauma care across England, Wales and the Republic of Ireland and has been supporting trauma receiving trusts for over twenty years by providing each NHS trust with analysis of process, case mix adjusted outcome analysis and comparisons of trauma care. The data collected follows the patient pathway from incident through to discharge from hospital and focuses on key observations, interventions, investigations and attendants treating the injured patient. An equivalent audit, TARNlet, has been developed for children.

Equality	The audit data will include the collection of data for children, young people, adults and older adults.
Study design	A retrospective cohort study using prospectively recorded data from the Trauma and Audit Research Network (TARN) database for patients presenting with major trauma. Longer term outcomes will be recorded. Temporal trends in these outcomes will then be observed over time as clinical practice and services respond to audit feedback. The resources involved (above and beyond usual care) in collecting the longer term outcome data (for example the recording and storing data, quality assurance of data (inclusive of ensuring completeness and accuracy), general governance and administration of the audit and the training costs of staff members involved). The benefit of national audit is that many of these services and costs can be centralised
Feasibility	None identified
Other comments	Economic evaluation assessing the resource use and costs associated with the costs of collecting the data should be undertaken. The cost savings of any changes to clinical practice or service configuration as a result of recording longer term outcomes should also be conducted.
Importance	This research recommendation is of high importance: the research is essential to inform future updates of key recommendations in the guideline

N.2 Rehabilitation

Research question: To identify the barriers to people with major trauma receiving early rehabilitation following early rehabilitation assessment.To identify the implications on service delivery of the barriers identified

Why this is important: Major trauma often results in people living with disability that results in a reduced quality of life. It is thus imperative to maximise access to rehabilitation to speed physical and psychological recovery after injury.

A proportion of patients will have complex needs necessitating inpatient rehabilitation from a multidisciplinary team with expertise. A larger group of patients will need ongoing support, rehabilitation and re-enablement once they are discharged home. The major trauma best practice tariff advises that every patient with an Injury Severity Score ≥9 in either a major trauma centre or a trauma unit should have their rehabilitation needs assessed, and that a rehabilitation prescription should be provided for all patients with rehabilitation needs. The rehabilitation prescription is used to document the rehabilitation needs of patients and identify how their needs should be addressed. It is unclear if adequate in- and out-patient service exists for trauma patients and what barriers prevent people from accessing these services.

Criteria for selecting high priority research recommendations:

PICO question	Population • People who have suspected major trauma and use trauma healthcare

	services Intervention • Early rehabilitation (physiotherapy, occupational therapy, speech, mental health) following early rehabilitation assessment (within 72 hrs) Outcomes • Barriers identified in the papers
Importance to patients or the population	The GDG emphasised that rehabilitation should start as soon as possible, and that waiting is inappropriate. Delayed rehabilitation may result in: • An inappropriate use of other resources. Whilst waiting for rehabilitation a person may well be occupying space in another setting that is equally in demand. • The development of 'complications' while waiting for example physical problems such as skin pressure ulcers, joint contracture and psychological complications such as depression, apathy and anger • Loss of employment to both patient and carer/ family member
Relevance to NICE guidance	The NICE major trauma service delivery made no recommendations on this topic as no evidence was identified to inform this question. The identification of barriers to trauma rehabilitation could lead to the development of clinical and cost-effective rehabilitation services to improve patient satisfaction, clinical outcomes and trauma system effectiveness. (These would link with the CG83 on how to deliver rehabilitation after critical illness)
Relevance to the NHS	It is thought that whilst the majority of patients treated within an MTC receive a rehabilitation prescription (incentivised by the best practice tariff which requires an assessment by a rehabilitation medicine consultant within 72 h of admission), there are significant delays in the delivery of early rehabilitation. The identification of barriers to trauma rehabilitation could lead to the development of clinical and cost-effective rehabilitation services to improve patient satisfaction, clinical outcomes and trauma system effectiveness
National priorities	Department of Health initiative on regional trauma networks. . The National Service Framework (NSF) for Long-Term Conditions highlights the need for MDT rehabilitation and some patients could suffer long term conditions after trauma such as brain injuries or spinal cord injuries. This could contribute to the NHS Outcome Framework in England, Domain 3 (helping people recover from episodes of ill health or following injury) to produce more detailed information, on barriers to recovery which are service related.
Current evidence base	No evidence identified
Equality	The study should stratify according to: Age: child (0-15 years); young people (16-17 years); adults (18-65 years; >65 years)
Study design	A qualitative study design would be the most appropriate
Feasibility	No issues identified
Other comments	Economic evaluation assessing the resource use and costs associated with the

	intervention should be undertaken.
Importance	This research recommendation is of high importance: the research is essential to inform future updates of key recommendations in the guideline

N.3 Retrieval

Research question: Is it clinically and cost effective to provide a dedicated service to transfer patients with major trauma from the emergency department for ongoing care?

Why this is important: Patients with major trauma may need rapid transfer from the local emergency department to a major trauma centre for specialist care. The local trauma unit's clinical team can transfer them without delay but may not be able to provide specialist treatment during the transfer. A specialist team sent by the receiving centre can provide this care care during transfer but the transfer may be delayed while waiting for the specialist team to arrive at the local trauma unit.

Criteria for selecting high priority research recommendations:

PICO question	Population • Children, young people and adults with major trauma Intervention • Retrieval service for secondary transfer Comparison: • Transfer by trauma unit clinical team Outcomes: • Mortality up to 12months • Health-related quality of life • Time taken to transfer • Delay to admission at MTC • Complications during transfer/due to transfer • Length of hospital stay
Importance to patients or the population	The fast transfer of critically injured patients who require rapid specialist care will have benefits in reducing patient mortality (and injury related morbidity)
Relevance to NICE guidance	The NICE major trauma service delivery made recommendations on the general principles relevant to transferring critically ill patients but there was insufficient evidence to recommend a specialist retrieval service.
Relevance to the NHS	It is imperative that a person with major trauma is in the right place to receive the best definitive treatment as quickly as possible. Some patients may need to be transferred from a trauma unit to a major trauma centre as soon as possible to receive the specialist care they need. How a service should be configured to retrieve the patient from the trauma unit to the major trauma centre is critical with respect to improving patient outcomes.
National priorities	Department of Health initiative on regional trauma networks.
Current evidence base	Several hospital trusts in the UK have implemented a dedicated transfer service,

	where clinicians with the skills required for the transfer of critically injured patients are available (24/7) to transfer patients requiring urgent specialised treatment between centres. However, there are no published studies to evaluate the clinical and cost effectiveness of these services.
Equality	The study should stratify according to: Age: child (0-15 years); young people (16-17 years); adults (18-65 years; >65 years)
Study design	A randomised control trial would be the most appropriate
Feasibility	None identified
Other comments	Economic evaluation assessing the resource use and costs associated with the intervention should be undertaken.
Importance	This research recommendation is of high importance: the research is essential to inform future updates of key recommendations in the guideline

N.4 Triage tools

Research question: To develop and validate a national pre-hospital triage tool for major trauma

Why this is important: Pre-hospital triage tools identify patients who need to be taken to a major trauma centre, bypassing the local emergency department. They are also used to generate pre-alert or standby calls for a trauma team. Most triage tools in the UK use physiological parameters with diagnostic cut-offs and categorical variables such as mechanism of injury. However, the parameters used, and the weighting given to each parameter, differ across the tools. A national pre-hospital triage tool should be developed and validated that will accurately identifies where a patient needs to be transported to which will in turn lead to improved patient outcomes and reduced costs.

Criteria for selecting high priority research recommendations:

PICO question	Population • Children, young people and adults with suspected major trauma Triage tool parameters could include • Physiological • Anatomical • Mechanism of injury Stratify/subgroup • Children • Older adults Outcome • Injury Severity Score of 15 of more

Importance to patients or the population	If a national trauma triage tool could be developed which accurately identified patients who needed to be transported directly to a major trauma centre this would improve patient outcomes and reduce resource use.
Relevance to NICE guidance	The NICE major trauma service delivery guideline recommends that a triage should be used but there was insufficient evidence to recommend which tool should be used.
Relevance to the NHS	An accurate triage tool for England and Wales would reduce the over and under-triaging of trauma patients. This would lead to improved patient outcomes and reduce resource use as patients would be transported to the destination most appropriate for the injuries (major trauma centre, trauma unit or local emergency department). Furthermore, a standardised national triage tool (although there may still be a need to modify it to suit local requirements e.g., distance to major trauma centre versus trauma unit) would facilitate the standardised of pre-hospital documentation.
National priorities	Department of Health initiative on regional trauma networks.
Current evidence base	Currently, there is no published accuracy data on the accuracy of adult trauma triage tools used in England and Wales. There are studies on a tool developed in the USA, ASC-COT, but sensitivity is poor. One study compared the accuracy of paediatric (less than 16 yrs of age) UK trauma tools. Specificity ranged from 0.77 to 0.97 and sensitivity from 0.17 to 0.41.
Equality	Specific tools or modifications of tools would be developed for children and older adults.
Study design	A retrospective cohort study using data from a national or European trauma database to explore the diagnostic accuracy of individual parameters and following on from this different triage tools.
Feasibility	How feasible? Costs? Technical issues?
Other comments	None identified
Importance	This research recommendation is of high importance: the research is essential to inform future updates of key recommendations in the guideline

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Appendix O: NICE technical team

Name	Role
Sharon Summers-Ma	Guideline Lead
Phil Alderson	Clinical Advisor
Nichole Taske	Clinical Lead
Bhash Naidoo	Health Economist
Ben Doak	Guideline Commissioning Manager
Thomas Feist	Guideline Coordinator
Judith McBride	Editor

Appendix P: Qualitative study checklist (per theme)

Question	Study 1 (ref id)	Study 2 (ref id)	Study 3 (ref id)	Study 4 (ref id)	Overall limitations per theme
Were qualitative studies/ surveys an appropriate approach?					
Were the studies approved by an ethics committee?					
Were the studies clear in what they seek to do?					
Is the context clearly described?					
Is the role of the researcher clearly described?					
How rigorous was the research design/methods?					
Is the data collection rigorous?					
Is the data analysis rigorous?					
Are the data rich (for qualitative study and open ended survey questions)?					
Are the findings relevant to the aims of the study?					
Are the findings and conclusions convincing?					
OVERALL LIMITATIONS per theme **No limitations/ Minor limitations/ Major limitations**					**Major limitations**

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