National Clinical Guideline Centre

Final

Major trauma: assessment and initial management

Major trauma: assessment and management of major trauma

NICE Guideline NG39

Methods, evidence and recommendations

February 2016

Final

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Update information

November 2020: We clarified our advice in recommendation 1.5.23 on crystalloids and tetrastarches for patients with or without active bleeding.

See www.nice.org.uk/NG39 for more details.

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1 Foreword

Major trauma describes serious and often multiple injuries that may require lifesaving interventions. Trauma has a bimodal age distribution with the first peak in the under-20s and then the second peak in the over-65 age group. It is the biggest killer of people aged below 45 years in the UK and in those people that survive a traumatic injury; a large number will have permanent disabilities. The estimated costs of major trauma are between £0.3 and £0.4 billion a year in immediate treatment. The cost of any subsequent hospital treatments, rehabilitation, home care support or informal carer costs are unknown. The National Audit Office estimated that the annual lost economic output as a result of major trauma is between £3.3 billion and £3.7 billion.

In the UK over the last 25 years there has been substantial improvement in outcomes for patients.

This has been due to a variety of reasons, which include better education as well as improvements in pre-hospital, emergency department and hospital management.

More recently, the development of integrated Trauma networks has aimed to organise regional trauma care that provides co-ordinated multidisciplinary care that is provided at a time and place that benefits the patient most. The benefits of the networks are demonstrated by progressive improvements in patient outcomes reported by The Trauma Audit and Research Network (TARN).

There are still improvements to be made and the Department of Health asked NICE to develop the following four clinical guidelines and one service delivery guideline related to the management of people with major trauma:

- **Spinal injury assessment**: assessment and imaging and early management for spinal injury (spinal column or spinal cord injury)
- Remit: To produce guidance on the assessment and imaging of patients at high risk of spinal injury.
- **Complex fractures**: assessment and management of complex fractures
- Remit: Complex fractures: assessment and management of complex fractures (including pelvic fractures and open fractures of limbs)
- **Fractures**: diagnosis, management and follow-up of fractures
- Remit: Fractures - Diagnosis, management and follow-up of fractures (excluding head and hip, pelvis, open and spinal)
- **Major trauma**: assessment and management of airway, breathing and ventilation, circulation, haemorrhage and temperature control.
- Remit: Assessment and management of major trauma including resuscitation following major blood loss associated with trauma
- **Service delivery of trauma services**

These guidelines are related topics with overlap in populations and key clinical areas for review. The guidelines have been developed together to avoid overlap and ensure consistency. However, each guideline ‘stands alone’ and addresses a specific area of care. See section 3.3 for more information on how the suite of guidelines was developed.

In summary, these guidelines represent the best current evidence available to support the trauma practitioner to optimally manage trauma patients, and that by encouraging increasing uniformity of care both mortality and morbidity will fall further.

2 Introduction

The National Audit Office (2010) report estimated that there are 20,000 cases of major trauma per year in England; 5,400 people die of their injuries with many others sustaining permanent disability. Every trauma death costs the nation in excess of £0.75 million and every major injury £50,000. (1). Data from TARNlet (children's component of the national clinical audit – the Trauma Audit Research Network) covering 183 hospitals recorded 23,771 incidents of trauma in children between 1988 and 2010. Of these, 30% were classed as major trauma, with an injury severity score of more than 15. This equates to approximately 300 children involved in major trauma in the UK per annum. (2)

Regional trauma networks went live across England in April 2012. Major trauma centres (MTCs) provide specialised care for patients with multiple, complex and serious major trauma injuries and work closely with a series of local trauma units. MTCs operate 24 hours a day, seven days a week. They are staffed by consultant-led specialist teams with access to the best diagnostic and treatment facilities, including orthopaedics, neurosurgery and radiology teams.

This guideline provides guidance on the assessment and management of major trauma, including resuscitation following major blood loss associated with trauma. For the purposes of this guideline, major trauma is defined as an injury or a combination of injuries that are life-threatening and could be life changing because it may result in long-term disability. This guideline covers both the pre-hospital and immediate hospital care of major trauma patients but does not include any management after definitive lifesaving intervention. It has been developed for health practitioners and professionals, patients and carers and commissioners of health services.

The key clinical areas are:

- Airway management
- Pre-hospital management of chest trauma
- Hospital management of chest trauma
- Management of haemorrhage
- Management of shock
- Heat loss
- Pain management
- Documentation and transfer of information
- Information and support
- Skills to be present in the multidisciplinary team.

3 Development of the guideline

3.1 What is a NICE clinical guideline?

NICE clinical guidelines are recommendations for the care of individuals in specific clinical conditions or circumstances within the NHS – from prevention and self-care through primary and secondary care to more specialised services. We base our clinical guidelines on the best available research evidence, with the aim of improving the quality of healthcare. We use predetermined and systematic methods to identify and evaluate the evidence relating to specific review questions.

NICE clinical guidelines can:

- provide recommendations for the treatment and care of people by health professionals
- be used to develop standards to assess the clinical practice of individual health professionals
- be used in the education and training of health professionals
- help patients to make informed decisions
- improve communication between patient and health professional.

While guidelines assist the practice of healthcare professionals, they do not replace their knowledge and skills.

We produce our guidelines using the following steps:

- Guideline topic is referred to NICE from the Department of Health.
- Stakeholders register an interest in the guideline and are consulted throughout the development process.
- The scope is prepared by the National Clinical Guideline Centre (NCGC).
- The NCGC establishes a Guideline Development Group.
- A draft guideline is produced after the group assesses the available evidence and makes recommendations.
- There is a consultation on the draft guideline.
- The final guideline is produced.

The NCGC and NICE produce a number of versions of this guideline:

- the ‘full guideline’ contains all the recommendations, plus details of the methods used and the underpinning evidence
- the ‘NICE guideline’ lists the recommendations
- ‘information for the public’ is written using suitable language for people without specialist medical knowledge
- NICE Pathways brings together all connected NICE guidance.

This version is the full version. The other versions can be downloaded from NICE at www.nice.org.uk.

3.2 Remit

NICE received the remit for this guideline from the Department of Health. They commissioned the NCGC to produce the guideline.

The remit for this guideline is: Assessment and management of major trauma including resuscitation following major blood loss associated with trauma.

3.3 Who developed the trauma guidelines?

As noted in section 1 the four clinical guidelines and service delivery guidance consist of related topics with overlap in populations and key clinical areas for review. The guidelines have been developed together to avoid overlap and ensure consistency. This required careful planning to ensure the guideline development groups had the support they needed. Senior clinical expertise was recruited in addition to the standard guideline development group.

Project Executive Team

The overlap in the content of the four clinical guidelines and the service delivery guidance required an approach that ensured coherence and avoided duplication across the guidelines. To address this, clinical experts from across the guidelines were recruited to form an umbrella group, the Project Executive Team (PET). The PET met quarterly throughout the development of the guidelines. At the PET meetings, the members provided expert advice to the technical team and GDGs on the crossover of reviews across guidelines. (See the list of project executive team members). Also see the list of Guideline Development Group members and the acknowledgements.

Guideline Development Group expert members

Expert members were healthcare professionals who worked across the four clinical guidelines and the service delivery guidance, and attended the GDGs that were relevant to their expertise. The expert members provided an additional level of coherence across the guidelines, helping to identify potential duplication in the areas of their expertise (see the list of the Guideline Development Group expert members).

Guideline Development Group (GDG)

Each guideline 'stands alone' and addresses a specific area of care. A dedicated, multidisciplinary Guideline Development Group (GDG), comprising health professionals, researchers and lay members developed this guidance. See the list of Guideline Development Group members and the acknowledgements.

The GDG was convened by the NCGC and chaired by Professor Karim Brohi in accordance with guidance from NICE.

The GDG met for two days every 6 weeks during the development of the guideline. At the start of the guideline development process all GDG members declared interests including consultancies, fee-paid work, share-holdings, fellowships and support from the healthcare industry. At all subsequent GDG meetings, members declared new and arising conflicts of interest.

Members were either required to withdraw completely, or for part of the discussion, if their declared interest made it appropriate. The details of declared interests and the actions taken are shown in Appendix B.

Staff from the NCGC provided methodological support and guidance for the development process. The technical team working on the guideline included a project manager, systematic reviewers, health economists and information scientists. The team undertook systematic searches of the literature, appraised the evidence, conducted meta-analysis and cost-effectiveness analysis where appropriate, and drafted the guideline in collaboration with the GDG.

3.3.1 What this guideline covers

Groups that will be covered

Adults, young people and children who present with a suspected major traumatic injury.

Key clinical issues that will be covered

- Assessment and management of pain relief (including opiates and Entonox)
- Airway management with cervical spine protection
- Breathing and ventilation
- Circulation with haemorrhage control
- Exposure
- Skills to be present within the multidisciplinary team
- Documentation of clinical assessments and management for people with major trauma
- Information and support needs of patients and their families and carers when appropriate.

For further details please refer to the scope in Appendix A and the review questions in Section 4.1.

3.3.2 What this guideline does not cover

Groups that will not be covered

- People with burns
- People with spinal injuries
- People with complex fractures

Clinical issues that will not be covered

- Prevention of major trauma
- Any management after definitive lifesaving intervention
- Major trauma resulting from burns

3.3.3 Relationships between the guideline and other NICE guidance

Related NICE Technology appraisals:

Pre-hospital initiation of fluid replacement therapy in trauma. NICE technology appraisal 74 (2004).

Related NICE medical technologies guidance:

CardioQ-ODM (oesophageal Doppler monitor). NICE medical technologies guidance 3 (2011).

Related NICE Clinical guidelines:

Patient experience in adult NHS services. NICE clinical guideline 138 (2012).

Organ donation for transplantation. NICE clinical guideline 135 (2011).

Venous thromboembolism. NICE clinical guideline 92 (2010).

Intravenous fluid therapy in adults in hospital. NICE clinical guideline 174 (2013).

Head injury. NICE clinical guideline 176 (2014).

Pressure ulcers. NICE clinical guideline 179 (2014).

Blood transfusion. NICE guideline 24. (2015)

Intravenous fluid therapy in children and young people in hospital. NICE guideline 29 (2015)

Related NICE guidance currently in development:

Spinal injuries assessment. NICE clinical guideline. Publication expected Feb 2016.

Fractures. NICE clinical guideline. Publication expected Feb 2016.

Complex fractures. NICE clinical guideline. Publication expected Feb 2016.

Major trauma services. NICE clinical guideline. Publication expected Feb 2016.

4 Methods

This chapter sets out in detail the methods used to review the evidence and to generate the recommendations that are presented in subsequent chapters. This guidance was developed in accordance with the methods outlined in the NICE guidelines manual 2012[100].

Sections 4.1 to 4.3 describe the process to review clinical evidence (summarised in Figure 1) and section 4.4 the process to review the cost-effectiveness evidence.

Figure 1: Step-by-step process of review of evidence in the guideline

4.1 Developing the review questions and outcomes

Review questions were developed in a PICO framework (patient, intervention, comparison and outcome) for intervention reviews. Review questions were developed with a framework of population, prognostic factor and outcomes for prognostic reviews, and with a framework of population, index tests, reference standard and target condition for reviews of diagnostic test accuracy. This was to guide the literature searching process, critical appraisal and synthesis of evidence, and to facilitate the development of recommendations by the guideline development group (GDG). They were drafted by the NCGC technical team and refined and validated by the GDG. The questions were based on the key clinical areas identified in the scope (Appendix A).

A total of 31 review questions were identified.

Full literature searches, critical appraisals and evidence reviews were completed for all the specified review questions.

Table 1: Review questions

Chapter	Review questions	Outcomes
Airway management	What is the most clinically and cost effective strategy for managing the airway in patients with trauma pre-hospital?	Critical: • Mortality at 48 hours, 30 days/1 month, 1 year • Health-related quality of life (Glasgow outcome scale or other functional outcome score; SF-36, functional independence measure, rehabilitation complexity scale, SF-12, EQ5D) • Brain injury management (oxygenation, control of carbon dioxide levels) • Aspiration events • Failure to intubate or secure airway • Adverse events (hypotension, unrecognised oesophageal intubation) Important • Patient reported outcomes (psychological wellbeing)
Assessment and management of chest trauma	What is the clinical and cost effectiveness of performing FAST compared to clinical examination pre-hospital in children, young people and adults who have suffered a suspected major chest trauma?	Critical: • Mortality at 24 hours, 30 days/1 month and 1 year • Health-related quality of life • Length of intensive care stay Adverse events: • parenchymal lung damage • infection, bleeding • lung damage • air embolism • empyema • numbers with inappropriate treatments Important: Patient-reported outcomes (psychosocial wellbeing) Destination Population size and directness: • No limitations on sample size • Studies with indirect populations will not be considered.
Assessment and management of chest trauma	What is the most clinically and cost effective technique (pre-hospital) to manage tension pneumothoraces?	Critical: • Mortality at 24 hours, 30 days/1 month, and 12 months • Health-related quality of life

Chapter	Review questions	Outcomes

		• Length of intensive care stay
		• Adverse events:
		  ○ Infection
		  ○ Air embolism
		  ○ Nerve damage
		  ○ Tissue damage
		
		Important:
		• Patient-reported outcomes:
		  ○ Pain/discomfort
		  ○ Return to normal activities
		  ○ Psychological wellbeing

Assessment and management of chest trauma	Which occlusive dressing used in the pre-hospital setting is the most clinically and cost effective in improving outcomes for patients with open pneumothoraces as a part of major trauma?	Critical: • Mortality at 24 hours, 30 days/1 month, and 12 months • Health-related quality of life • Adverse effects (conversion to tension pneumothorax, infection) Important: • Patient-reported outcomes (pain/discomfort, return to normal activities, psychological wellbeing)

In-hospital tension pneumothoraces	What is the most clinically and cost effective technique (in-hospital) to manage tension pneumothoraces?	Critical:
		• Mortality at 24 hours, 30 days/1 month, and 12 months
		• Health-related quality of life
		• Length of intensive care stay
		• Adverse events:
		  ○ Infection
		  ○ Air embolism
		  ○ Nerve damage
		  ○ Tissue damage
		
		Important:
		• Patient-reported outcomes:
		  ○ Pain/discomfort
		  ○ Return to normal activities
		  ○ Psychological wellbeing).

Imaging assessment of chest trauma	What are the most clinically and cost effective hospital strategies for assessing chest trauma (tension pneumothorax, haemothorax, cardiac tamponade, pneumothorax, pulmonary contusion, flail chest and aortic injury) in patients with major trauma on initial presentation?	Critical: • Mortality at 24 hours, 30 days/1 month and 1 year • Health-related quality of life • Length of intensive care stay • Complications – parenchymal lung damage, infection, bleeding, lung damage, air embolism, empyema • Numbers with inappropriate treatments

Chapter	Review questions	Outcomes
		Important: • Patient-reported outcomes (psychosocial wellbeing) • Destination Population size and directness: • No limitations on sample size • Studies with indirect populations will not be considered.
Imaging assessment of chest trauma	Diagnostic accuracy of hospital imaging strategies in people presenting with major trauma	• Diagnostic accuracy

Assessment and management of haemorrhage	Are haemostatic dressings clinically and cost effective in improving outcomes in patients with haemorrhage in major trauma?	Critical:
		• Mortality at 24 hours, 30 days/1month and 12 months
		• Health-related quality of life
		• Adverse effects
		  ○ skin burns
		  ○ delayed wound healing
		  ○ necrosis
		  ○ surgical complications
		• Length of ICU stay
		• Blood product use
		
		Important:
		• Patient-reported outcomes (psychological wellbeing)

Assessment and management of haemorrhage	Is the use of pneumatic or mechanical tourniquets clinically and cost effective in improving outcomes in patients with haemorrhage in major trauma?	Critical • Mortality at 24 hours, 30 days/1 month and 12 months • Health-related quality of life • Blood product use (RBCs, platelets, plasma, cryoprecipitate) • Length of ICU stay • Adverse effects: amputation, nerve palsies, renal failure. Important • Time to definitive control of haemorrhage • Patient-reported outcomes (psychological wellbeing)
Assessment and management of haemorrhage	Is the application of pelvic binders pre-hospital in patients suspected of pelvic fracture clinically and cost effective in improving outcomes?	Critical: • Mortality at 24 hours, 30 days/1 month and 12 months • Volume of blood components • Health-related quality of life • Adverse effects (unnecessary

Chapter	Review questions	Outcomes
		imaging) Important: • Patient-reported outcomes (pain/discomfort) • Improvement in haemodynamics (blood pressure and heart rate)

Assessment and management of haemorrhage	Is the use of systemic haemostatic agents clinically and cost effective in improving outcomes in patients with confirmed or suspected haemorrhage in major trauma?	Critical:
		• Mortality at 24 hours, 30 days/1 month and 12 months
		• Health-related quality of life
		• Adverse effects
		  ○ venous thromboembolism
		  ○ thrombotic events (MI/Stroke, pulmonary embolism)
		  ○ over-transfusion related morbidity
		  ○ infections
		• Blood product use:
		  ○ RBCs
		  ○ Platelets
		  ○ Plasma
		  ○ cryoprecipitate
		
		Important:
		• Time to definitive control of haemorrhage
		• Patient-reported outcomes (psychological wellbeing).

Assessment and management of haemorrhage	What is the most clinically and cost effective regimen for reversal of pre-existing therapeutic anticoagulation (laboratory effect) in major trauma?	Critical:
		• Mortality at 24 hours, 30 days/1month and 12 months
		• Health-related quality of life
		• Adverse events:
		  ○ Stroke
		  ○ Myocardial infarction
		  ○ Thromboembolism (PA and venous)
		• Reversal of anti-coagulation as measured by laboratory assessment
		• Neurological outcome (brain injured patients)
		• Blood product use
		
		Important:
		• Patient-reported outcomes (pain/discomfort, return to normal activities, psychological wellbeing)

Assessment and management of	What is the most accurate risk tool to predict the need for massive transfusion in patients with major trauma (pre-hospital and	• Diagnostic accuracy • Outcomes from false positive/false negative results, adverse effects

Chapter	Review questions	Outcomes
haemorrhage	hospital)?	
Assessment and management of haemorrhage	What is the most clinically and cost effective technique for circulatory access in patients with major trauma, including following a failed attempt at initial peripheral access?	Critical: • Mortality at 24 hours, 30 days/1 month and 12 months • Health-related quality of life • Adverse effects: pain, infection, thrombosis, multiple access failures, compartment syndrome, fracture • Time to establish access Important: • Patient-reported outcomes (psychological wellbeing).
Assessment and management of haemorrhage	What are the most clinically and cost effective fluid resuscitation strategies in the major trauma patient (hypotensive versus normotensive)?	Critical: • Mortality at 24 hours, 30 days/1 month, and 12 months • Health-related quality of life • Neurological outcome • Length of intensive care stay • Blood product use Important: • Multi organ failure • Time to definitive control of haemorrhage • Patient-reported outcomes: pain/discomfort return to normal activities psychological wellbeing).

Assessment and management of haemorrhage	What is the best volume expansion fluid to use in the resuscitation of haemorrhagic shock?	Critical:
		• Mortality at 24 hours, 30 days/1 month and 12 months
		• Health-related quality of life
		• Length of intensive care stay
		• Acute transfusion reaction
		  ○ Haemolytic transfusion reaction – acute
		  ○ Haemolytic transfusion reaction – delayed
		  ○ Post-transfusion purpura
		  ○ Previously uncategorised complications of transfusion
		  ○ Transfusion associated graft versus host disease
		  ○ Transfusion associated circulatory overload
		  ○ Transfusion associated dyspnoea
		  ○ Transfusion-related acute lung injury
		  ○ Transfusion transmitted infections

Chapter	Review questions	Outcomes
		Important: • Time to definitive control of haemorrhage • Patient-reported outcomes: ○ return to normal activities ○ psychological wellbeing
Control of haemorrhage in hospital	What type of major haemorrhage protocol is the most clinically and cost effective for improving outcomes in patients with major trauma?	Critical: • Mortality at 24 hours, 30 days/1 month, 12 months • Health-related quality of life • Blood product use (RBCs, platelets, plasma, cryoprecipitate) • Length of intensive care stay • Adverse effects: over-transfusion related morbidity, thromboembolism, transfusion-reactions, and infections Important: • Patient reported outcomes (psychological wellbeing) • Blood product waste
Control of haemorrhage in hospital	What are the most clinically and cost effective imaging strategies for detecting life threatening internal haemorrhage in major trauma patients?	Critical: • Mortality (24 hours, 30 days/1 month and 1 year) • Health related quality of life • Blood product use: • RBCs • Platelets • Plasma • cryoprecipitate) • Length of intensive care stay Adverse events: • Infarction • Infection • surgical complications) Important: • Time to definitive control of haemorrhage • Patient reported outcomes: • pain/discomfort • return to normal activities • psychological wellbeing) Population size and directness: • No limitations on sample size • Studies with indirect populations will not be considered.

Chapter	Review questions	Outcomes
Control of haemorrhage in hospital	What is the diagnostic accuracy of imaging strategies for detecting life threatening internal haemorrhage in major trauma patients?	• Diagnostic accuracy (including sensitivity, specificity, positive predictive value, negative predictive value).
Control of haemorrhage in hospital	What is the clinical and cost effectiveness of whole-body CT imaging in major trauma?	Critical: • Mortality at 24 hours, 30 days/1month and 12 months • Health-related quality of life • Blood product use: ○ RBCs ○ Platelets ○ Plasma ○ cryoprecipitate) • Length of intensive care stay Important: • Time to definitive control of haemorrhage • Time to surgery • Patient reported outcomes (psychosocial wellbeing) • Long-term radiation risk • Delayed/missed injury
Control of haemorrhage in hospital	What are the most clinically and cost-effective surgical intervention strategies in the major trauma patient with active haemorrhage (damage control versus definitive surgery)?	Critical: • Mortality at 24 hours (post damage control surgery and pre-definitive surgery), 30 days/1 month and 12 months • Health-related quality of life • Adverse effects (complications of surgery) Important: • Patient-reported outcomes (psychological wellbeing). • Blood components • Length of stay on ICU
Control of haemorrhage in hospital	Is the use of interventional radiology for definitive haemorrhage control in major trauma patients clinically and cost effective?	Critical: • Mortality at 24 hours, 30 days/1 month and 12 months • Health-related quality of life • Failure rate or re-intervention rate • Adverse effects ○ ischaemic damage ○ necrosis ○ renal failure • Blood product use • Length of intensive care stay • Time to definitive control of

Chapter	Review questions	Outcomes
		haemorrhage Important: • Patient-reported outcomes: ○ pain/discomfort ○ return to normal activities ○ psychological wellbeing
Monitoring	a) Is the use of point -of -care coagulation testing versus laboratory coagulation testing clinically and cost effective in people with major trauma? b) What is the diagnostic accuracy of point- of -care coagulation testing versus laboratory coagulation testing in people with major trauma?	Critical: • Mortality at 24 hours, 30 days/1month and 12 months • Health-related quality of life • Length of intensive care stay • Blood product use Important: • Time to definitive control of haemorrhage • Time to availability of result
Monitoring	What is the most clinically and cost effective frequency of blood test monitoring for people with suspected haemorrhage following major trauma?	Critical: • Mortality at 24 hours, 30 days/1 month, and 12 months • Health-related quality of life • Length of intensive care stay • Blood product use: ○ RBCs ○ Platelets ○ Plasma ○ Cryoprecipitate Important: • Patient-reported outcomes: ○ pain/discomfort ○ return to normal activities ○ psychological wellbeing • Time to definitive control of shock/haemorrhage
Monitoring	Does monitoring of lactate levels to guide management of hypovolemic shock improve outcomes?	Critical: • Mortality at 24 hours, 30 days and 12-months • Health-related quality of life • Length of intensive care stay • Adverse effects: over-transfusion-related morbidity, thromboembolism, transfusion-reactions • Blood product use (red blood cells, platelets, plasma, cryoprecipitate) Important: • Patient reported outcomes

Chapter	Review questions	Outcomes
		(psychological wellbeing) • Time to definitive control of haemorrhage
Warming	Is warming clinically and cost effective in people who have experienced major trauma?	Critical: • Mortality at 24 hours, 30days/1month, and 12 months • Health-related quality of life • Length of intensive care stay • Adverse effects: ○ skin burns ○ hyperthermia ○ infection) • Neurological outcome Important: • Patient-reported outcomes: ○ pain/discomfort ○ return to normal activities, psychological wellbeing).
Pain	What is the most appropriate pain assessment tool (pre-hospital and hospital) in patients with major trauma?	Critical: • Patient satisfaction • Health-related quality of life Important: • Patient-reported outcomes (psychological wellbeing).
Pain	What are the most clinically and cost effective first-line pharmacological pain management strategies (pre-hospital and hospital) in patients with major trauma?	Critical: • Pain levels (Pictorial scales, Numerical scales, Verbal scales, Visual scales) • Health-related quality of life • Adverse effects: nausea and respiratory depression, hallucinations • Level of consciousness Important: • Patient-reported outcomes (psychological wellbeing).
Documentation	Is documentation using a standard form across all clinical settings (pre-hospital and hospital) in which a major trauma patient might be treated clinically and cost effective?	Critical: • Mortality at 24 hours • Mortality at 30 days/1 month • Mortality at 12 months • Health-related quality of life • Complications Important: • Length of stay • Patient-reported outcome: return to

Chapter	Review questions	Outcomes
		normal activities • Patient-reported outcome: psychological wellbeing. • Missing data • Timing of transfers
Information and support	What information and support do people with major trauma and their families/carers want in-hospital/on discharge from ED?	• Thematic analysis

4.2 Searching for evidence

4.2.1 Clinical literature search

The aim of the literature search was to systematically identify all published clinical evidence relevant to the review questions. Searches were undertaken according to the parameters stipulated within the NICE Guidelines Manual.[100] Databases were searched using medical subject headings and free-text terms. Foreign language studies were not reviewed and, where possible, searches were restricted to articles published in the English language. All searches were conducted in MEDLINE, Embase, and the Cochrane Library, and were updated for the final time between 18th March and 26th April 2015. No papers added to the databases after this date were considered.

Search strategies were quality assured by cross-checking reference lists of highly relevant papers, analysing search strategies in other systematic reviews, and asking GDG members to highlight any additional studies. The questions, the study types applied, the databases searched and the years covered can be found in Appendix F.

The titles and abstracts of records retrieved by the searches were sifted for relevance, with potentially significant publications obtained in full text. These were then assessed against the inclusion criteria.

4.2.2 Health economic literature search

Systematic searches were undertaken to identify relevant health economic evidence within the published literature. The NHS Economic Evaluation Database (NHS EED), the Health Economic Evaluations Database (HEED) and Health Technology Assessment (HTA) database were searched using broad population terms and no date restrictions. A search was also run in MEDLINE and Embase using a specific economic filter with population terms. Where possible, searches were restricted to articles published in the English language. Economics search strategies are included in Appendix F. All searches were updated for the final time between 18th March and 26th April 2015 except in HEED which ceased production in 2014. No papers added to the databases after this date were considered.

4.2.2.1 Call for evidence

There were no calls for evidence.

4.3 Evidence gathering and analysis

The tasks of the research fellow are listed below and described in further detail in sections 4.3.1 to 4.3.6. The research fellow:

- Identified potentially relevant studies for each review question from the relevant search results by reviewing titles and abstracts, and deciding which should be ordered as full papers. Full papers were then obtained.
- Reviewed full papers against pre-specified inclusion / exclusion criteria to identify studies that addressed the review question in the appropriate population, and reported on outcomes of interest (see Appendix C for review protocols).
- Critically appraised relevant studies using the appropriate study design checklists as specified in The Guidelines Manual [National Institute for Health and Clinical Excellence (2012)[100]. Available from: https://www.nice.org.uk/article/PMG6/chapter/1Introduction
- Critically appraised relevant studies with a qualitative study design NCGC checklist (see Appendix R).
- Extracted key information about interventional study methods and results using Evibase, NCGC purpose-built software. Evibase produces summary evidence tables, with critical appraisal ratings. Key information about non-interventional study methods and results were manually extracted onto standard evidence tables and critically appraised separately (see Appendix G for the evidence tables).
- Generated summaries of the evidence by outcome. Outcome data is combined, analysed and reported according to study design:
  - Randomised data is meta analysed where appropriate and reported in GRADE profiles
  - Observational data presented as a range of values in GRADE profiles
  - Diagnostic data is meta-analysed if appropriate or presented as a range of values in adapted GRADE profiles
  - Prognostic data is meta-analysed where appropriate and reported in GRADE profiles.
  - Qualitative data is summarised across studies where appropriate and reported in themes.
- A sample of a minimum of 20% of the abstract lists of the first three sifts by new reviewers were double sifted by a senior research fellow. As no papers were missed by any reviewers, no further double sifting was carried out. All of the evidence reviews were quality assured by a senior research fellow. This included checking:
  - papers were included or excluded appropriately
  - a sample of the data extractions,
  - correct methods were used to synthesis data
  - a sample of the risk of bias assessments.

4.3.1 Inclusion and exclusion criteria

The inclusion and exclusion of studies was based on the criteria defined in the review protocols (see Appendix C). Excluded studies by review question (with the reasons for their exclusion) are listed in Appendix J. The GDG was consulted about any uncertainty regarding inclusion or exclusion.

The key population inclusion criterion was:

- People of all ages with suspected major trauma

The key population exclusion criterion was:

- People with burns.
- People with spinal injuries (this will be covered in another guideline)
- People with complex fractures (this will be covered in another guideline)

Conference abstracts were not automatically excluded from any review. No relevant conference abstracts were identified for this guideline. Literature reviews, posters, letters, editorials, comment articles, unpublished studies and studies not in English were excluded.

4.3.2 Type of studies

Randomised trials, non-randomised trials, and observational studies (including diagnostic or prognostic studies) were included in the evidence reviews as appropriate.

For most intervention reviews in this guideline, parallel randomised controlled trials (RCTs) were included because they are considered the most robust type of study design that could produce an unbiased estimate of the intervention effects. Crossover RCTs were not appropriate for any of the questions. If non-randomised studies were appropriate for inclusion, that is, non-drug trials with no randomised evidence, the GDG identified a-priori in the protocol the variables which must either be equivalent at baseline or that the analysis had to adjust for any baseline differences. If the study did not fulfil either criterion it was excluded. Please refer to Appendix C for full details on the study design of studies selected for each review question.

For diagnostic reviews, diagnostic RCTs, cross-sectional and retrospective studies were included. For prognostic reviews, prospective and retrospective cohort studies were included. Case–control studies were not included.

Where data from observational studies were included the results for each outcome were presented separately for each study and meta-analysis was not conducted.

4.3.3 Methods of combining evidence

4.3.3.1 Data synthesis for intervention reviews

Where possible, meta-analyses were conducted to combine the data from the studies for each of the outcomes in the review question using RevMan5 software.[4]

All analyses were stratified for age (under 18 years and 18 years or over), which meant that different studies with predominant age-groups in different age strata were not combined and analysed together. For some questions additional stratification was used, and this is documented in the individual question protocols (see Appendix C). If additional strata were used this led to sub-strata (for example, 2 stratification criteria would lead to 4 sub-strata categories, or 3 stratification criteria would lead to 9 sub-strata categories) which would be analysed separately.

Analysis of different types of data

Dichotomous outcomes

Fixed-effects (Mantel-Haenszel) techniques (using an inverse variance method for pooling) were used to calculate risk ratios (relative risk) for the binary outcomes, which included:

- Mortality
- Failure rate or re-intervention
- Adverse events

The absolute risk difference was also calculated using GRADEpro software[1], using the median event rate in the control arm of the pooled results.

For binary variables where there were zero events in either arm, Peto odds ratios, rather than risk ratios, were calculated. Peto odds ratios are more appropriate for data with a low number of events.

Where there was sufficient information provided, Hazard Ratios were calculated in preference for outcomes such as mortality.

Continuous outcomes

The continuous outcomes were analysed using an inverse variance method for pooling weighted mean differences. These outcomes included:

- Heath-related quality of life (HRQL)
- Length of stay (hospital/spinal cord injury centre)
- Blood product use
- Patient-reported outcomes

Where the studies within a single meta-analysis had different scales of measurement, standardised mean differences were used, where each different measure in each study was 'normalised' to the standard deviation value pooled between the intervention and comparator groups in that same study.

The means and standard deviations of continuous outcomes are required for meta-analysis. However, in cases where standard deviations were not reported, the standard error was calculated if the p values or 95% confidence intervals (CIs) were reported, and meta-analysis was undertaken with the mean and standard error using the generic inverse variance method in Cochrane Review Manager (RevMan5) software. [4] Where p values were reported as 'less than', a conservative approach was undertaken. For example, if a p value was reported as "p ≤0.001", the calculations for standard deviations were based on a p value of 0.001. If these statistical measures were not available then the methods described in section 16.1.3 of the Cochrane Handbook (version 5.1.0, updated March 2011)[2] were applied.

Generic inverse variance

If a study reported only the summary statistic and 95% CIs, the generic-inverse variance method was used to enter data into RevMan5.[4] If the control event rate was reported, this was used to generate the absolute risk difference in GRADEpro.[1] If multivariate analysis was used to derive the summary statistic but no adjusted control event rate was reported no absolute risk difference was calculated.

Heterogeneity

Statistical heterogeneity was assessed for each meta-analysis estimate by considering the chi-squared test for significance at p<0.1, or an I-squared inconsistency statistic of more than 50%, as indicating significant heterogeneity. Where significant heterogeneity was present, a priori subgrouping of studies was carried out for:

- age (children under 17 years or adult 18 years or over)

If the subgroup analysis reduced heterogeneity within all of the derived subgroups, then each of the derived subgroups were adopted as separate outcomes. For example, instead of the single outcome of 'missed diagnosis', this would be separated into two outcomes 'missed diagnosis in people aged under 65 years' and 'missed diagnosis in people aged 65 years and over'. Assessments of potential differences in effect between subgroups were based on the chi-squared tests for heterogeneity statistics between subgroups. Any subgroup differences were interpreted with caution as separating the groups breaks the study randomisation and as such are subject to uncontrolled confounding.

For some questions, additional subgrouping was applied, and this is documented in the individual question protocols (see Appendix C). These additional subgrouping strategies were applied independently, so subunits of subgroups were not created, unlike the situation with strata. Other

subgrouping strategies were only used if the age category subgroup was unable to explain heterogeneity, and then these further subgrouping strategies were applied in order of priority. Again, once a sub-grouping strategy was found to explain heterogeneity from all derived sub-groups, further sub-grouping strategies were not used.

If all pre-defined strategies of sub-grouping were unable to explain statistical heterogeneity within each derived sub-group, then a random effects (DerSimonian and Laird) model was employed to the entire group of studies in the meta-analysis. A random-effects model assumes a distribution of populations, rather than a single population. This leads to a widening of the CIs around the overall estimate, thus providing a more realistic interpretation of the true distribution of effects across more than 1 population. If, however, the GDG considered the heterogeneity was so large that meta-analysis was inappropriate, then the results were described narratively.

Complex analysis /further analysis

Network meta-analysis was considered for the comparison of interventional treatments, but was not pursued because of insufficient data available for the outcomes..

Where studies had used a cross-over design, paired continuous data were extracted where possible, and forest plots were generated in RevMan5[4] with the Generic Inverse Variance function. When a cross-over study had categorical data, the standard error (of the log RR) was calculated using the simplified Mantel Haenszel method for paired outcomes, when the number of subjects with an event in both interventions was known. Forest plots were generated in RevMan5[4] with the Generic Inverse Variance function. If paired continuous or categorical data were not available from the cross-over studies, the separate group data were analysed in the same way as data from parallel groups, on the basis that this approach would over-estimate the CIs and thus artificially reduce study weighting resulting in a conservative effect. Where a meta-analysis had a mixture of studies using both paired and parallel group approaches, all data were entered into RevMan5[4] using the Generic Inverse Variance function.

4.3.3.2 Data synthesis for diagnostic test accuracy reviews

Two separate review protocols were produced to reflect the two different diagnostic study designs:

Diagnostic RCTs

Diagnostic RCTs (sometimes referred to as test and treat trials) are a randomised comparison of two diagnostic tests, with study outcomes being clinically important consequences of diagnostic accuracy (patient outcomes similar to those in intervention trials, such as mortality). Patients are randomised to receive test A or test B, followed by identical therapeutic interventions based on the results of the test (that is, someone with a positive result would receive the same treatment regardless of whether they were diagnosed by test A or test B). Downstream patient outcomes are then compared between the two groups. As treatment is the same in both arms of the trial, any differences in patient outcomes will reflect the accuracy of the tests in correctly establishing who does and does not have the condition. Diagnostic RCTs were searched for first in preference to diagnostic accuracy studies (see below). Data were synthesised using the same methods for intervention reviews (see dichotomous or continuous outcomes above)

Diagnostic accuracy studies

For diagnostic test accuracy studies, a positive result on the index test was found in two different ways, according to whether the index test was measured on a continuous scale or was bivariate.

For continuous index test measures, a positive result on the index test was found if the patient had values of the chosen measured quantity above or below a threshold value, and different thresholds

could be used. The threshold of a diagnostic test is defined as the value at which the test can best differentiate between those with and without the target condition and, in practice, it varies amongst studies. Diagnostic test accuracy measures used in the analysis were sensitivity and specificity, and, if different diagnostic thresholds were used within a single study, area under the receiver operating characteristics (ROC) curve

For bivariate index test measures, a positive result on the index test was found if a particular clinical sign was detected. For example, a positive test would be recorded if a fracture was observed. Diagnostic test accuracy measures used in the analysis were sensitivity and specificity.

Coupled forest plots of sensitivity and specificity with their 95% CIs across studies (at various thresholds) were produced for each test, using RevMan5.[4] In order to do this, 2x2 tables (the number of true positives, false positives, true negatives and false negatives) were directly taken from the study if given, or else were derived from raw data or calculated from the set of test accuracy statistics.

Diagnostic meta-analysis was conducted where appropriate; that is, when 5 or more studies were available per threshold. Test accuracy for the studies was pooled using the bivariate method modelled in Winbugs®.[84] The bivariate method uses logistic regression on the true positives, true negatives, false positives and false negatives reported in the studies. Overall sensitivity and specificity and confidence regions were plotted (using methods outlined by Novielli et al. 2010)[108]. For scores with less than five studies, median sensitivity and the paired specificity were reported where possible. If an even number of studies were reported the lowest value of the two middle pairs was reported.

Heterogeneity or inconsistency amongst studies was visually inspected in the forest plots.

4.3.3.3 Data synthesis for risk prediction rules

Evidence reviews on risk prediction rules/tools results were presented separately for discrimination and calibration. The discrimination data was analysed according to the principles outlined under the section on data synthesis for diagnostic accuracy studies. Calibration data e.g., R^2 , if reported was presented separately to the discrimination data. The results were presented for each study separately along with the quality rating for the study. Inconsistency and imprecision were not assessed.

4.3.3.4 Data synthesis for qualitative reviews

For each included paper subthemes were identified and linked to a generic theme. An example of a subtheme identified by patients and carers is 'keeping an open channel of communication about reasons for any delays in the emergency room' and this is linked to a broader generic theme of 'information'. In some cases, subthemes would relate to more than one generic theme. A summary evidence table of generic themes and underpinning subthemes was then produced alongside the quality of the evidence.

4.3.4 Appraising the quality of evidence by outcomes

4.3.4.1 Interventional studies

The evidence for outcomes from the included RCT and observational studies were evaluated and presented using an adaptation of the 'Grading of Recommendations Assessment, Development and Evaluation (GRADE) toolbox' developed by the international GRADE working group (http://www.gradeworkinggroup.org/). The software (GRADEpro[1]) developed by the GRADE working

group was used to assess the quality of each outcome, taking into account individual study quality and the meta-analysis results.

Each outcome was first examined for each of the quality elements listed and defined in Table 2.

Table 2: Description of quality elements in GRADE for intervention studies

Quality element	Description
Risk of bias	Limitations in the study design and implementation may bias the estimates of the treatment effect. Major limitations in studies decrease the confidence in the estimate of the effect. Examples of such limitations are selection bias (often due to poor allocation concealment), performance and detection bias (often due to a lack of blinding of the patient, health care professional and assessor) and attrition bias (due to missing data causing systematic bias in the analysis).
Indirectness	Indirectness refers to differences in study population, intervention, comparator and outcomes between the available evidence and the review question.
Inconsistency	Inconsistency refers to an unexplained heterogeneity of effect estimates between studies in the same meta-analysis.
Imprecision	Results are imprecise when studies include relatively few patients and few events (or highly variable measures) and thus have wide CIs around the estimate of the effect relative to clinically important thresholds. 95% CIs denote the possible range of locations of the true population effect at a 95% probability, and so wide CIs may denote a result that is consistent with conflicting interpretations (for example a result may be consistent with both clinical benefit AND clinical harm) and thus be imprecise.
Publication bias	Publication bias is a systematic underestimate or an overestimate of the underlying beneficial or harmful effect due to the selective publication of studies. A closely related phenomenon is where some papers fail to report an outcome that is inconclusive, thus leading to an over-estimate of the effectiveness of that outcome.
Other issues	Sometimes randomisation may not adequately lead to group equivalence of confounders, and if so this may lead to bias, which should be taken into account. Potential conflicts of interest, often caused by excessive pharmaceutical company involvement in the publication of a study, should also be noted.

Details of how the four main quality elements (risk of bias, indirectness, inconsistency and imprecision) were appraised for each outcome are given below. Publication or other bias was only taken into consideration in the quality assessment if it was apparent.

Risk of bias

The main domains of bias for RCTs are listed in Table 3. Each outcome had its risk of bias assessed within each paper first. For each paper, if there were no risks of bias in any domain, the risk of bias was given a rating of 0. If there was risk of bias in just one domain, the risk of bias was given a 'serious' rating of -1, but if there was risk of bias in two or more domains the risk of bias was given a 'very serious' rating of -2. A weighted average score was then calculated across all studies contributing to the outcome, by taking into account the weighting of studies according to study precision. For example if the most precise studies tended to each have a score of -1 for that outcome, the overall score for that outcome would tend towards -1.

Table 3: Principle domains of bias in RCTs

Limitation	Explanation
Selection bias – sequence generation and allocation	If those enrolling patients are aware of the group to which the next enrolled patient will be allocated, either because of a non-random sequence that is predictable, or because a truly random sequence was not concealed from the researcher, this may translate into systematic selection bias. This may occur if the researcher chooses not

Limitation	Explanation
concealment	to recruit a participant into that specific group because of 1) knowledge of that participant's likely prognostic characteristics and 2) a desire for one group to do better than the other.
Performance and detection bias - Lack of patient and health care professional blinding	Patients, caregivers, those adjudicating and/or recording outcomes, and data analysts should not be aware of the arm to which patients are allocated. Knowledge of group can influence 1) the experience of the placebo effect, 2) performance in outcome measures, 3) the level of care and attention received, and 4) the methods of measurement or analysis, all of which can contribute to systematic bias.
Attrition bias	Attrition bias results from loss of data beyond a certain level (a differential of 10% between groups) which is not accounted for. Loss of data can occur when participants are compulsorily withdrawn from a group by the researchers (for example, when a per-protocol approach is used) or when participants do not attend assessment sessions. If the missing data are likely to be different from the data of those remaining in the groups, and there is a differential rate of such missing data from groups, systematic attrition bias may result.
Selective outcome reporting	Reporting of some outcomes and not others on the basis of the results can also lead to bias, as this may distort the overall impression of efficacy.
Other limitations	For example: • Stopping early for benefit observed in randomised trials, in particular in the absence of adequate stopping rules • Use of unvalidated patient-reported outcomes • lack of washout periods to avoid carry-over effects in cross-over trials • Recruitment bias in cluster randomised trials

Indirectness

Indirectness refers to the extent to which the populations, intervention, comparisons and outcome measures are dissimilar to those defined in the inclusion criteria for the reviews. Indirectness is important when these differences are expected to contribute to a difference in effect size, or may affect the balance of harms and benefits considered for an intervention. As for risk of bias, each outcome had its indirectness assessed within each paper first. For each paper, if there were no sources of indirectness, indirectness was given a rating of 0. If there was indirectness in just one source (for example, in terms of population), indirectness was given a 'serious' rating of -1, but if there was indirectness in two or more sources (for example, in terms of population and treatment) the indirectness was given a 'very serious' rating of -2. A weighted average score was then calculated across all studies contributing to the outcome, by taking into account study precision. For example, if the most precise studies tended to have an indirectness score of -1 each for that outcome, the overall score for that outcome would probably tend towards -1.

Inconsistency

Inconsistency refers to an unexplained heterogeneity of results for an outcome across different studies. When estimates of the treatment effect across studies differ widely, this suggests true differences in underlying treatment effect, which may be due to differences in populations, settings or doses. When heterogeneity existed within an outcome (chi-square $p<0.1$ or I^2 inconsistency statistic of more than 50%), but no plausible explanation could be found, the quality of evidence for that outcome was downgraded. Inconsistency for that outcome was given a 'serious' score of -1 if the I^2 was 50-74, and a 'very serious' score of -2 if the I^2 was 75 or more.

If inconsistency could be explained based on pre-specified subgroup analysis (that is, each subgroup had an I^2 less than 50), the GDG took this into account and considered whether to make separate

recommendations on new outcomes based on the subgroups defined by the assumed explanatory factors. In such a situation the quality of evidence was not downgraded for those emergent outcomes.

Since the inconsistency score was based on the meta-analysis results, the score represented the whole outcome and so weighted averaging across studies was not necessary.

Imprecision

The criteria applied for imprecision were based on the CIs for the pooled estimate of effect, and the minimal important differences (MID) for the outcome. The MIDs are the threshold for appreciable benefits and harms, separated by a zone either side of the line of no effect where there is assumed to be no clinically important effect. If either of the 95% CIs of the overall estimate of effect crossed **one** of the MID lines, imprecision was regarded as serious and a 'serious' score of -1 was given. This was because the overall result, as represented by the span of the CIs, was consistent with two interpretations as defined by the MID (for example, no clinically important effect and either clinical benefit or harm). If **both** MID lines were crossed by either or both of the CIs then imprecision was regarded as very serious and a 'very serious' score of -2 was given. This was because the overall result was consistent with three interpretations defined by the MID (no clinically important effect and clinical benefit and clinical harm). This is illustrated in Figure 2. As for inconsistency, since the imprecision score was based on the meta-analysis results, the score represented the whole outcome and so weighted averaging across studies was not necessary.

The position of the MID lines is ideally determined by values as reported in the literature. 'Anchor-based' methods aim to establish clinically meaningful changes in a continuous outcome variable by relating or 'anchoring' them to patient-centred measures of clinical effectiveness that could be regarded as gold standards with a high level of face validity. For example, the minimum amount of change in an outcome necessary to make a patient decide that they felt their quality of life had 'significantly improved' might define the MID for that outcome. MIDs in the literature may also be based on expert clinician or consensus opinion concerning the minimum amount of change in a variable deemed to affect quality of life or health. For binary variables, any MIDs reported in the literature will inevitably be based on expert consensus, as such, MIDs relate to all-or-nothing population effects rather than measurable effects on an individual, so are not amenable to patient-centred 'anchor' methods.

In the absence of literature values, the alternative approach to deciding on MID levels is the 'default' method, as follows:

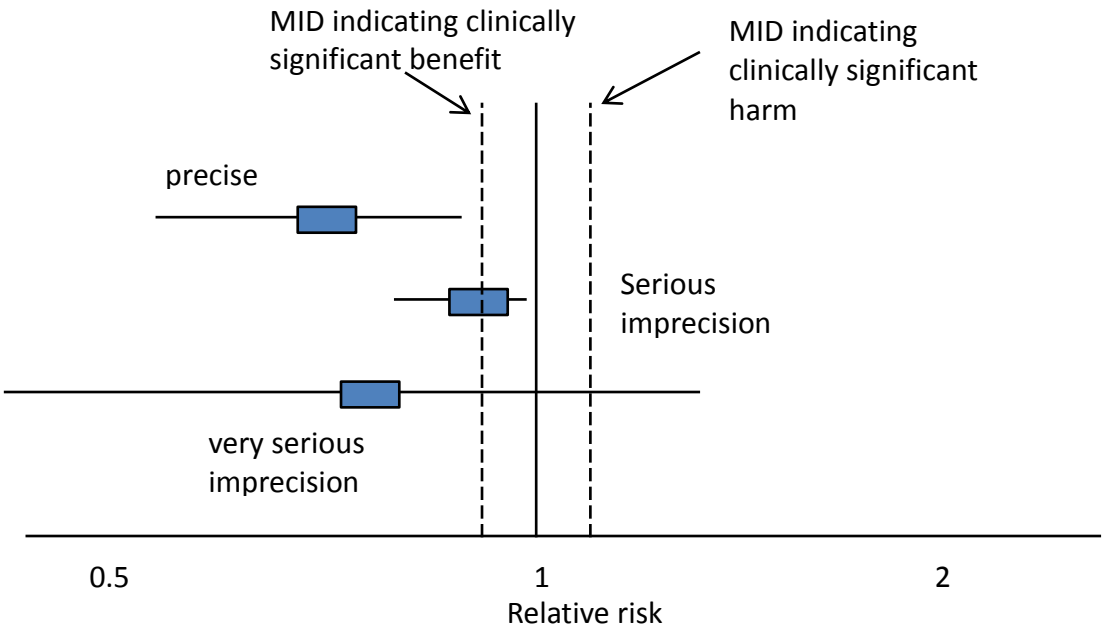
- For categorical outcomes the MIDs are taken as risk ratios (RRs) of 0.75 and 1.25. For 'positive' outcomes, such as 'patient satisfaction', the RR of 0.75 is taken as the line denoting the boundary between no clinically important effect and a clinically significant harm, whilst the RR of 1.25 is taken as the line denoting the boundary between no clinically important effect and a clinically significant benefit. For 'negative' outcomes, such as 'bleeding', the opposite occurs, so the RR of 0.75 is taken as the line denoting the boundary between no clinically important effect and a clinically significant benefit, whilst the RR of 1.25 is taken as the line denoting the boundary between no clinically important effect and a clinically significant harm.
- For continuous outcome variables the MID is taken as half the median baseline standard deviation of that variable, across all studies in the meta-analysis. Hence the MID denoting the minimum clinically significant benefit will be a positive for a 'positive' outcome (for example, a quality of life measure where a higher score denotes better health), and negative for a 'negative' outcome (for example, a VAS pain score). Clinically significant harms will be the converse of these. If baseline values are unavailable, then half the median comparator group standard deviation of that variable will be taken as the MID.

- If standardised mean differences have been used, then the MID will be set at the absolute value of +0.5. This follows because standardised mean differences are mean differences normalised to the pooled standard deviation of the two groups, and are thus effectively expressed in units of 'numbers of standard deviation'. The 0.5 MID value in this context therefore indicates half a standard deviation, the same definition of MID as used for non-standardised mean differences.

The default MID value was subject to amendment after discussion with the GDG. If the GDG decided that the MID level should be altered, after consideration of absolute as well as relative effects, this was allowed, provided that any such decision was not influenced by any bias towards making stronger or weaker recommendations for specific outcomes.

For this guideline, no appropriate MIDs for continuous or dichotomous outcomes were found in the literature, and so the default method was used.

Figure 2: Illustration of precise and imprecise outcomes based on the CI of dichotomous outcomes in a forest plot. Note that all three results would be pooled estimates, and would not, in practice, be placed on the same forest plot



Overall grading of the quality of clinical evidence

Once an outcome had been appraised for the main quality elements, as above, an overall quality grade was calculated for that outcome. The scores from each of the main quality elements (0, −1 or −2) were summed to give a score that could be anything from 0 (the best possible) to −8 (the worst possible). However scores were capped at −3. This final score was then applied to the starting grade that had originally been applied to the outcome by default, based on study design. For example, all RCTs started as High and the overall quality became Moderate, Low or Very low if the overall score was −1, −2 or −3 points, respectively. The significance of these overall ratings is explained in Table 3. The reasons or criteria used for downgrading were specified in the footnotes of the GRADE tables.

On the other hand, observational interventional studies started at LOW, and so a score of −1 would be enough to take the grade to the lowest level of Very low. Observational studies could, however,

be upgraded if there was: a large magnitude of effect, a dose-response gradient, and if all plausible confounding would reduce a demonstrated effect.

Table 4: Overall quality of outcome evidence in GRADE

Level	Description
High	Further research is very unlikely to change our confidence in the estimate of effect
Moderate	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate
Low	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate
Very low	Any estimate of effect is very uncertain

4.3.4.2 Prognostic studies

The quality of evidence for prognostic studies was evaluated according to the criteria given in Table 5. If data were meta-analysed the quality for pooled studies was presented. If the data was not pooled then a quality rating was presented for each study.

Table 5: Description of quality elements for prospective studies

Quality element	Description of cases where the quality measure would be downgraded
Study design	If case control rather than prospective cohort
Patient recruitment	If potential for selection bias
Validity of risk factor measure(s)	If non-validated and no reasonable face validity
Validity of outcome measure	If non-validated and no reasonable face validity
Blinding	if assessors of outcome not blinded to risk factor measurement (or vice versa)
Adequate follow up (or retrospective) duration	If follow up/retrospective period inadequate to allow events to occur, or retrospective period so short that causality is in doubt because the outcome may have preceded the risk factor
Confounder consideration	If there is a lack of consideration of all reasonable confounders in a multivariable analysis
Attrition	If attrition is too high and there is no attempt to adjust for this.
Directness	If the population, risk factors or outcome differ from that in the review question.

Because prognostic reviews were not usually based on multiple outcomes per study, quality rating was assigned by study. However, if there was more than one outcome involved in a study, then the quality rating of the evidence statements for each outcome was adjusted accordingly. For example, if one outcome was based on an invalidated measurement method, but another outcome in the same study wasn't, the latter outcome would be graded one grade higher than the other.

Quality rating started at High for prospective studies, and each major limitation (see Table 5) brought the rating down by one increment to a minimum grade of Low, as explained for interventional studies.

4.3.4.3 Diagnostic studies

Quality of evidence for diagnostic data was evaluated by study using the Quality Assessment of Diagnostic Accuracy Studies version 2 (QUADAS-2) checklists. Risk of bias and applicability in primary diagnostic accuracy studies in QUADAS-2 consists of 4 domains (see Figure 3):

- Patient selection

- Index test
- Reference standard
- Flow and timing

Figure 3: Summary of QUADAS-2 with list of signalling, risk of bias and applicability questions.

Domain	Patient selection	Index test	Reference standard	Flow and timing
Description	Describe methods of patient selection. Describe included patients (prior testing, presentation, intended use of index test and setting)	Describe the index test and how it was conducted and interpreted	Describe the reference standard and how it was conducted and interpreted	Describe any patients who did not receive the index test(s) and/or reference standard or who were excluded from the 2x2 table (refer to flow diagram). Describe the time interval and any interventions between index test(s) and reference standard
Signalling questions (yes/no/unclear)	Was a consecutive or random sample of patients enrolled?	Were the index test results interpreted without knowledge of the results of the reference standard?	Is the reference standard likely to correctly classify the target condition?	Was there an appropriate interval between index test(s) and reference standard?
	Was a case-control design avoided?	If a threshold was used, was it pre-specified?	Were the reference standard results interpreted without knowledge of the results of the index test?	Did all patients receive a reference standard?
	Did the study avoid inappropriate exclusions?			Did all patients receive the same reference standard?
				Were all patients included in the analysis?
Risk of bias; (high/low/unclear)	Could the selection of patients have introduced bias?	Could the conduct or interpretation of the index test have introduced bias?	Could the reference standard, its conduct or its interpretation have introduced bias?	Could the patient flow have introduced bias?
Concerns regarding applicability (high/low/unclear)	Are there concerns that the included patients do not match the review question?	Are there concerns that the index test, its conduct, or interpretation differ from the review question?	Are there concerns that the target condition as defined by the reference standard does not match the review question?	

4.3.4.4 Qualitative reviews

Table 6 below summarises the factors which were assessed to inform the quality rating for each subtheme. The quality for each theme is presented in a summary table with the findings.

Table 6: Summary of factors assessed in qualitative reviews

Quality element	Factors
Limitations of evidence	• 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?
Coherence of findings	• Do the subthemes identified complement, reinforce or contradict each other?
Applicability of evidence	• Are the findings of the study applicable to the evidence review? For example population and setting

4.3.5 Assessing clinical importance

The GDG assessed the evidence by outcome in order to determine if there was, or potentially was, a clinically important benefit, a clinically important harm or no clinically important difference between interventions. To facilitate this, binary outcomes were converted into absolute risk differences (ARDs) using GRADEpro[56,56] software: the median control group risk across studies was used to calculate the ARD and its 95% CI from the pooled risk ratio.

The assessment of clinical benefit, harm, or no benefit or harm was based on the point estimate of absolute effect for intervention studies which was standardised across the reviews. The GDG considered for most of the outcomes in the intervention reviews that if at least 100 participants per 1000 (10%) achieved (if positive) the outcome of interest in the intervention group compared with the comparison group then this intervention would be considered beneficial. The same point estimate but in the opposite direction would apply if the outcome was negative. For the critical outcomes of mortality, any reduction represented a clinical benefit. For adverse events, 50 events or more represented clinical harm. For continuous outcomes, if the mean difference was greater than the minimally important difference then this presented a clinical benefit or harm. For outcomes such as mortality any reduction or increase was considered to be clinically important.

This assessment was carried out by the GDG for each critical outcome, and an evidence summary table was produced to compile the GDG's assessments of clinical importance per outcome, alongside the evidence quality and the uncertainty in the effect estimate (imprecision).

4.3.6 Clinical evidence statements

Clinical evidence statements are summary statements that are presented after the GRADE profiles, summarising the key features of the clinical effectiveness evidence presented. The wording of the evidence statements reflects the certainty/uncertainty in the estimate of effect. The evidence statements were presented by outcome and encompassed the following key features of the evidence:

- The number of studies and the number of participants for a particular outcome.

- An indication of the direction of clinical importance (if one treatment is beneficial or harmful compared with the other or whether there is no difference between the two tested treatments).
- A description of the overall quality of evidence (GRADE overall quality).

4.4 Evidence of cost-effectiveness

Evidence on cost-effectiveness related to the key clinical issues being addressed in the guideline was sought. The health economist:

- Undertook a systematic review of the economic literature
- Undertook new cost-effectiveness analysis in priority areas

4.4.1 Literature review

The Health Economist:

- Identified potentially relevant studies for each review question from the economic search results by reviewing titles and abstracts – full papers were then obtained.
- Reviewed full papers against pre-specified inclusion / exclusion criteria to identify relevant studies (see below for details).
- Critically appraised relevant studies using the economic evaluations checklist as specified in The Guidelines Manual[101]
- Extracted key information about the study's methods and results into evidence tables (See Appendix H. Studies considered eligible but were excluded can be found in Appendix L)
- Generated summaries of the evidence in NICE economic evidence profiles (included in the relevant chapter write-ups) – see below for details.

4.4.1.1 Inclusion and exclusion

Full economic evaluations (studies comparing costs and health consequences of alternative courses of action: cost–utility, cost-effectiveness, cost-benefit and cost-consequence analyses) and comparative costing studies that addressed the review question in the relevant population were considered potentially applicable as economic evidence.

Studies that only reported cost per hospital (not per patient) or only reported average cost effectiveness without disaggregated costs and effects were excluded. Abstracts, posters, reviews, letters and editorials, foreign language publications and unpublished studies were excluded. Studies judged to have an applicability rating of 'not applicable' were excluded (this included studies that took the perspective of a non-OECD country).

Remaining studies were prioritised for inclusion based on their relative applicability to the development of this guideline and the study limitations. For example, if a high quality, directly applicable UK analysis was available other less relevant studies may not have been included. Where exclusions occurred on this basis, this is noted in the relevant section.

For more details about the assessment of applicability and methodological quality see the economic evaluation checklist (The Guidelines Manual, Appendix H[101] and the health economics research protocol in Appendix C.

When no relevant economic analysis was found from the economic literature review, relevant UK NHS unit costs related to the compared interventions were presented to the GDG to inform the possible economic implication of the recommendation being made.

4.4.1.2 NICE economic evidence profiles

The NICE economic evidence profile has been used to summarise cost and cost-effectiveness estimates. The economic evidence profile shows, for each economic study, an assessment of

applicability and methodological quality, with footnotes indicating the reasons for the assessment. These assessments were made by the health economist using the economic evaluation checklist from The Guidelines Manual, Appendix H.[101] It also shows incremental costs, incremental outcomes (for example, QALYs) and the incremental cost-effectiveness ratio from the primary analysis, as well as information about the assessment of uncertainty in the analysis. See Table 7 for more details.

If a non-UK study was included in the profile, the results were converted into pounds sterling using the appropriate purchasing power parity http://stats.oecd.org/Index.aspx?datasetcode=SNA_TABLE4

Table 7: Content of NICE economic profile

Item	Description
Study	First author name, reference, date of study publication and country perspective.
Limitations	An assessment of methodological quality of the study[a]: • Minor limitations – the study meets all quality criteria, or the study fails to meet one or more quality criteria, but this is unlikely to change the conclusions about cost effectiveness. • Potentially serious limitations – the study fails to meet one or more quality criteria, and this could change the conclusion about cost effectiveness • Very serious limitations – the study fails to meet one or more quality criteria and this is very likely to change the conclusions about cost effectiveness. Studies with very serious limitations would usually be excluded from the economic profile table.
Applicability	An assessment of applicability of the study to the clinical guideline, the current NHS situation and NICE decision-making[a]: • Directly applicable – the applicability criteria are met, or one or more criteria are not met but this is not likely to change the conclusions about cost effectiveness. • Partially applicable – one or more of the applicability criteria are not met, and this might possibly change the conclusions about cost effectiveness. • Not applicable – one or more of the applicability criteria are not met, and this is likely to change the conclusions about cost effectiveness.
Other comments	Particular issues that should be considered when interpreting the study.
Incremental cost	The mean cost associated with one strategy minus the mean cost of a comparator strategy.
Incremental effects	The mean QALYs (or other selected measure of health outcome) associated with one strategy minus the mean QALYs of a comparator strategy.
ICER	Incremental cost-effectiveness ratio: the incremental cost divided by the respective QALYs gained.
Uncertainty	A summary of the extent of uncertainty about the ICER reflecting the results of deterministic or probabilistic sensitivity analyses, or stochastic analyses of trial data, as appropriate.

(a) Limitations and applicability were assessed using the economic evaluation checklist from The Guidelines Manual, Appendix H[101]

Where economic studies compare multiple strategies, results are presented in the economic evidence profiles for the pair-wise comparison specified in the review question, irrespective of whether or not that comparison was 'appropriate' within the analysis being reviewed. A comparison is 'appropriate' where an intervention is compared with the next most expensive non-dominated option – a clinical strategy is said to 'dominate' the alternatives when it is both more effective and less costly. Footnotes indicate if a comparison was 'inappropriate' in the analysis.

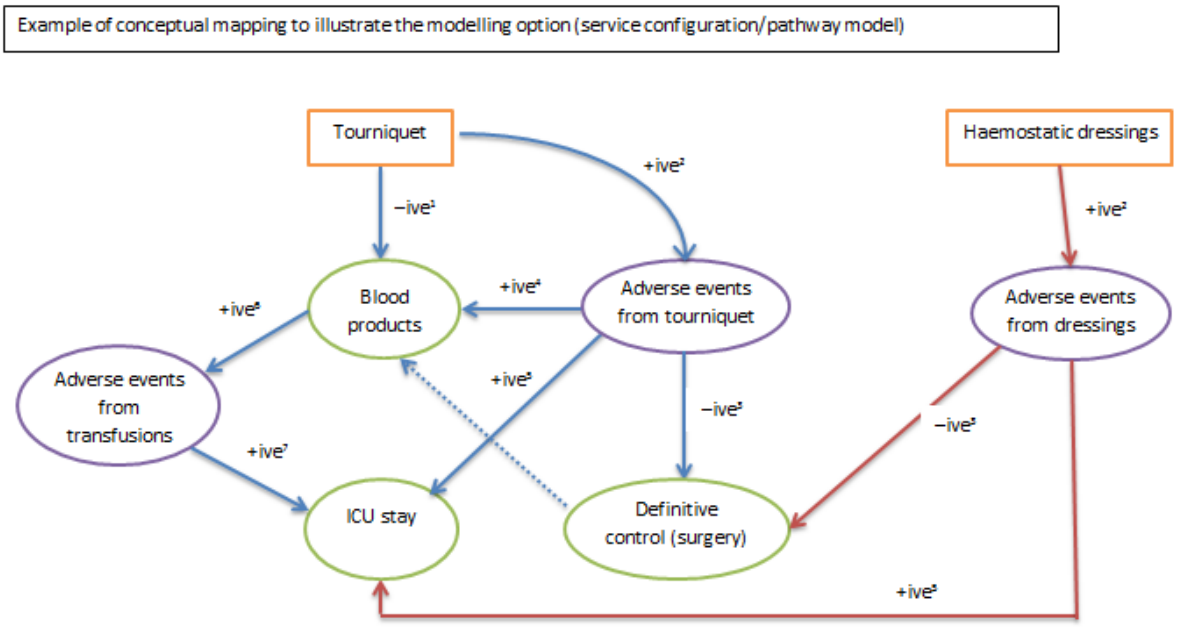
4.4.2 Undertaking new health economic analysis

As well as reviewing the published economic literature for each review question, as described above, new economic analysis was attempted by the Health Economist in priority areas. Priority areas for the new health economic analysis were agreed by the GDG after formation of the review questions and consideration of the available health economic evidence.

Additional data for the analysis was explored through the use of audit data and discussion with the GDG. Model structure, inputs and assumptions were explained to and agreed by the GDG members during meetings, and they commented on subsequent revisions.

One method that was used to try and link together the questions in this guideline, which are inter-related and have complex interactions (particularly around haemorrhage control), was conceptual mapping. This is an activity that involves diagrammatically representing the relationships between different areas and the interactions between interventions and outcomes, and was suggested as a softer approach of looking at the effect of different interventions and interactions between interventions on outcomes, rather than economic modelling in its more traditional form of cost utility. An example of this method is shown below.

Figure 4: Conceptual mapping example



[1] This is a negative relationship because an effective tourniquet will control bleeding better and lead to less use of blood products.
[2] This is a positive relationship because the interventions can lead to adverse events.
[3] This is a negative relationship because adverse events can lead to a delay in surgery.
[4] This is a positive relationship because adverse events of tourniquets can lead to increased bleeding and thus more use of blood products.
[5] Adverse events can lead to longer ICU stay.
[6] Use of blood products can lead to transfusion related complications.
[7] Transfusion related complicated can lead to longer ICU stay.
Dotted arrow: surgery could also impact the use of blood products

See Appendix M for details of the health economic analysis attempted for the guideline.

4.4.3 Cost-effectiveness criteria

NICE's report 'Social value judgements: principles for the development of NICE guidance' sets out the principles that GDGs should consider when judging whether an intervention offers good value for money.[99]

In general, an intervention was considered to be cost effective if either of the following criteria applied (given that the estimate was considered plausible):

a. The intervention dominated other relevant strategies (that is, it was both less costly in terms of resource use and more clinically effective compared with all the other relevant alternative strategies), or
b. The intervention cost less than £20,000 per quality-adjusted life-year (QALY) gained compared with the next best strategy.

If the GDG recommended an intervention that was estimated to cost more than £20,000 per QALY gained, or did not recommend one that was estimated to cost less than £20,000 per QALY gained, the reasons for this decision are discussed explicitly in the 'from evidence to recommendations' section of the relevant chapter with reference to issues regarding the plausibility of the estimate or to the factors set out in the 'Social value judgements: principles for the development of NICE guidance' [99].

In the absence of economic evidence

When no relevant published studies were found, and a new analysis was not prioritised, the GDG made a qualitative judgement about cost effectiveness by considering expected differences in resource use between options and relevant UK NHS unit costs, alongside the results of the clinical review of effectiveness evidence.

The UK NHS costs reported in the guideline are those that were presented to the GDG and were correct at the time recommendations were drafted. They may have changed subsequently before the time of publication.

4.5 Developing recommendations

Over the course of the guideline development process, the GDG was presented with:

- Evidence tables of the clinical and economic evidence reviewed from the literature. All evidence tables are in Appendix G.
- Summary of clinical and economic evidence and quality as presented in chapters 6-17.
- Forest plots and summary ROC curves (Appendix J)
- A description of the methods and results of the cost-effectiveness analysis undertaken for the guideline (Appendix M)

Recommendations were drafted on the basis of the GDG interpretation of the available evidence, taking into account the balance of benefits, harms and costs. When clinical and economic evidence was of poor quality, conflicting or absent, the GDG drafted recommendations based on their expert opinion. The considerations for making consensus-based recommendations include the balance between potential harms and benefits, economic or implications compared with the benefits, current practices, recommendations made in other relevant guidelines, patient preferences and equality issues. The consensus recommendations were done through discussions in the GDG. The GDG also considered whether the uncertainty was sufficient to justify delaying making a recommendation to await further research, taking into account the potential harm of failing to make a clear recommendation (See section 0).

The main considerations specific to each recommendation are outlined in the Evidence to Recommendation Section preceding the recommendation section.

4.5.1 Research recommendations

When areas were identified for which good evidence was lacking, the GDG considered making recommendations for future research. Decisions about inclusion were based on factors such as:

- the importance to patients, including patient safety, or the population
- national priorities
- potential impact on the NHS and future NICE guidance
- ethical and technical feasibility

4.5.2 Validation process

The guidance is subject to an eight week public consultation and feedback as part of the quality assurance and peer review the document. All comments received from registered stakeholders are responded to in turn and posted on the NICE website when the pre-publication check of the full guideline occurs.

4.5.3 Updating the guideline

Following publication, and in accordance with the NICE guidelines manual[101], NICE will consider whether the evidence base has progressed sufficiently to alter the guideline recommendations and warrant an update.

4.5.4 Disclaimer

Health care providers need to use clinical judgement, knowledge and expertise when deciding whether it is appropriate to apply guidelines. The recommendations cited here are a guide and may not be appropriate for use in all situations. The decision to adopt any of the recommendations cited here must be made by the practitioners in light of individual patient circumstances, the wishes of the patient, clinical expertise and resources.

The National Clinical Guideline Centre disclaims any responsibility for damages arising out of the use or non-use of these guidelines and the literature used in support of these guidelines.

4.5.5 Funding

The National Clinical Guideline Centre was commissioned by the National Institute for Health and Care Excellence to undertake the work on this guideline.

5 Guideline summary

5.1 Full list of recommendations

1. Use drug-assisted rapid sequence induction (RSI) of anaesthesia and intubation as the definitive method of securing the airway in patients with major trauma who cannot maintain their airway and/or ventilation.
2. If RSI fails, use basic airway manoeuvres and adjuncts and/or a supraglottic device until a surgical airway or assisted tracheal placement is performed.
3. Aim to perform RSI as soon as possible and within 45 minutes of the initial call to the emergency services, preferably at the scene of the incident.

If RSI cannot be performed at the scene:

- consider using a supraglottic device if the patient's airway reflexes are absent
- use basic airway manoeuvres and adjuncts if the patient's airway reflexes are present or supraglottic device placement is not possible
- transport the patient to a major trauma centre for RSI provided the journey time is 60 minutes or less
- only divert to a trauma unit for RSI before onward transfer if a patent airway cannot be maintained or the journey time to a major trauma centre is more than 60 minutes.

4. Use clinical assessment to diagnose pneumothorax for the purpose of triage or intervention.
5. Consider using eFAST (extended focused assessment with sonography for trauma) to augment clinical assessment only if a specialist team equipped with ultrasound is immediately available and onward transfer will not be delayed.
6. Be aware that a negative eFAST of the chest does not exclude a pneumothorax.
7. Only perform chest decompression in a patient with suspected tension pneumothorax if there is haemodynamic instability or severe respiratory compromise.
8. Use open thoracostomy instead of needle decompression if the expertise is available, followed by a chest drain via the thoracostomy in patients who are breathing spontaneously.
9. Observe patients after chest decompression for signs of recurrence of the tension pneumothorax.
10. In patients with an open pneumothorax:
    - cover the open pneumothorax with a simple occlusive dressing and
    - observe for the development of a tension pneumothorax.

11. In patients with tension pneumothorax, perform chest decompression before imaging only if they have either haemodynamic instability or severe respiratory compromise.
12. Perform chest decompression using open thoracostomy followed by a chest drain in patients with tension pneumothorax.
13. Imaging for haemorrhage in patients with suspected haemorrhage should be performed urgently, and the images should be interpreted immediately by a healthcare professional with training and skills in this area.
14. Consider immediate chest X-ray and/or eFAST (extended focused assessment with sonography for trauma) as part of the primary survey to assess chest trauma in adults (16 or over) with severe respiratory compromise.
15. Consider immediate CT for adults (16 or over) with suspected chest trauma without severe respiratory compromise who are responding to resuscitation or whose haemodynamic status is normal (see also recommendation 50 on whole-body CT).
16. Consider chest X-ray and/or ultrasound for first-line imaging to assess chest trauma in children (under 16s).
17. Do not routinely use CT for first-line imaging to assess chest trauma in children (under 16s).
18. Use simple dressings with direct pressure to control external haemorrhage.
19. In patients with major limb trauma use a tourniquet if direct pressure has failed to control life-threatening haemorrhage.
20. If active bleeding is suspected from a pelvic fracture after blunt high-energy trauma:
    - apply a purpose-made pelvic binder or
    - consider an improvised pelvic binder, but only if a purpose-made binder does not fit.
21. Use intravenous tranexamic acid as soon as possible in patients with major trauma and active or suspected active bleeding.
22. Do not use intravenous tranexamic acid[a] more than 3 hours after injury in patients with major trauma unless there is evidence of hyperfibrinolysis.
23. Rapidly reverse anticoagulation in patients who have major trauma with haemorrhage.
24. Hospital trusts that admit patients with major trauma should have a protocol for the rapid identification of patients who are taking anticoagulants and the reversal of anticoagulation agents.
25. Use prothrombin complex concentrate immediately in adults (16 or over) with major trauma who have active bleeding and need emergency reversal of a vitamin K antagonist.
26. Do not use plasma to reverse a vitamin K antagonist in patients with major trauma.
27. Consult a haematologist immediately for advice on adults (16 or over) who have active bleeding and need reversal of any anticoagulant agent other than a vitamin K antagonist.

28. Consult a haematologist immediately for advice on children (under 16s) with major trauma who have active bleeding and may need reversal of any anticoagulant agent.

29. Do not reverse anticoagulation in patients who do not have active or suspected bleeding.

30. Use physiological criteria that include the patient's haemodynamic status and their response to immediate volume resuscitation to activate the major haemorrhage protocol.

31. Do not rely on a haemorrhagic risk tool applied at a single time point to determine the need for major haemorrhage protocol activation.

32. For circulatory access in patients with major trauma in pre-hospital settings:
    - use peripheral intravenous access or
    - if peripheral intravenous access fails, consider intra-osseous access.

33. For circulatory access in children (under 16s) with major trauma, consider intra-osseous access as first-line access if peripheral access is anticipated to be difficult.

34. For circulatory access in patients with major trauma in hospital settings:
    - use peripheral intravenous access or
    - if peripheral intravenous access fails, consider intra-osseous access while central access is being achieved.

35. For patients with active bleeding use a restrictive approach to volume resuscitation until definitive early control of bleeding has been achieved.

36. In pre-hospital settings, titrate volume resuscitation to maintain a palpable central pulse (carotid or femoral).

37. In hospital settings, move rapidly to haemorrhage control, titrating volume resuscitation to maintain central circulation until control is achieved.

38. For patients who have haemorrhagic shock and a traumatic brain injury:
    - if haemorrhagic shock is the dominant condition, continue restrictive volume resuscitation or
    - if traumatic brain injury is the dominant condition, use a less restrictive volume resuscitation approach to maintain cerebral perfusion.

39. In pre-hospital settings only use crystalloids to replace fluid volume in patients with active bleeding if blood components are not available.

40. In hospital settings do not use crystalloids for patients with active bleeding (See the section on resuscitation in the NICE guideline ‘Intravenous fluid therapy in adults in hospital’ and the section on fluid resuscitation in the NICE guideline ‘Intravenous fluid therapy in children and young people in hospital’ for advice on tetrastarches.

41. For adults (16 or over) use a ratio of 1 unit of plasma to 1 unit of red blood cells to replace fluid volume.

42. For children (under 16s) use a ratio of 1 part plasma to 1 part red blood cells, and base the volume on the child’s weight.

43. Hospital trusts should have specific major haemorrhage protocols for adults (16 or over) and children (under 16s).

44. For patients with active bleeding, start with a fixed-ratio protocol for blood components and change to a protocol guided by laboratory coagulation results at the earliest opportunity.
45. Limit diagnostic imaging (such as chest and pelvis X-rays or FAST [focused assessment with sonography for trauma]) to the minimum needed to direct intervention in patients with suspected haemorrhage and haemodynamic instability who are not responding to volume resuscitation.
46. Be aware that a negative FAST does not exclude intraperitoneal or retroperitoneal haemorrhage.
47. Consider immediate CT for patients with suspected haemorrhage if they are responding to resuscitation or if their haemodynamic status is normal.
48. Do not use FAST or other diagnostic imaging before immediate CT in patients with major trauma.
49. Do not use FAST as a screening modality to determine the need for CT in patients with major trauma.
50. Use whole-body CT (consisting of a vertex-to-toes scanogram followed by a CT from vertex to mid-thigh) in adults (16 or over) with blunt major trauma and suspected multiple injuries. Patients should not be repositioned during whole-body CT.
51. Use clinical findings and the scanogram to direct CT of the limbs in adults (16 or over) with limb trauma.
52. Do not routinely use whole-body CT to image children (under 16s). Use clinical judgement to limit CT to the body areas where assessment is needed.
53. Use damage control surgery in patients with haemodynamic instability who are not responding to volume resuscitation.
54. Consider definitive surgery in patients with haemodynamic instability who are responding to volume resuscitation.
55. Use definitive surgery in patients whose haemodynamic status is normal.
56. Use interventional radiology techniques in patients with active arterial pelvic haemorrhage unless immediate open surgery is needed to control bleeding from other injuries.
57. Consider interventional radiology techniques in patients with solid-organ (spleen, liver or kidney) arterial haemorrhage.
58. Consider a joint interventional radiology and surgery strategy for arterial haemorrhage that extends to surgically inaccessible regions.
59. Use an endovascular stent graft in patients with blunt thoracic aortic injury.
60. Minimise ongoing heat loss in patients with major trauma.
61. See the NICE guideline on patient experience in adult NHS services for advice on assessing pain in adults.
62. Assess pain regularly in patients with major trauma using a pain assessment scale suitable for the patient's age, developmental stage and cognitive function.
63. Continue to assess pain in hospital using the same pain assessment scale that was used in the pre-hospital setting.

64. For patients with major trauma, use intravenous morphine as the first-line analgesic and adjust the dose as needed to achieve adequate pain relief.

65. If intravenous access has not been established, consider the intranasal route for atomised delivery of diamorphine or ketamine.

66. Consider ketamine in analgesic doses as a second-line agent.

67. Record the following in patients with major trauma in pre-hospital settings:

- catastrophic haemorrhage
- airway with in line spinal immobilisation
- breathing
- circulation
- disability (neurological)
- exposure and environment

(<C>ABCDE)

68. If possible, record information on whether the assessments show that the patient's condition is improving or deteriorating.

69. Record pre-alert information using a structured system and include all of the following:

- the patient's age and sex
- time of incident
- mechanism of injury
- injuries suspected
- signs, including vital signs and Glasgow Coma Score
- treatment so far
- estimated time of arrival at emergency department
- special requirements
- the ambulance call sign, name of the person taking the call and time of call.

70. A senior nurse or trauma team leader in the emergency department should receive the pre-alert information and determine the level of trauma team response according to agreed and written local guidelines.

71. The trauma team leader should be easily identifiable to receive the handover and the trauma team ready to receive the information.

72. The pre-hospital documentation, including the recorded pre-alert information, should be quickly available to the trauma team and placed in the patient's hospital notes.

73. Record the items listed in recommendation 67, as a minimum, for the primary survey.

74. One member of the trauma team should be designated to record all trauma team findings and interventions as they occur (take 'contemporaneous notes').

75. The trauma team leader should be responsible for checking the information recorded to ensure that it is complete.

76. Follow a structured process when handing over care within the emergency department (including shift changes) and to other departments. Ensure that the handover is documented.

77. Ensure that all patient documentation, including images and reports, goes with patients when they are transferred to other departments or centres.

78. Produce a written summary, which gives the diagnosis, management plan and expected outcome, and:

- is aimed at and sent to the patient's GP within 24 hours of admission
- includes a summary written in plain English that is understandable by patients, family members and carers
- is readily available in the patient's records.

79. When communicating with patients, family members and carers:

- manage expectations and avoid misinformation
- answer questions and provide information honestly, within the limits of your knowledge
- do not speculate and avoid being overly optimistic or pessimistic when discussing information on further investigations, diagnosis or prognosis
- ask if there are any other questions.

80. The trauma team structure should include a clear point of contact for providing information to patients, family members and carers.

81. If possible, ask the patient if they want someone (a family member, carer or friend) with them.

82. If the patient agrees, invite their family member, carer or friend into the resuscitation room. Ensure that they are accompanied by a member of staff and their presence does not affect assessment, diagnosis or treatment.

83. Allocate a dedicated member of staff to contact the next of kin and provide support for unaccompanied children and vulnerable adults.

84. Contact the mental health team as soon as possible for patients who have a pre-existing psychological or psychiatric condition that might have contributed to their injury, or a mental health problem that might affect their wellbeing or care in hospital.

85. For a child or vulnerable adult with major trauma, enable their family members or carers to remain within eyesight if appropriate.

86. Work with family members and carers of children and vulnerable adults to provide information and support. Take into account the age, developmental stage and cognitive function of the child or vulnerable adult.

87. Include siblings of an injured child when offering support to family members and carers.

88. Explain to patients, family members and carers what is happening and why it is happening. Provide:

- information on known injuries
- details of immediate investigations and treatment, and if possible include time schedules

- information about expected outcomes of treatment, including time to returning to usual activities and the likelihood of permanent effects on quality of life, such as pain, loss of function or psychological effects.

89. Provide information at each stage of management (including the results of imaging) in face-to-face consultations.

90. Document all key communications with patients, family members and carers about the management plan.

91. For patients who are being transferred from an emergency department to another centre, provide verbal and written information that includes:

    - the reason for the transfer
    - the location of the receiving centre and the patient's destination within the receiving centre
    - the name and contact details of the person responsible for the patient's care at the receiving centre
    - the name and contact details of the person who was responsible for the patient's care at the initial hospital.

    The recommendations listed here are directed at clinical staff. The recommendations aimed at organisations are in the Major trauma services guidance.

5.1.1 Additional recommendations

The evidence for the following recommendations was reviewed in other guidelines from this suite of 5 guidelines.

Immediate destination after injury

- Be aware that the optimal destination for patients with major trauma is usually a major trauma centre. In some locations or circumstances intermediate care in a trauma unit might be needed for urgent treatment, in line with agreed practice within the regional trauma network.

Training and skills

- Ensure that each healthcare professional within the trauma service has the training and skills to deliver, safely and effectively, the interventions they are required to give, in line with this guideline and the NICE guidelines on non-complex fractures, complex fractures and spinal injury.
- Enable each healthcare professional who delivers care to patients with trauma to have up-to-date training in the interventions they are required to give.
- Provide education and training courses for healthcare professionals who deliver care to children with major trauma that include the following components:
    - Safeguarding
    - Taking into account the radiation risk of CT to children when discussing imaging for them
    - The importance of the major trauma team, the roles of team members and the team leader, and working effectively in a major trauma team
    - Managing the distress families and carers may experience and breaking bad news
    - The importance of clinical audit and case review.

5.2 Key research recommendations

1. **What is the clinical and cost effectiveness of point-of-care coagulation testing using rotational thromboelastrometry (ROTEM) or thromboelastography (TEG) to target treatment, compared with standard laboratory coagulation testing?**

2. **Is lactate monitoring in patients with major trauma clinically and cost effective?**

3. **Is morphine clinically and cost effective compared with ketamine for first-line pharmacological pain management (in both pre-hospital and hospital settings) in patients with major trauma?**

4. **Is warming clinically and cost effective in patients with major trauma? If so, which groups of patients will benefit from warming and what is the best method of warming?**

6 Airway management

6.1 Introduction

Due to the injuries trauma patients sustain they may require support pre-hospital to maintain their airway. This may include patients who stop breathing, those that are unable to maintain adequate ventilation, or those that require airway support for head and chest trauma management. A lack of oxygen pre-hospital can result in a higher risk of mortality, and can also cause brain injury, which can have long-term implications for function and patient quality of life. The effective airway management pre-hospital is therefore a critical clinical issue. There are a number of airway strategies currently used pre-hospital:

- Basic airway adjuncts (including bag valve mask, naso and oro-pharyngeal airway). Bag valve mask enables clinicians to provide adequate ventilation for patients requiring airway support and allows enough time to establish a more controlled approach to airway management, such as tracheal intubation. Oropharyngeal airways should be used in unconscious (unresponsive) patients as they are quite stimulating and generate a gag reflex. A nasopharyngeal airway is an adjunct for use in patients with potential or actual airway obstruction, particularly in circumstances where an oropharyngeal airway is inappropriate (e.g. patient has trismus or an intact gag reflex)
- Laryngeal masks are a type of supra-glottic device. They are designed to be used above the vocal cords, or glottis opening. They're placed using a blind technique and create a seal around the glottic opening but do not cross the vocal cords. They cannot be used in patients with an intact gag reflex.
- Tracheal intubation (Drug assisted, non-drug assisted, Rapid sequence induction of anaesthesia). Tracheal intubation is where an orotracheal tube is placed under direct vision or assisted vision (e.g videolaryngoscopes) through the larynx into the trachea. It has the advantage of providing a protected airway whilst enabling ventilation, a route for oxygenation and suctioning. In the unconscious patients with no gag or laryngeal reflex, tracheal intubation can be performed without the use of drugs.
- Rapid sequence induction (RSI) of anaesthesia and intubation is a method to facilitate emergency tracheal intubation. The overall aim is to rapidly provide optimal conditions for tracheal intubation, as this is thought to reduce the risk of aspiration. RSI of anaesthesia and intubation is the administration of a potent induction agent (anaesthetic) followed by a rapidly acting neuromuscular blocking agent to induce unconsciousness and motor paralysis for tracheal intubation
- Surgical airway (cricothyroidotomy). This procedure provides a temporary emergency airway in situations where there is obstruction at or above the level of the larynx, such that oral/nasal tracheal intubation is impossible

This review considers the optimum airway management strategy that should be used for trauma patients pre-hospital

6.2 Review question: What is the most clinically and cost effective strategy for managing the airway in patients with trauma pre-hospital?

For full details see review protocol in Appendix C.

Table 8: PICO characteristics of review question

Population	Children, young people and adults experiencing a traumatic incident, including: • people able to be intubated without drugs (GCS=3), • people unable to maintain or protect their own airway (GCS <9, <12 and <15), and • people who are able to maintain their own airway, but who need to be intubated for other reasons (for example, people who may lose their airway during transport and people who require ventilatory support for chest or head trauma management)
Intervention(s)	• Drug-assisted tracheal intubation • Non-drug assisted tracheal intubation • Rapid sequence induction of anaesthesia (RSI) • Supraglottic devices • Surgical airway/ assisted tracheal placement (cricothyroidotomy)
Comparison(s)	• Basic airway adjuncts (including bag-valve mask, naso- and oropharyngeal airway) • No intervention • A comparison of those listed above
Outcomes	Critical: • Mortality at 48 hours, 30 days/1 month, 1 year • Health-related quality of life (Glasgow outcome scale or ther functional outcome score; SF-36, functional independence measure (FIM), rehabilitation complexity scale, SF-12, EQ5D) • Brain injury management (oxygenation, control of carbon dioxide levels) • Aspiration events • Failure to intubate or secure airway • Adverse events (hypotension, unrecognised oesophageal intubation) Important • Patient reported outcomes (psychological wellbeing)
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

We searched for RCTs and cohort studies that compared airway management strategies as listed in the review protocol. Studies were excluded if (i) the intervention received by patients was unclear, (ii) patients in the same group may have received different interventions, or (iii) patients received multiple interventions (for example, if an intervention was unsuccessful).

6.3 Clinical evidence

No clinical evidence was found to be relevant for this question.

6.4 Economic evidence

Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow chart in Appendix E.

Unit costs

Table 9: Resources and costs involved in tracheal intubation

Resources needed	Cost	Cost per patient	Source
Equipment used			
Endotracheal tube cuffed with murphy eye	£12.17 Box of 10	£1.22	NHS supply chain [3]
Endotracheal tube introducer (single-use bougie)	£59.24 Box of 20	£2.96	NHS supply chain
Compact HME with expandable catheter mount	£21.48 Box of 25	£0.86	NHS supply chain
Oropharyngeal airway	£2.85 Pack of 10	£0.29	NHS supply chain
laryngoscope handle and blade combination single use	£63.82 Pack of 20	£7.25	NHS supply chain
Resuscitator manual (bag-valve-mask) disposable		£6.44	NHS supply chain
Electrostatic filter with sampling port - Adult: Co_2 detector (easycap)	£37.14 case of 6	£6.19	NHS supply chain
		Non-drug assisted tracheal intubation **TOTAL: £25.21**	
Drugs used			
Anaesthetic: Ketamine	£5.06 20-mL vial (10 mg/mL so =200mg)	£5.06	BNF [73]
Muscle relaxant:Rocuronium	£3 5ml vial (10mg/ml so = 50mg)	£3	BNF
1x2 ml syringe	£5.18 Box of 100	£0.05	NHS supply chain
2x10 ml syringe	£26.30 Box of 100	£0.53	NHS supply chain
20 ml (sodium chloride)	£3.36 Pack of 10 x 10 ml	£0.67	NHS supply chain
		RSI and drug assisted tracheal intubation **Total: £34.52** [a]	

(a) This is the total of the equipment and the drugs used (including drug administering equipment)

Table 10: Resources and costs of other airway interventions and comparators

Intervention	Resources needed	Cost	Cost per patient	Source
Supraglottic devices	Airway supraglottic (i-gel) (adult)	£128.34 Case of 25	£5.13	NHS supply chain [3]
	Catheter mount extendable tube 15f/22m straight connector	£20.73 Box of 50	£0.41	NHS supply chain

Intervention	Resources needed	Cost	Cost per patient	Source
			Total: £5.55	
Surgical airway (cricothyroidotomy)	disposable scalpel	£2.35 Box of 10	£0.24	NHS supply chain
	Endotracheal tube introducer (single use bougie)	£59.24 Box of 20	£2.96	NHS supply chain
	Standard Endotracheal Tube cuffed with murphy eye	£12.07 Box of 10	£1.21	NHS supply chain
			Total: £4.40	
	OR Cricothyroidotomy emergency kit		**Total: £16.99**	NHS supply chain
Basic airway adjuncts	Resuscitator manual (bag-valve-mask) disposable		£6.44	NHS supply chain
	Oropharyngeal airway	£2.85 Pack of 10	£0.29	NHS supply chain
	NasoSafe nasopharyngeal airway	£18.79 Pack of 10	£1.88	NHS supply chain

6.5 Evidence statements

Clinical

No clinical evidence identified.

Economic

No relevant economic evaluations were identified.

6.6 Recommendations and link to evidence

Recommendations	**This section should be read in conjunction with section 17 in the NICE full guideline on major trauma services: service delivery for major trauma.** **1. Use drug-assisted rapid sequence induction (RSI) of anaesthesia and intubation as the definitive method of securing the airway in patients with major trauma who cannot maintain their airway and/or ventilation.** **2. If RSI fails, use basic airway manoeuvres and adjuncts and/or a supraglottic device until a surgical airway or assisted tracheal placement is performed.** **Pre-hospital settings** **3. Aim to perform RSI as soon as possible and within 45 minutes of the initial call to the emergency services, preferably at the scene of the**

	incident. **If RSI cannot be performed at the scene:** • **consider using a supraglottic device if the patient's airway reflexes are absent** • **use basic airway manoeuvres and adjuncts if the patient's airway reflexes are present or supraglottic device placement is not possible** • **transport the patient to a major trauma centre for RSI provided the journey time is 60 minutes or less** • **only divert to a trauma unit for RSI before onward transfer if a patent airway cannot be maintained or the journey time to a major trauma centre is more than 60 minutes.**
	The recommendations on airway management were identified as key areas to evaluate in the Major Trauma service delivery guidance scope area, 'Access to Services'. See Major Trauma Service Guidance chapter 17 for details on the development of the airway management service delivery recommendation.
Relative values of different outcomes	The following outcomes were critical to decision making: mortality up to 12 months, health-related quality of life, brain injury management, aspiration events, failure to intubate or secure airway, and adverse events (hypotension and unrecognised oesophageal intubation). Outcomes important to decision making were patient-reported outcomes, such as psychological well-being.
Trade-off between clinical benefits and harms	There was no published evidence to inform a recommendation on the use of airway management strategies in adult or child major trauma patients. The GDG discussed the associated risks of RSI of anaesthesia and intubation, for example, there is a greater risk of mortality if the tube enters the oesophagus rather than the lungs. However, the GDG felt that when the procedure is delivered by a team/clinician with appropriate training and experience (including experience conducting intubation, and maintaining sedation and ventilation after induction), the benefits of drug-assisted RSI in resuscitating the patient outweigh the risks. The GDG proposed that RSI of anaesthesia and intubation achieves improved ventilation increasing the probability of survival and reduces long-term morbidity compared with other methods of intubation. RSI is the preferred method of tracheal intubation because it results in rapid unconsciousness and neuromuscular blockade. This is important in patients who have not fasted and are at much greater risk for vomiting and aspiration. The GDG had a strong belief that RSI of anaesthesia and intubation delivered by a competent person is the gold standard of care when maintaining the airway of both adults and children and made a recommendation for RSI of anaesthesia and intubation accordingly. The GDG also noted that in the UK only physicians trained in RSI of anaesthesia or intubation or paramedics trained in the technique under the direct supervision of a physician can deliver this intervention as part of a team therefore availability of people in the pre-hospital setting to perform the procedure is limited. Taking this into account the GDG therefore recommended other airway management strategies that can be used to maintain a patient's airway while awaiting the clinical expertise to perform RSI of anaesthesia and intubation safely.

	The GDG suggested that the second best device for airway management was the supraglottic device. This device provides less protection than RSI of anaesthesia and intubation against aspiration; however this device provides greater protection than basic airway adjuncts, and can be administered safely by in the pre-hospital environment by paramedics or physicians staff. An additional advantage of supraglottic devices over other methods is that they can be easily inserted and removed. However, the GDG noted that supraglottic devices can only be used in patients without airway reflexes to avoid stimulating vomiting or laryngospasm,, and are therefore only appropriate for use in patients with a reduced level of consciousness. For patients with airway reflexes, where a supraglottic device cannot be used, the GDG recommended the use of basic airway manoeuvres and adjuncts until such time as RSI of anaesthesia and intubation is available. If RSI of anaesthesia and intubation fails a surgical airway or assisted tracheal intubation should be performed. This is required only in a very small minority of patients, for example patients with extensive facial injuries or an obstructed upper airway The GDG considered evidence regarding outcomes of patients related to pre-hospital scene and transfer times. The evidence suggested that outcomes were worse where there were long transport times (greater than 60 minutes) without a definitive airway, regardless of final destination. The GDG therefore concluded that where possible, RSI should be delivered at scene and within a timeframe than minimised pre-hospital time. Pre-hospitals systems should develop to make this widely available. Where pre-hospital RSI is not possible within a 45-minute window, the GDG recommended transporting the patient with supraglottic or basic airway adjuncts to a MTC within 60 minutes, otherwise to a TU. Overall, this was felt to be the most effective method of securing a definitive airway within this clinically important timeframe.
Trade-off between net health benefits and resource use	No published economic evidence was identified to inform this question. Unit costs were presented showing that basic airway adjuncts had the lowest intervention costs (£1.88), supraglottic devices had low cost (£5.55) and RSI and drug-assisted tracheal intubation had the highest unit cost (£34.52). The differential in unit cost for the devices is likely to expand once staff costs are added, in that the cheapest interventions also require the least competence to undertake, whereas RSI and drug assisted tracheal intubation needs higher skill and expertise to deliver. The key issue is that a competent person needs to be present on scene to deliver RSI of anaesthesia and intubation. Trained doctors hold this competency and are currently only on scene when an enhanced critical care team or individual doctors (for example, BASICS) are dispatched. Dispatch of such teams is dependent on the triaging decision of the 999 call handler and/or the first attendants on scene. There are two main ways this can be provided; RSI of anaesthesia and intubation is immediately available at the scene (this implies a person with these skills will be one of the first responders to the scene) or a team with the skills are called out. A recommendation proposing RSI of anaesthesia and intubation is available immediately whenever an airway may need to be maintained could lead to highly qualified and costly staff members being displaced from other clinical duties and increase the overall cost of the strategy substantially. The cost effectiveness in part will depend on who is trained to undertake RSI, and also the extent other populations (such as those with acute medical emergencies) may also benefit from having expertise in RSI routinely available on scene.

	In the other model of provision skilled staff could be called to the scene to provide RSI of anaesthesia and intubation. Currently, pre-hospital teams will consider whether the patient triggers the trauma bypass tool for triage direct to a major trauma centre (MTC). The severity of the patients other injuries, the time to reach the nearest ED and whether the nearest ED is a trauma unit or MTC, and whether travel time to the ED is more or less time than waiting for expertise to come to scene is all taken into account before transporting a patient. Although waiting on scene and calling out expertise only where necessary is potentially a less expensive model, this strategy is only likely to be clinically and cost effective if the on scene triage is accurate, the wait for expertise to arrive on scene is quick and there is high benefit in transport direct to an MTC without bypass. Many of the costs and benefits accrued in each strategy depend on economies of scale (that is, the more patients needing RSI intubation on scene, the less down time of the attending specialist staff) and economies of scope (that is, the ability of the attending staff to clinically manage other aspects of the trauma beside the airway), and these economies depend on local circumstance. The most cost-effective option may differ according to local circumstance. If the value of maximising population health gain by not exceeding the £20,000 per QALY threshold is upheld, this may mean different healthcare provision (and potential health gain) according to local circumstance. Overall, cost effectiveness of the interventions, when access implications are taken into account, remain unclear. It was GDG consensus, that RSI tracheal intubation (if undertaken by a competent person), despite having a risk of adverse events, would ensure an effective secure airway and potentially avoid downstream transfer costs. RSI leads to an increased probability of survival and reduces long-term morbidity compared with other methods of intubation. Other benefits of intubation include the administration of anaesthesia and effective ventilation (for example, in patients with significant chest injuries). It was concluded that the benefits would increase QALYs of the intervention and would offset its cost, therefore, the GDG felt this strategy would be more cost effective than the use of other airway management strategies, especially where possible to implement according to local service provision. Equally, where RSI tracheal intubation was not possible, use of a supraglottic device if possible would be more cost effective than airway adjuncts, such as bag and mask (provided the patients reflexes allow). This recommendation is likely to be a change a practice, as traditional teaching involves beginning with the least invasive airway device (bag and mask) and increasing the complexity of the interventions until the patient's airway is secure. The aim of this recommendation, however, is to encourage beginning with RSI (if the skills are available) as this would be the definitive method of securing the airway and the most appropriate in major trauma patients who cannot maintain their own airway. This recommendation is also likely to have a cost impact as resourcing of staff capable of undertaking RSI will be an issue.
Quality of evidence	No clinical or economic evidence was found for this question.
Other considerations	The GDG noted the importance of the early identification and of patients who require RSI or a surgical airway and early preparation of equipment for these procedures. The GDG noted that in a recent retrospective review of RSI performed by physician/critical care paramedics in the UK, there was only one case out of 142 of failure to intubate [87]. The GDG did not identifying any considerations specific to children.

	The GDG noted that the Trauma service delivery guidance would be evaluating the service delivery impact of the access to RSI as part of the operational model assessing access to services.

7 Assessment and management of chest trauma

7.1 Introduction

Major trauma incidents, particularly motor vehicle accidents, frequently involve serious injuries to the thorax. Such injuries include pneumothorax, haemothorax, pulmonary contusion, cardiac tamponade, flail chest and aortic laceration. The direct effects of these injuries on pulmonary and cardiovascular function can be life threatening, accounting for 25% of all deaths from trauma. In the UK this is over 4000 deaths per year. It is vital that these injuires are diagnosed as accurately and as quickly as possible.

7.2 Pre-hospital chest imaging

7.2.1 Introduction

In the pre-hospital setting, hand-held ultrasound (US) devices are becoming increasingly available. However, there is little understanding of the diagnostic accuracy of such devices for use in this setting and for the different types of chest trauma injuries. It is also important to consider whether these devices have a positive impact on patient outcomes or lead to longer times on scene and delaying potentially life-saving intervention.

7.2.2 Review question: What is the clinical and cost effectiveness of performing FAST compared to clinical examination pre-hospital in children, young people and adults who have suffered a suspected major chest trauma?

For full details see review protocol in Appendix C.

Table 11: PICO characteristics of review question

Population	Children, young people and adults who have experienced a suspected major chest trauma as follows: tension pneumothorax, haemothorax, cardiac tamponade, pneumothorax, pulmonary contusion, flail chest and aortic injury.
Intervention	Extended focused assessment with sonography for trauma (eFAST) scan Treatments that are acceptable in any RCTs comparing these tests (availability must be the same in each arm of each RCT): • chest drain (haemothorax) • needle decompression (tension pneumothorax) • needle aspiration (pericardiocentesis for cardiac tamponade) • thoracostomy • thoracotomy
Comparison	Clinical examination
Outcomes	Critical: • Mortality at 24 hours, 30 days/1 month and 1 year • Health-related quality of life • Length of intensive care stay Adverse events: • parenchymal lung damage

	• infection, bleeding • lung damage • air embolism • empyema • numbers with inappropriate treatments Important: Patient-reported outcomes (psychosocial wellbeing) Destination Population size and directness: • No limitations on sample size • Studies with indirect populations will not be considered.
Study designs	RCT, systematic reviews of RCTs, Quasi-RCT

7.2.3 Clinical evidence

No clinical evidence identified.

7.2.4 Review question: What is the diagnostic accuracy of performing (i) ultrasound compared to clinical examination pre-hospital in children, young people and adults who have suffered a suspected major chest trauma (ii) clinical examination pre-hospital compared to later imaging in children, young people and adults who have suffered a suspected major chest trauma?

For full details see review protocol in Appendix C.

Table 12: PICO Characteristics of review question

Population	Children, young people and adults who have experienced a suspected major chest trauma as follows: tension pneumothorax, haemothorax, cardiac tamponade, pneumothorax, pulmonary contusion, flail chest and aortic injury.
Index tests	Pre-hospital: • US/eFAST scan • No imaging/clinical examination (including different clinical examinations compared with each other or with no imaging)
Reference standards	• Later imaging (X-ray or CT, or in-hospital imaging) or surgical findings
Outcomes	Diagnostic accuracy Population size and directness: • No limitations on sample size • Studies with indirect populations will not be considered.
Study design	Observational studies

Diagnostic accuracy of chest trauma will depend on the exact nature of the trauma. For example, a particular test may be sensitive for detection of pneumothorax but not sensitive for detection of haemothorax. Hence, separate analyses were conducted for detection of specific thoracic injuries (as presented in the single study identified).

7.2.5 Clinical evidence

One prospective observational study[115,116] in an adult trauma population was found that evaluated the diagnostic accuracy of eFAST performed in-flight by helicopter emergency medical services (HEMS) providers to detect pneumothorax only and pneumothorax that required intervention (thoracostomy or thoracotomy). No evidence was identified comparing clinical examination pre-hospital with later imaging.

Table 13: Summary of studies included in the review

Study	Intervention and comparison	Population	Reference standard	Comments
Press 2014[115,116]	eFAST (performed in-flight by HEMS providers)	Adult trauma patients	CT or later surgical intervention findings.	Prospective study with unclear blinding of those interpreting the reference standard.

eFAST for detection of pneumothorax in the pre-hospital setting

Table 14: Diagnostic accuracy profile for pre-hospital eFAST in detecting pneumothorax only and pneumothorax requiring intervention (gold standard=CT, chest radiography and clinical evaluation) in adults

Number of studies	Number of patients	Risk of bias	Inconsistency	Indirectness	Imprecision	Pooled Sensitivity (95% CI)	Pooled Specificity (95% CI)	Quality
Pre-hospital eFAST for detecting pneumothorax (with CT, chest radiography and clinical evaluation as the gold standard) in adults								
1	293	Very serious[a]	NA	None	Serious[b]	0.19 (0.08 to 0.33)	1.00 (0.98 to 1.00)	VERY LOW
Pre-hospital eFAST for detecting pneumothorax requiring intervention (with CT, chest radiography and clinical evaluation as the gold standard) in adults								
1	293	Very serious[a]	NA	None	Very serious[b]	0.47 (0.24 to 0.71)	1.00 (0.99 to 1.00)	VERY LOW

(a) Risk of bias mainly due to lack of information on interval between tests, and that there were various reference standards used.
(b) Precision of specificity good, but a high range in sensitivity.

7.2.6 Economic evidence

Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow chart in Appendix E.

Unit costs

Table 15: Intervention cost

Imaging modality	Description	Cost
FAST scan[a]	US Scan, less than 20 minutes	£59 [37]

(a) US cost being used as a proxy for FAST.

7.2.7 Evidence statements

Clinical

Adults

Diagnostic accuracy of pre-hospital eFAST for pneumothorax

Very low quality evidence from 1 study comprising 293 adults showed that eFAST performed in-flight by the pre-hospital HEMS providers has a low and variable sensitivity of 0.19 (95% CI, 0.08 to 0.33) and a high specificity of 1.00 (95% CI, 0.98 to 1.00) for diagnosing pneumothorax only. Very low quality evidence from the same study showed pre-hospital eFAST has a low and variable sensitivity of 0.47 (95% CI, 0.24 to 0.71) and a high specificity of 1.00 (95% CI, 0.99 to 1.00) for diagnosing pneumothorax requiring intervention by either thoracostomy or thoracotomy.

Children

No evidence was identified.

Economic

No relevant economic evaluations were identified.

7.2.8 Recommendations and link to evidence

Recommendations	**4. Use clinical assessment to diagnose pneumothorax for the purpose of triage or intervention.** **5. Consider using eFAST (extended focused assessment with sonography for trauma) to augment clinical assessment only if a specialist team equipped with ultrasound is immediately available and onward transfer will not be delayed.** **6. Be aware that a negative eFAST of the chest does not exclude a pneumothorax.**

Relative values of different outcomes	The outcomes for this diagnostic review question are sensitivity and specificity of the index tests relative to a reference test (which is assumed to give the 'true' diagnosis). Sensitivity is an important outcome, because poor sensitivity may result in people with potentially serious chest trauma being undiagnosed and therefore, untreated or directed to the wrong destination. In contrast, low specificity, leading to incorrect positive diagnoses, will lead to unnecessary treatments or wrong destination. Though carrying a risk of unnecessary adverse events and higher costs, such additional treatments secondary to misdiagnoses are unlikely to be as much of a risk to the patient as missed diagnoses.
Trade-off between clinical benefits and harms	In the pre-hospital environment, the identification of tension pneumothorax causing hypoxia, ventilator difficulty or haemodynamic compromise is critical so that immediate intervention can be delivered (see recommendations on the management of chest trauma) and the patient transferred to a major trauma centre. The GDG were confident that this could be identified by clinical signs and symptoms alone and that eFAST would not provide any additional benefit. Furthermore, conducting an eFAST examination increases on-scene time and delays transportation of the patient to hospital. In addition, the pre-hospital environment (for example, poor lighting conditions) makes it difficult to conduct the eFAST examination. Although, the GDG acknowledge that the single paper identified as evidence for accuracy of eFAST was performed by trained pre-hospital providers and conducted in-flight and therefore, would not be considered as holding up transit from the scene to the appropriate hospital. While diagnostic cohort studies can tell us about the relative accuracy of a diagnostic test compared with a reference standard, they do not tell us whether adopting a particular diagnostic strategy improves patient outcomes. Evidence on patient outcomes is only available from diagnostic RCTs which compare two diagnostic interventions with identical subsequent treatment as indicated by the diagnostic test. No such evidence was identified. The evidence identified that eFAST had very low sensitivity (19%) for correctly identifying adult trauma patients who had pneumothoraces. Similarly, while the sensitivity did increase when specifying pneumothoraces that required intervention (thoracostomy and thoracotomy), this was still lower than chance (47%). The specificity for both outcomes was high (100%) indicating that there would be a very low number of false-positive diagnoses. Therefore, the GDG felt that while they could not recommend using eFAST in isolation, they acknowledged that there was weak evidence showing that when used by a specialist team in transit, eFAST may help to rule in (confirm) pneumathoraces suspected on clinical assessment. The high specificity indicates that false-positives would be minimised and this could prevent unnecessary pre-hospital clinical intervention. However, the GDG wanted to highlight that the low sensitivity indicates that eFAST is of no use to rule out pneumothoraces and stipulate that pre-hospital providers cannot rely upon a negative scan result. The GDG acknowledged that eFAST is currently an over-relied upon test given the lack of high quality evidence for its accuracy in diagnosing different types of chest trauma. Therefore, the GDG wanted to stipulate that while eFAST may be of use to augment clinical assessment, the current evidence base does not justify people changing the way they carry out clinical assessment and their subsequent management of the injured person. eFAST should be used by teams comprised of health professionals and practitioners who have received specialist training in its use.
Trade-off between net	No economic evidence was identified for this question.

health benefits and resource use	The accuracy of a clinical assessment is unknown and can also vary depending on who is undertaking it. This is likely to have a lower sensitivity and specificity than eFAST and lead to more false positives and interventions, such as chest drains, which could be harmful. There is limited availability of eFAST pre-hospital. There is a trade-off in terms of the benefit of undertaking an eFAST being dependent on whether it will lead to a change in management versus the time that it will take. Identifying clinically relevant injuries that need immediate intervention is the key. The accuracy of eFAST also varies depending on who is undertaking it and the training they have in assessment using eFAST. Correct identification of injuries could also have an impact on triage. eFAST is not currently widely available and is most commonly found on air ambulances. Therefore, if a doctor was undertaking eFAST (compared with a paramedic), this is likely to influence intervention choice which may then negate the need to be directed for emergency intervention. The accuracy of eFAST is highly operator dependant, and also the higher skill level of a doctor can undertake a wider choice of decompression interventions compared with a paramedic. The sensitivity of eFAST from the single paper identified was very poor; however, the specificity was high. This means there will be many people missed. When looking at clinically relevant pneumothoraces, the sensitivity of this still means around half of clinically relevant pneumothoraces will be missed which could result in serious health consequences. The GDG felt that clinical assessment is not consistent across the country and the accuracy of the assessment depends on how in depth the examination is and also who is interpreting the findings. There are also some difficulties in undertaking eFAST in a pre-hospital environment. The GDG considered that recommending eFAST would have large cost and training implications given its current limited availability and the evidence identified showed a high proportion of missed injuries. However, it was recognised that if eFAST is available, this could have value alongside clinical assessment to rule in pneumothoraces, but care must be taken when ruling out because a negative eFAST scan cannot definitively exclude pneumothoraces because of the high false negative rates. Given the high specificity, eFAST is minimising the number of false positives and therefore those that undergo unnecessary intervention, which is not uncommon in practice. Intervention for chest injuries should not be based solely on the identification of an injury through eFAST, but when accompanied with clinical signs and symptoms of respiratory distress. Therefore, it was felt that the added benefit of eFAST is limited (the value is specifically around ruling in) and thus, cost effectiveness remains uncertain. It is important to note that there is no set training or accreditation for FAST and training courses can vary. Hence, this recommendation does not aim to encourage investment in FAST, but highlights that there may be a benefit in addition to clinical assessment where it is already available and used by specialist staff. In summary, it was agreed a recommendation should focus on clinical assessment that can identify specific injuries (that are caused by the chest trauma and could lead to respiratory difficulty) that would need intervention.
Quality of evidence	The evidence retrieved from the single study included was of very low quality.

	Chief limitations were a lack of information about the time interval between when eFAST was performed and when the confirmatory reference test was performed, and the use of a variety of reference tests (CT, X-ray and clinical observation) so that the population did not all get measured against the same gold standard. The included evidence was in an adult population, no evidence was found in children.
Other considerations	The GDG did not identify any considerations specific to children.

7.3 Pre-hospital tension pneumothorax

7.3.1 Introduction

A tension pneumothorax is the rapid accumulation of extrapleural air that compresses intrathoracic vessels and obstructs venous returns to the heart. This leads to circulatory instability and may result in traumatic cardiac arrest. It is a life-threatening condition and it is important to recognise and treat it quickly. No treatment is not an option. Treatment comprises a method to allow air to escape from the pleural space; the interventions include needle decompression, open thoracostomy or chest drain. An open thoracostomy can only be used on intubated patients. A surgical incision is made, blunt dissection is performed, and the pleura penetrated. The wound is then left open. This is a rapid way of decompressing a tension pneumothorax in a critically injured trauma patient who is intubated. The positive pressure ventilation prevents the thoracostomy wound from acting as an open, 'sucking', chest wound. There are many additional challenges when undertaking these interventions in the pre-hospital setting as compared with the in-hospital setting. This is due to the varyied and unpredictable environments where pre-hospital care takes place.

7.3.2 Review question: What is the most clinically and cost effective technique (pre-hospital) to manage tension pneumothoraces?

For full details see review protocol in Appendix C.

Table 16: PICO characteristics of review question

Population	Children and adults with a suspected tension pneumothorax after experiencing a traumatic incident.
Intervention(s)	• Needle decompression • Chest drain (placement of chest tube) • Open thoracostomy (intubated patients only)
Comparison(s)	A comparison of the above

Outcomes	Critical:
	• Mortality at 24 hours, 30 days/1 month, and 12 months
	• Health-related quality of life
	• Length of intensive care stay
	• Adverse events:
	  ○ infection
	  ○ air embolism
	  ○ nerve damage
	  ○ tissue damage
	
	Important:

	• Patient-reported outcomes: ○ pain/discomfort ○ return to normal activities ○ psychological wellbeing
Study design	RCTs or systematic reviews of RCTs; cohort/case control studies if RCT evidence is insufficient. Only cohort/case control studies accounting for important confounding factors will be considered (severity of shock, severity of injury, degree of head injury, age, cardiac arrest)

7.3.3 Clinical evidence

No relevant clinical studies were identified.

7.3.4 Economic evidence

Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow chart in Appendix E.

Unit costs

Some interventions can be undertaken using a combination of equipment, or there are also purpose made devices available. The table below illustrates the costs of these products.

Table 17: Intervention equipment costs

Intervention	Resources needed	Cost	Cost per patient	Source
Needle decompression *(micro-costing approach)*	14 g IV cannula	£0.97 each	£0.97	NHS Supply Chain[3]
	Alcohol prep pad - Medi-Prep	£2.57 (Box of 500)	£0.01	The Air Ambulance Service
	10 ml syringe	£84.32 (Case of 1600)	£0.05	NHS Supply Chain
	10 ml sodium chloride	£3.36 (Pack of 10)	£0.34	Drug Tariff[106]
		Total	**£1.37**	
	ARS decompression needle *(purpose made device)*		£14.95	Bound Tree Medical [(a)]
	ThoraQuik chest decompression device *(purpose made device)*		£39.95	Bound Tree Medical [(a)]
Chest drain	Portex emergency chest drain kit		**£49.95**	SP Services [(a)]
Open thoracostomy	Gloves	£32.87 (Box of 50)	£0.66	
	Alcohol prep pad - Medi-Prep	£2.57	£0.01	The Air

		(Box of 500)		Ambulance Service
	Disposable scalpel	£2.35 (Box of 10)	£0.24	NHS supply chain
		Total	**£0.90**	

(a) Suppliers used by the East Midlands Ambulance Service. The prices listed here are the prices direct from the supplier, although prices to individual trusts may vary due to locally negotiated discounts.

7.3.5 Evidence statements

Clinical

No clinical studies were identified.

Economic

No relevant economic evaluations were identified.

7.3.6 Recommendations and link to evidence

Recommendations	**7. Only perform chest decompression in a patient with suspected tension pneumothorax if there is haemodynamic instability or severe respiratory compromise.** **8. Use open thoracostomy instead of needle decompression if the expertise is available, followed by a chest drain via the thoracostomy in patients who are breathing spontaneously.** **9. Observe patients after chest decompression for signs of recurrence of the tension pneumothorax.**
Relative values of different outcomes	The critical outcomes were mortality, health-related quality of life, length of intensive care stay, infection, air embolism, nerve damage and tissue damage. The GDG considered pain/discomfort, return to normal activities and psychological wellbeing to be important outcomes.
Trade-off between clinical benefits and harms	No clinical evidence was found to evaluate the trade-off between clinical benefits and harms between the pre-hospital treatments for tension pneumothorax. Therefore, the GDG made recommendations based on expert consensus. The GDG acknowledged that most people thought to have a tension pneumothorax in the pre-hospital setting actually do not have one and for those that do, most are not life-threatening. It is hard to make a definite diagnosis in the pre-hospital setting, so the likelihood of causing harm by carrying out an unnecessary procedure is potentially high. But where there is a life threatening tension pneumothorax intervention is required immediately. To reduce the number of unnecessary decompressions, the GDG limited the recommendation to intervene to people who are haemodynamically unstable or have severe respiratory compromise. The GDG agreed that people who have signs of a tension pneumothorax but are haemodynamically normal can wait until hospital for a more definitive diagnosis and possible decompression. **Technique** The GDG discussed the benefits and harms of each method of decompression. Needle decompression is a simpler technique to perform than insertion of a chest drain but is associated with a number of complications. These include the device

	blocking, the catheter not being long enough and therefore, not penetrating the thoracic parietal pleura, or incorrect placement of the needle, all of which result in the decompression not being successful. The GDG agreed by consensus that open thoracostomy is more effective and stable than needle decompression. In patients who are ventilated, there is no need to insert a chest drain prior to arrival in hospital. Chest drain insertion is a definitive procedure but more complex to perform. Incorrect placement of the chest drain can result in serious adverse events and decompression not being successful. Imaging to confirm correct placement of the chest tube is more limited in the pre-hospital setting. In the GDGs opinion, incorrect placement of the chest drain is common in current practice. The GDG stated that tension pneumothoraces that have been decompressed require close observation to detect reoccurrence of the tension pneumothorax.
Trade-off between net health benefits and resource use	No economic evidence was identified for this question. The insertion of a chest drain is the most expensive method, not only because of the equipment needed, but also because of the staff time and skill. However, most patients will eventually get a chest drain later in hospital and this cost will apply at some point. The intervention used will depend on the skill of the professional. Needle decompression can be undertaken by all registered paramedics, whereas thoracostomies can be performed by critical care trained paramedics but are usually undertaken by a doctor, and chest drains are only performed by doctors. The effectiveness of an intervention and the feasibility has to be considered, the only procedure routinely done by paramedics on scene currently is needle decompression. Some interventions may take more time (for example, a chest drain takes longer than a needle decompression) which can delay transfer to hospital. A larger proportion of the cost is likely to come from the potential presence of more highly skilled staff. Most people thought to have a tension pneumothorax do not actually have a tension pneumothorax or have a life threatening tension pneumothorax and there may be unnecessary decompression occurring in the pre-hospital setting. Thus, the correct identification of a life threatening tension pneumothorax is vital. If the appropriately skilled professional is available pre-hospital and undertakes an intervention, such as inserting a chest drain, then this will not have to be done later in hospital. Therefore, the timing of the interventions might be an issue, which is directly influenced by the staff available pre-hospital, it may also be a case of earlier treatment leading to better outcomes, however, this may only be in a small proportion of life-threatening tension pneumothoraces. Clinical resource would be freed up later when the patient arrives in the ED to deal with their other injuries. There can be significant risk of adverse events associated with some of the interventions if not undertaken correctly, for example, nerve damage and lung injury. Infection is also more likely pre-hospital than in hospital because of the environment. Potential adverse events of a chest drain include converting an open pneumothorax to a tension pneumothorax which can be life threatening. The GDG thought incorrect placement of a chest drain was common pre-hospital. Also important to consider is the precision with which tension pneumothoraces can be identified pre-hospital, as needle decompression, for example, can cause a tension

	pneumothorax in someone who did not have a tension pneumothorax to begin with. The GDG felt that decompression should be limited to haemodynamically unstable patients, and were aware of the of the service delivery implications of needing higher skilled staff on the scene for the more complex decompression methods. After weighing up the benefits and risks of each intervention, the GDG felt that open thoracostomy was a better method than needle decompression, and should be undertaken if the skills are available. Open thoracostomy is preferred in ventilated patients because the intervention involves making a hole, so is not associated with problems the other methods might have, such as blocking, the cannula falling out or the needle not being long enough. The ventilated patients do not have to be unstable as well as being suspected of a tension pneumothorax, as it is more of a prophylactic measure to avoid waiting for complications to develop because having an assisted airway means there is more risk of developing a tension pneumothorax.
Quality of evidence	No relevant clinical studies were identified.
Other considerations	The GDG did not identify any considerations specific to children.

7.4 Management of open pneumothorax

7.4.1 Introduction

An open pneumothorax is an accumulation of air in the pleural space with an open communication to the atmosphere through a defect of the chest wall or tracheobronchial tree. The defects can be caused by injury to the chest wall, such as stab or bullet wounds. These injuries create a wound that appears to be 'sucking air' into the chest and may be visibly bubbling. In the pre-hospital setting the treatment options are: occlusive dressing (vented or non-vented), improvised three-sided dressing or alternatively, no treatment until the person reaches hospital. The dressings can be used alone or in conjunction with a chest drain.

7.4.2 Review question: Which occlusive dressing used in the pre-hospital setting is the most clinically and cost effective in improving outcomes for patients with open pneumothoraces as a part of major trauma?

For full details see review protocol in Appendix C.

Table 18: PICO characteristics of review question

Population	Children and adults with an open pneumothorax after experiencing a traumatic incident.
Intervention(s)	• Occlusive dressing (non-vented) • Occlusive dressing (with vent/valve) • Improvised dressing (three-sided) • Occlusive/improvised dressing (any) and chest drain
Comparison(s)	No dressing A comparison of the above
Outcomes	Critical: • Mortality at 24 hours, 30 days/1 month and 12 months • Health-related quality of life • Adverse effects (conversion to tension pneumothorax, infection) Important: • Patient-reported outcomes (pain/discomfort, return to normal activities,

	psychological wellbeing)
Study design	RCTs or systematic reviews of RCTs; cohort/case control studies if RCT evidence is insufficient. Only cohort/case control studies accounting for important confounding factors will be considered (severity of shock, severity of injury, degree of head injury, age).

7.4.3 Clinical evidence

No relevant clinical studies were identified.

7.4.4 Economic evidence

Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow chart in Appendix E.

Unit costs

Table 19: Intervention costs

Intervention	Detail	Cost per patient	Source[a]
Non-vented dressings	Nightingale dressing	£10.95	SP services
Vented dressings	Asherman chest seal	£10.50	SP services
	Bolin chest seal	£19.95	SP services
	Russell chest seal	£22.95	SP services
	SAM chest seal	£19.95	SP services
Dressing plus chest drain	Chest drain kit plus occlusive dressing	£49.95 plus occlusive dressing	SP services

(a) A supplier used by the East Midlands Ambulance Service. The prices listed here are the prices direct from the supplier, although prices to individual trusts may vary due to locally negotiated discounts. These products were unavailable on the NHS supply chain catalogue.

Improvised three sided dressings are unlikely to have many costs associated with them as this would involve using materials found at the scene and would thus not have any direct cost to the NHS.

7.4.5 Evidence statements

Clinical

No clinical evidence was identified.

Economic

No relevant economic evaluations were identified.

7.4.6 Recommendations and link to evidence

Recommendations	**10.In patients with an open pneumothorax:** • **cover the open pneumothorax with a simple occlusive dressing and** • **observe for the development of a tension pneumothorax.**
Relative values of different outcomes	Critical outcomes for decision making were mortality, health-related quality of life and infection. Outcomes considered important by the GDG were pain/discomfort, return to normal activities and psychological wellbeing.
Trade-off between clinical benefits and harms	No clinical evidence was found to evaluate the trade-off between clinical benefits and harms between treatments for open pneumothoraces in the pre-hospital setting. The GDG agreed that given the lack of evidence, no recommendation could be made around whether an occlusive dressing for an open pneumothorax should be vented or three-sided. Additionally, the GDG accepted there was no evidence to make a recommendation around supplementing the dressing with a chest drain in the pre-hospital setting. The GDG decided through expert consensus to recommend using a simple occlusive dressing to treat an open pneumothorax in the pre-hospital setting. The GDG emphasised the importance of a 'simple' dressing that provides an airtight seal that is fast and straightforward to apply. The GDG discussed the potential benefits of placing an air-occlusive dressing over the site and taping it on three sides allowing trapped air to escape from the untaped edge during exhalation. However, the time required to apply this dressing and the limited effectiveness of the adhesive to stick to a diaphoretic bleeding patient often results in dressing failure. Although a simple (adhesive) occlusive dressing doesn't allow for escape of pleural air, the adhesive resolves the problems of too much time needed to tape three sides of the dressing and failure of the adhesive to stick to the patient's chest wall. The priority should be transporting the patient to a hospital where a chest drain can be inserted. The airtight property of occlusive dressings aids in preventing transition to a tension pneumothorax but the patient will require close monitoring. The GDG stated that gauze alone would not be appropriate as it does not provide an airtight seal over an open chest wound.
Trade-off between net health benefits and resource use	No economic evidence was identified for this question. The purpose-made dressings available vary in price from around £10–£25. Additional to the dressings, a chest drain may also be applied. However, the insertion of a chest drain is a skill which can only be undertaken by a doctor. If a chest drain was inserted pre-hospital this could save time later in hospital, when everyone with an occlusive dressing will eventually receive a chest drain. In other words, a chest drain will always be inserted to an open pneumothorax at some stage. This cost would always apply regardless of whether it was inserted pre-hospital or in hospital, but the cost of a pre-hospital doctor would be additional if this was done on scene. On the other hand, inserting a chest drain pre-hospital could take time which could have been better spent getting the patient to hospital earlier. Adverse events from dressings and/or chest drain include conversion to a tension pneumothorax and infection. No clinical evidence has been identified to provide information on the effectiveness of the different interventions or on their risk of adverse events. So, it is unclear whether purpose-made dressings are more effective than improvised dressings and

	also whether there is benefit to early insertion of a chest drain. This also meant that the cost-effectiveness of different dressings could not be determined. The GDG discussed that ideally, in the pre-hospital setting, you do not want to be spending time trying to put on an occlusive dressing correctly, as this time would be better spent dressing the wound as quickly as possible so you can then transfer the patient to an appropriate destination where they can have a chest drain inserted. Therefore, it was important to stress that a simple dressing that provides an airtight seal for the wound and can be applied quickly would be adequate, and investing in high-cost occlusive dressings would not add any benefit.
Quality of evidence	No relevant clinical studies were identified.
Other considerations	The GDG did not identify any considerations specific to children.

8 In-hospital tension pneumothoraces

8.1 Introduction

A tension pneumothorax is the rapid accumulation of extrapleural air that compresses intrathoracic vessels and obstructs venous returns to the heart. This leads to circulatory instability and may result in traumatic arrest. It is a life-threatening condition and it is important to recognise and treat it quickly. No treatment is not an option. Treatment comprises a method to allow air to escape from the pleural space; the interventions include needle decompression, open thoracostomy or chest drain. An open thoracostomy can only be used on intubated patients.

8.2 Review question: What is the most clinically and cost effective technique (in-hospital) to manage tension pneumothoraces?

For full details see review protocol in Appendix C.

Table 20: PICO characteristics of review question

Population	Children and adults with a tension pneumothorax after experiencing a traumatic incident.
Intervention(s)	• Needle decompression • Chest drain (placement of chest tube) • Open thoracostomy (intubated patients only)
Comparison(s)	A comparison of the above

Outcomes	Critical:
	• Mortality at 24 hours, 30 days/1 month, and 12 months
	• Health-related quality of life
	• Length of intensive care stay
	• Adverse events:
	  ○ infection
	  ○ air embolism
	  ○ nerve damage
	  ○ tissue damage
	
	Important:
	• Patient-reported outcomes:
	  ○ pain/discomfort
	  ○ return to normal activities
	  ○ psychological wellbeing).

Study design	RCTs or systematic reviews of RCTs; cohort/case control studies if RCT evidence is insufficient. Only cohort/case control studies accounting for important confounding factors will be considered (severity of shock, severity of injury, degree of head injury, age)

8.3 Clinical evidence

No relevant clinical studies were identified.

8.4 Economic evidence

Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow chart in Appendix E.

Unit costs

These costs are the same as those used for the pre-hospital management of tension pneumothorax question. Although it is important to note that if an intervention has taken place pre-hospital, this may negate the need for it to take place in hospital (for example; insertion of a chest drain).

Table 21: Intervention equipment costs

Intervention	Resources needed	Cost	Cost per patient	Source
Needle decompression *(micro-costing approach)*	14 g IV cannula	£0.97 each	£0.97	NHS Supply Chain[3]
	Alcohol prep pad - Medi-Prep	£2.57 (Box of 500)	£0.01	The Air Ambulance Service
	10 ml syringe	£84.32 (Case of 1600)	£0.05	NHS Supply Chain
	10 ml sodium chloride	£3.36 (Pack of 10)	£0.34	Drug Tariff[106]
		Total	**£1.37**	
	ARS decompression needle *(purpose made device)*		£14.95	Bound Tree Medical [(a)]
	ThoraQuik chest decompression device *(purpose made device)*		£39.95	Bound Tree Medical [(a)]
Chest drain	Portex emergency chest drain kit		**£49.95**	SP Services [(a)]
Open thoracostomy	Gloves	£32.87 (Box of 50)	£0.66	
	Alcohol prep pad - Medi-Prep	£2.57 (Box of 500)	£0.01	The Air Ambulance Service
	Disposable scalpel	£2.35 (Box of 10)	£0.24	NHS supply chain
		Total	**£0.90**	

(a) Suppliers used by the East Midlands Ambulance Service. The prices listed here are the prices direct from the supplier, although prices to individual trusts may vary due to locally negotiated discounts.

8.5 Evidence statements

Clinical

No clinical evidence was identified.

Economic

No relevant economic evaluations were identified.

8.6 Recommendations and link to evidence

Recommendations	**11. In patients with tension pneumothorax, perform chest decompression before imaging only if they have either haemodynamic instability or severe respiratory compromise.** **12. Perform chest decompression using open thoracostomy followed by a chest drain in patients with tension pneumothorax.**
Relative values of different outcomes	The critical outcomes for decision making were mortality, health-related quality of life, length of intensive care stay, infection, air embolism, nerve damage and tissue damage. Pain/discomfort, return to normal activities and psychological wellbeing were important outcomes.
Trade-off between clinical benefits and harms	No clinical evidence was found to evaluate the trade-off between clinical benefits and harms between the in-hospital treatments for tension pneumothorax. The GDG stated that needle decompression is rarely appropriate in the hospital setting compared with open thoracostomy. It was considered to be an often inadequate treatment for tension pneumothoraces that does not allow for definitive control of air in the pleural space and can be associated with complications. However, it is the faster of the two techniques and has a use for patients who are haemodynamically unstable or have severe respiratory compromise and are suspected of a tension pneumothorax. The GDG agreed through consensus that the most effective treatment for tension pneumothorax is open thoracostomy followed by placement of a chest drain. This is more time consuming than needle thoracostomy, however, placement of a chest drain allows for definitive control of air in the pleural space. In the GDGs opinion, this technique has fewer complications and better outcomes for patients
Trade-off between net health benefits and resource use	No economic evidence was identified for this question. The insertion of a chest drain is the most expensive method, not only because of the equipment involved because of the kit needed, but also because of the staff. However, most patients would eventually receive a chest drain anyway, either already presenting with a chest drain applied pre-hospitally or have one inserted in hospital if patients: • have had an open thoracostomy pre-hospital • have had a needle decompression pre-hospital. These patients will quite likely have a chest drain inserted because this is likely to have caused a pneumothorax if there wasn't one initially. In hospital, the appropriately skilled staff (that is, a doctor) would be on hand to perform any of the interventions to treat a tension pneumothorax. Many people thought to have a tension pneumothorax do not turn out to have a tension pneumothorax, and decompressing in patients without a tension pneumothorax can lead to harm. There can be significant risk of adverse events associated with some of the interventions if not undertaken correctly, for example, nerve damage, tissue damage, lung injury and infection. Potential adverse events of a chest drain include converting an open pneumothorax to a tension pneumothorax which can be life threatening. The GDG agreed that the gold standard method of decompressing the chest is open thoracostomy followed by chest drain; however, as in the pre-hospital question for

	the management of tension pneumothoraces, this should be limited to haemodynamically unstable patients, when prior to a definitive diagnosis based on imaging.
Quality of evidence	No relevant clinical studies were identified.
Other considerations	It was noted that in patients who are not unstable, no intervention should be undertaken prior to imaging. However, after a definitive diagnosis, all tension pneumothoraces will be decompressed. The GDG did not identify any considerations specific to children.

9 Imaging assessment of chest trauma

9.1 Introduction

Major trauma incidents, particularly motor vehicle accidents, frequently involve serious injuries to the thorax. Such injuries include pneumothorax, haemothorax, pulmonary contusion, cardiac tamponade, flail chest and aortic laceration. The direct effects of these injuries on pulmonary and cardiovascular function can be life threatening, accounting for 25% of all deaths from trauma. In the UK this is over 4000 deaths per year. It is vital that these injuires are diagnosed as accurately and as quickly as possible. Various tests are used for diagnosis of these injuries, including US, X-ray and CT, but there is little consensus on the most accurate method to use for each type of injury.

9.2 Review question: What are the most clinically and cost effective hospital strategies for assessing chest trauma (tension pneumothorax, haemothorax, cardiac tamponade, pneumothorax, pulmonary contusion, flail chest and aortic injury) in patients with major trauma on initial presentation?

Table 22: PICO characteristics of review question

Population	Children, young people and adults who have experienced a suspected major trauma
Intervention	Tests: • X-ray • US • Extended focused assessment sonography for trauma (eFAST) • Chest CT • X-ray plus chest CT • US plus chest CT • X-ray plus US plus chest CT • FAST plus chest CT Appropriate treatments in response to test findings are the same as for the FAST protocol
Comparison	All tests will be compared with each other.
Population	Children, young people and adults who have experienced a suspected major trauma.
Outcomes	Critical: • Mortality at 24 hours, 30 days/1 month and 1 year • Health-related quality of life • Length of intensive care stay • Complications – parenchymal lung damage, infection, bleeding, lung damage, air embolism, empyema • Numbers with inappropriate treatments Important: • Patient-reported outcomes (psychosocial wellbeing)

	• Destination Population size and directness: • No limitations on sample size • Studies with indirect populations will not be considered.
Study designs	RCTs, Systematic reviews of RCTs or Quasi-RCTs

9.3 Clinical evidence

No clinical evidence identified.

9.4 Review question: Diagnostic accuracy of hospital imaging strategies in people presenting with major trauma

For full details see review protocol in Appendix C.

Table 23: PICO characteristics of review question

Population	Children, young people and adults who have experienced a suspected major trauma.
Index tests	Hospital imaging strategies as follows: • X-ray (supine) • US/eFAST • Chest CT (helical and/or multi-slice)
Reference standards	• CT (helical and/or multi-slice) or subsequent operative/clinical findings for pneumothorax/haemothorax/flail chest/cardiac tamponade/pulmonary contusion • Angiography or subsequent operative/clinical findings for aortic injury
Outcomes	Diagnostic accuracy
Study design	Observational studies

Diagnostic accuracy of chest trauma will depend on the exact nature of the trauma. For example, a particular test may be sensitive for detection of pneumothorax but not sensitive for detection of haemothorax. Hence, separate analyses were conducted for detection of each of the following specific thoracic injuries:

- tension pneumothorax
- other pneumothorax
- haemothorax
- cardiac tamponade
- pulmonary contusion
- flail chest
- aortic injury.

These were the only injuries considered as they were felt by the GDG to be the most important. Some of the papers used the term ultrasound which may have actually

9.5 Clinical evidence

9.5.1 Hospital imaging: tension pneumothorax

One study was identified that compared the diagnostic accuracy of eFAST and X-ray with CT for tension pneumothorax[133,133].

Table 24: Summary of study included in the review

Study	Population	Index test(s)	Reference test	Comments
Soult 2015[133,133]	Consecutive patients presenting at emergency department (ED) of a level 1 trauma centre n=345	eFAST and X-ray	CT	Retrospective design.

Table 25: Diagnostic accuracy profile for US in detecting pneumothorax (gold standard=CT) in studies with sufficient data for meta-analysis

Number of studies	Number of patients	Risk of bias	Inconsistency	Indirectness	Imprecision	Sensitivity (95% CI)	Specificity (95% CI)	Quality
eFAST for detecting tension pneumothorax (with CT as the gold standard) in adults								
1	345	Serious[a]	None	None	Serious[b]	0.40 (0.28 to 0.52	0.99 (0.97 to 1.00)[c]	VERY LOW
X-ray for detecting tension pneumothorax (with CT as the gold standard) in adults								
1	345	Serious[a]	None	None	Serious[b]	0.24 (0.13 to 0.45	1.00 (0.99 to 1.00[c]	VERY LOW

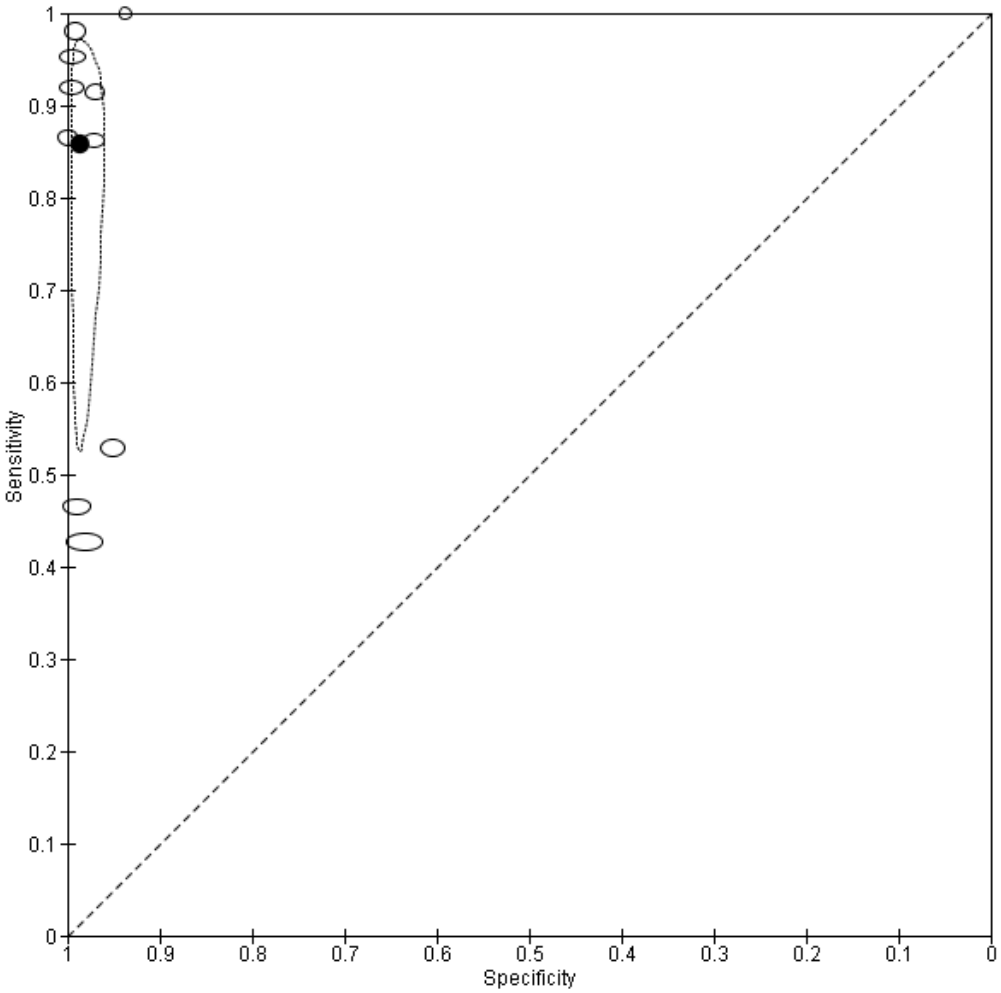
(a) Risk of bias mainly due to lack of information on interval between tests or a lack of blinding.
(b) Precision of specificity good, but a wide range in sensitivity.

9.5.2 Hospital imaging: other pneumothorax

Fifteen adult studies[5,6,7,12,14,15,19,23,40,68,95,123,131,138,145] and 1 child study[65,66] were found that evaluated the diagnostic accuracy of methods to detect pneumothorax (Table 26).

- Ten of these adult studies[5,6,14,19,40,68,95,123,131,145] assessed the diagnostic accuracy of US, all of which provided sufficient data for meta-analysis (Table 27 and Figure 5).

Figure 5: Diagnostic meta-analysis for US in detecting pneumothorax (gold standard=CT)



Note: The solid black circle represents the pooled value of sensitivity and specificity. The dotted curve drawn around this point represents the 95% CIs around this point. The open ovals represent the results of individual studies, and their area is proportional to the study size.

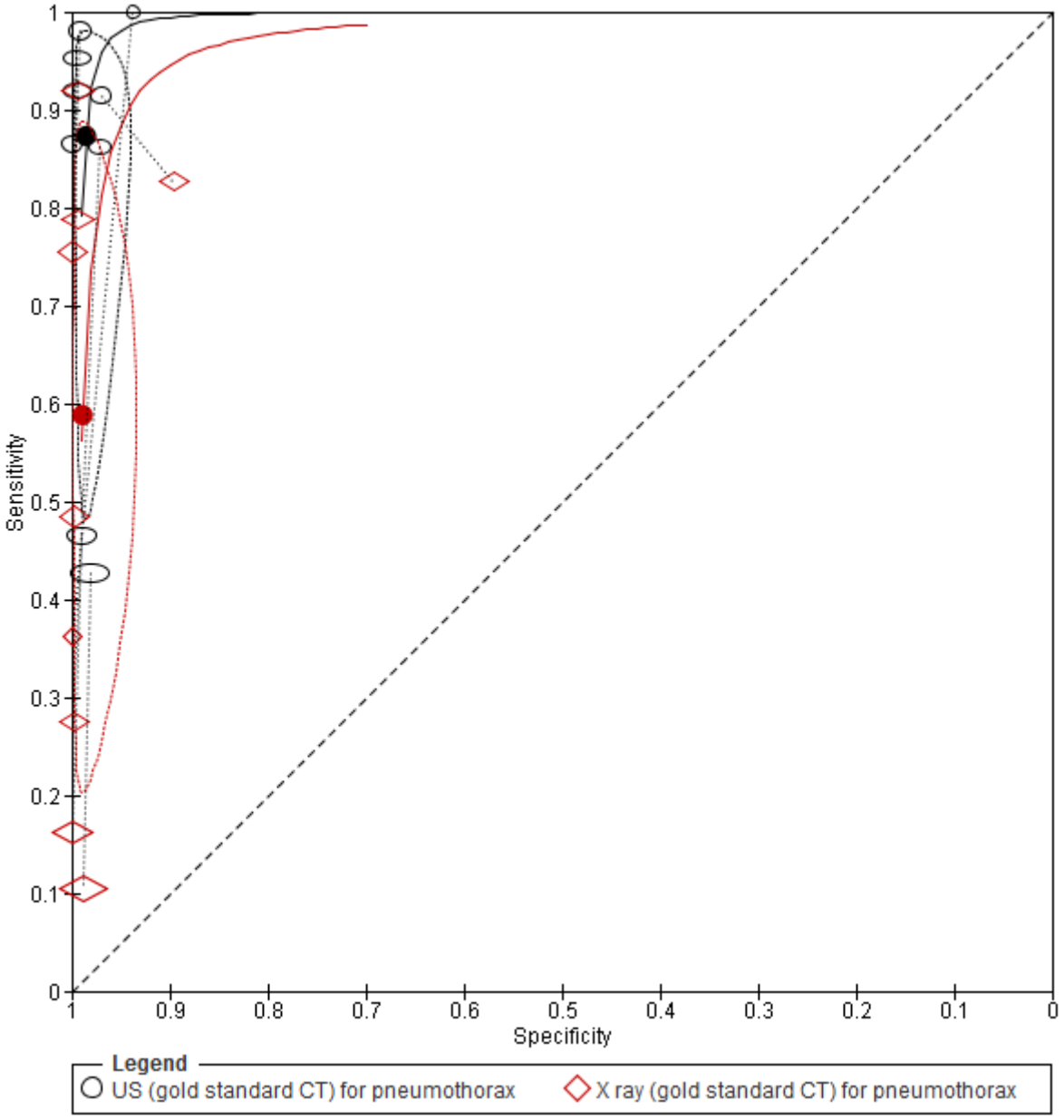
- Three of these studies[14,19,95] used eFAST US, but these were not analysed separately, since 3 would be too small a number of studies for a meta-analysis, and the results did not appear to differ in any appreciable way to the standard US studies.
- Fourteen adult studies [5,6, 7,12,14,15,19,23,40,95,123,131,138,145] assessed the diagnostic accuracy of X-ray, ten of which[5,6,14,19,40,95,123,131,138,145] provided sufficient data for meta-analysis (Table 28 and Figure 8).
- The other 4 adult studies[7,12,15,23] provided partial information, prohibiting a diagnostic meta-analysis (data summarised in Table 29). The child study[65,66] also provided partial information, prohibiting a diagnostic meta-analysis (data summarised in Table 28).

The positioning of patients for X-ray was believed to be an important covariate. The above studies were all believed to have carried out X-rays in supine, and this was based on an explicit description,

or, if this were absent, based on the majority of patients in the study having blunt trauma, who are usually, in contrast to some penetrating trauma patients, kept in a supine position.

Eight of the adult studies[5,14,19,40,95,123,131,145] with data sufficient for meta-analysis compared US with X-ray in the same study. The plot superimposing the meta-analysis results of these is illustrated in Figure 6.

Figure 6: Superimposed plot of diagnostic accuracy of US and X-ray for detecting pneumothorax, from studies comparing both against a common gold standard, and with data sufficient for meta-analysis.



Note: The dotted curves drawn around these points represent the 95% confidence intervals around these points. The open circles and diamonds respectively represent the US and X-ray results of individual studies, and their area is proportional to the study size. US and chest X-ray results from the same study are linked by dotted lines.

Table 26: Summary of studies included in the review

Study	Population	Index test(s)	Reference test	Comments

Study	Population	Index test(s)	Reference test	Comments
Abbasi 2013[5,5]	Adults admitted to ED with thoracic trauma; n=146	US and X-ray	CT	Adequately blinded
Abdulrahman 2015[6,6]	Adults admitted to trauma centre in Qatar; n=305	US and X-ray	CT	Adequately blinded
Alkadhi 2005[7,8]	Trauma patients; half with traffic accidents; age 48 (17-67) years; n=60	X-ray	CT	Unclear blinding. Study type unclear
Barrios 2010[11,12]	Patients at level 1 trauma unit; n=374	X-ray	CT	No blinding; no raw data provided or able to be extracted, and only sensitivity yielded.
Blaivas 2005[14,14]	Blunt trauma patients aged >17 years; 76% female; n=176	FAST US and X-ray	CT	Prospective. Blinded for US/CT only. Timing unclear.
Blasinska-Przerwa 2013[15]	Patients with chest trauma; n=30	X-ray	CT	Retrospective. No blinding reported.
Brook 2009[19,19]	Consecutive patients at trauma room in ED; ages ranged from 6 months to 88 years, with mean of 31 years; n=169	FAST US and X-ray	CT	Prospective. Blinded for US/CT only.
Chardoli 2013[23,23]	Patients with blunt chest trauma; n=200	X-ray	CT	No raw data presented
Donmez 2012[40,40]	Multiple trauma patients; n=68	US and X-ray	CT	Prospective. Blinded. Timing unclear
Holmes 2001B[66,66]	Children aged <16 years undergoing abdominal CT scan; n=538	X-ray	CT	Abdominal CT scan done but covered thoracic area as well
Hyacinthe 2012[68,68]	Patients with mainly blunt trauma with indication for thoracic CT scan; n=119	US	CT	Prospective
Nandipati 2011[95,95]	Blunt and penetrating trauma; 53.8% blunt trauma due to motor vehicle collision (MVC); n=204	FAST US and X-ray	CT	Prospective. Blinding unclear. Timing unclear
Rowan 2002[123,123]	Patients with blunt thoracic trauma; n=27	US and X-ray	CT	Prospective. Timing unclear
Soldati 2008[131,132]	Patients admitted	US and X-	CT	Study type unclear

Study	Population	Index test(s)	Reference test	Comments
	to emergency department for chest trauma or major trauma; aged >18 years; n=109	ray		
Varin 2009[138,138]	Consecutive patients at level 1 trauma unit with penetrating wounds; n=299	X-ray	CT/surgery	Unclear blinding
Zhang 2006[145,145]	Blunt trauma patients; MVC 61.5%; n=135	US and X-ray	CT	Prospective. Blinded for US/CT only.

US for detection of pneumothorax

Table 27: Diagnostic accuracy profile for US in detecting pneumothorax (gold standard=CT) in studies with sufficient data for meta-analysis

Number of studies	Number of patients	Risk of bias	Inconsistency	Indirectness	Imprecision	Pooled Sensitivity (95% CI)	Pooled Specificity (95% CI)	Quality
US for detecting pneumothorax (with CT as the gold standard) in adults								
10	1921	Serious[a]	Serious[b]	None	Serious[c]	0.845 (0.678 to 0.953)[d]	0.986 (0.974 to 0.994)[d]	VERY LOW

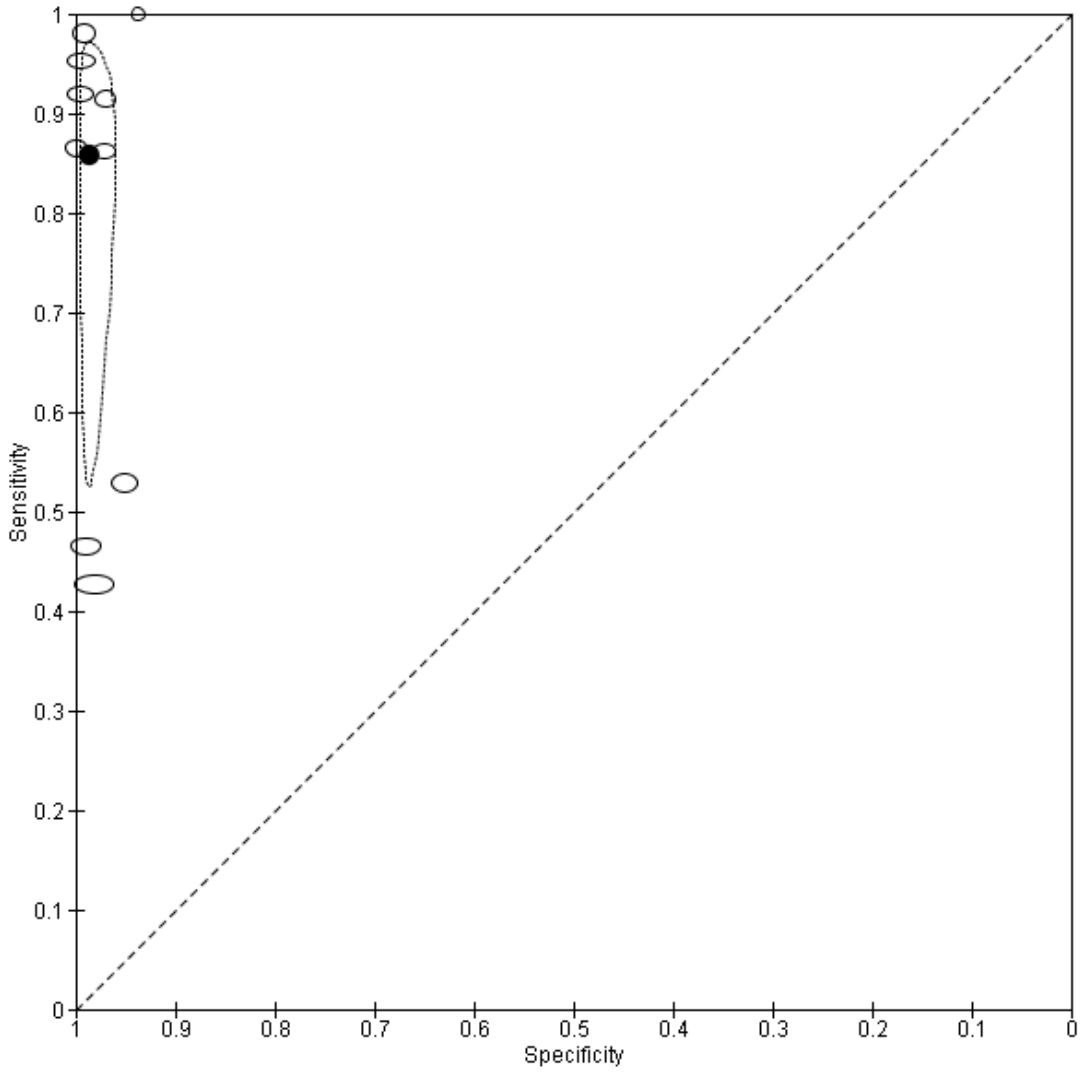
(a) Risk of bias mainly due to lack of information on interval between tests or a lack of blinding.

(b) Some lack of overlap of CIs on forest plot, but only 2 studies diverged from the others

(c) Precision of specificity good, but a high range in sensitivity.

(d) This is a conservative estimate. The WinBugs software[84] used to calculate the pooled sensitivity and specificity (and parameters for calculation of the 95% CIs) does not function when zeroes are present in the raw diagnostic data set. Hence where there were zero false negatives, or zero false positives, the zero had to be converted to the value of 1. This had the effect of creating less favourable sensitivity and specificity estimates than otherwise.

Figure 7: Diagnostic meta-analysis for US in detecting pneumothorax (gold standard=CT)



Source: The solid black circle represents the pooled value of sensitivity and specificity. The dotted curve drawn around this point represents the 95% confidence intervals around this point. The open ovals represent the results of individual studies, and their area is proportional to the study size.

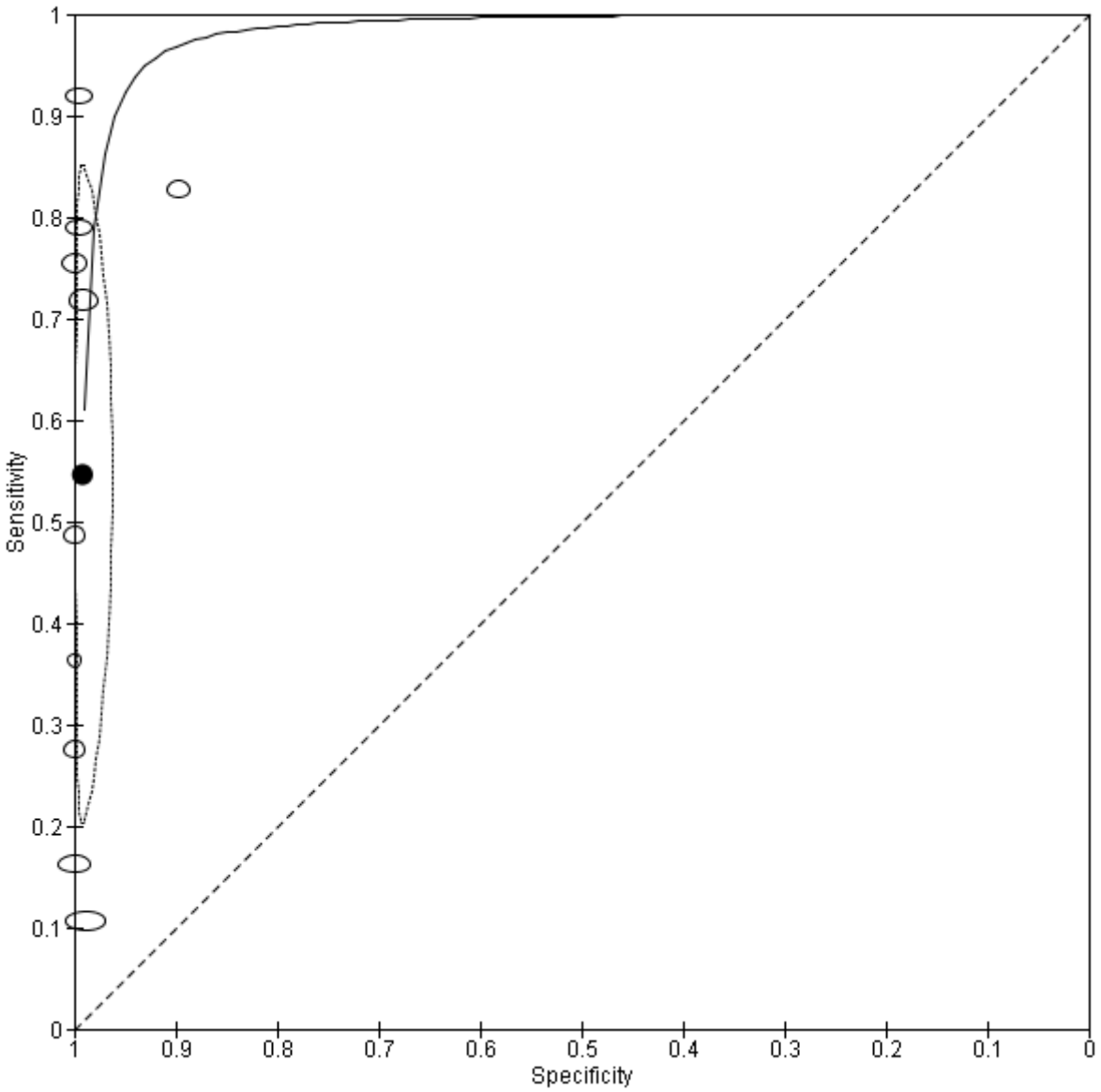
X-ray for detection of pneumothorax

Table 28: Diagnostic accuracy profile for X-ray in detecting pneumothorax (gold standard=CT) in studies with sufficient data for meta-analysis

Number of studies	Number of patients	Risk of bias	Inconsistency	Indirectness	Imprecision	Pooled Sensitivity (95% CI)	Pooled Specificity (95% CI)	Quality
X-ray for detecting pneumothorax (with CT as the gold standard) in adults								
10	1983	Very serious[a]	Very serious[b]	No serious indirectness	Very serious[c]	0.544(0.299 to 0.0.775)[d]	0.991(0.979 to 0.997) [d]	VERY LOW

(a) Risk of bias mainly due to lack of information on interval between tests and a lack of blinding.
(b) Significant lack of overlap of CIs on forest plot
(c) Precision of specificity good, but a very high range in sensitivity
(d) This is a conservative estimate. The WinBugs software[84] used to calculate the pooled sensitivity and specificity (and parameters for calculation of the 95% CIs) does not function when zeroes are present in the raw diagnostic data set. Hence where there were zero false negatives, or zero false positives, the zero had to be converted to the value of 1. This had the effect of creating less favourable sensitivity and specificity estimates than otherwise.

Figure 8: Diagnostic meta-analysis for X-ray in detecting pneumothorax (gold standard=CT)



Note: The solid black circle represents the pooled value of sensitivity and specificity. The dotted curve drawn around this point represents the 95% confidence intervals around this point. The open circles represent the results of individual studies, and their area is proportional to the study size.

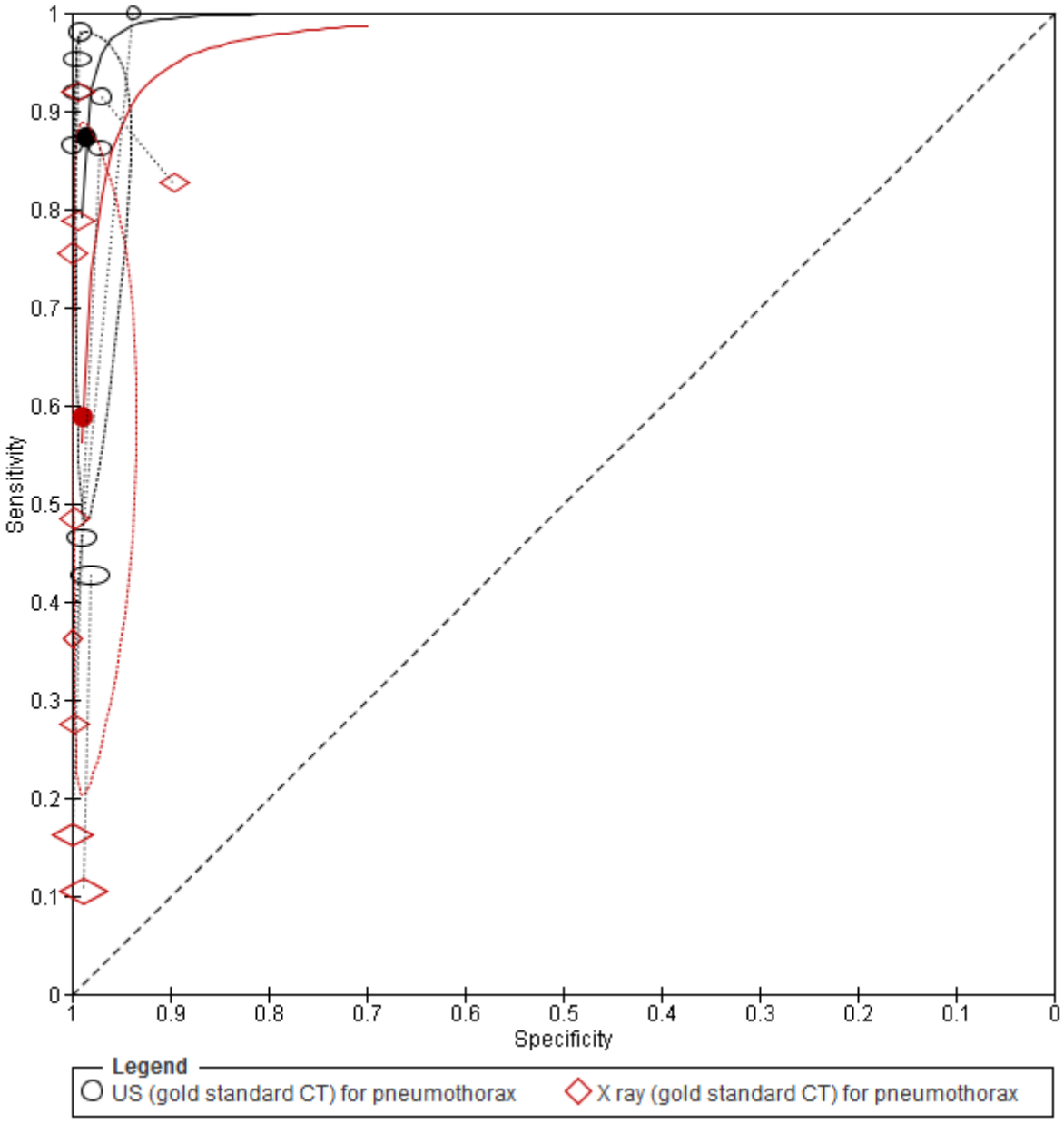
Table 29: Diagnostic accuracy profile for X-ray in detecting pneumothorax (gold standard=CT) in studies with insufficient data for meta-analysis

Number of studies	Number of patients	Risk of bias	Inconsistency	Indirectness	Imprecision	Sensitivity (95% CI) (in study order)	Specificity (95% CI)	Quality
X-ray for detecting pneumothorax (with CT as the gold standard) in adults								
4	1002	Very serious[a]	Serious[b]	None	NA[c]	0.579 0.6 0.45 0.44 Median 0.52	1 1 - -	VERY LOW
X-ray for detecting pneumothorax (with CT as the gold standard) in children								
1	200	Very serious[a]	NA	None	NA[c]	0	-	LOW

(a) Risk of bias mainly due to lack of information on interval between tests and a lack of blinding.
(b) Precision unevaluable

Comparison between US and X-ray (for paired US and X-ray data collected within the same study) for detecting pneumothorax.

Figure 9: Superimposed plot of diagnostic accuracy of US and X-ray for detecting pneumothorax, from studies comparing both against a common gold standard, and with data sufficient for meta-analysis. The filled black circle represent the summary point for US and the red filled circle for x-ray.



Note: The dotted curves drawn around these points represent the 95% confidence intervals around these points. The open circles and diamonds respectively represent the US and X-ray results of individual studies, and their area is proportional to the study size. US and chest X-ray results from the same study are linked by dotted lines.

9.5.3 Hospital imaging: haemothorax

Five adult studies[12,15,23,68,138] evaluated the diagnostic accuracy of methods to diagnose haemothorax (Table 30).

- One of these adult studies assessed the diagnostic accuracy of US[68,68] (Table 31).
- Four adult studies[12,15,23,138] assessed the diagnostic accuracy of X-ray. Of these, only 1 contained all raw diagnostic data, and so pooling of results was not possible (Table 32). The positioning of patients for X-ray was believed to be an important covariate. These studies were all believed to have carried out most X-rays in supine. This belief was based on an explicit description in the study, or, if this were absent, based on the majority of patients in the study having blunt trauma, who are usually, in contrast to some penetrating trauma patients, kept in a supine position.

Table 30: Summary of studies included in the review

Study	Population	Index test(s)	Reference test	Comments
Barrios 2010[11,12]	Patients at level 1 trauma unit; n=374	X-ray	CT	No blinding; no raw data provided or able to be extracted, and only sensitivity yielded.
Blasinska-Przerwa 2013[15]	Patients with chest trauma; n=30	X-ray	CT	Retrospective. No blinding reported.
Chardoli 2013[23,23]	Patients with blunt chest trauma; n=200	X-ray	CT	No raw data presented
Hyacinthe 2012[68,68]	Patients with mainly blunt trauma with indication for thoracic CT scan; n=119	US	CT	Prospective
Varin 2009[138,138]	Consecutive patients at level 1 trauma unit with penetrating wounds; n=299	X-ray	CT/surgery	Unclear blinding

US to detect haemothorax

Table 31: Diagnostic accuracy profile for the use of US to detect haemothorax

Number of studies	Number of patients	Risk of bias	Inconsistency	Indirectness	Imprecision	Sensitivity (95% CI) (in study order)	Specificity (95% CI)	Quality
US for detecting haemothorax (with CT as the gold standard) in adults								
1	119	No serious risk of bias	NA	None	NA[a]	0.37 (0.21-0.55)	0.96 (0.92-0.98)	MODERATE

(a) Precision not evaluable.

X-ray to detect haemothorax

Table 32: Diagnostic accuracy profile for the use of X-ray to detect haemothorax

Number of studies	Number of patients	Risk of bias	Inconsistency	Indirectness	Imprecision	Sensitivity (95% CI) (in study order)	Specificity (95% CI)	Quality
X-ray for detecting haemothorax (with CT/surgery as the gold standard) in adults								
4	299 374 200 30	Very serious[a]	Very serious[b]	None	NA[c]	0.63 (0.51-0.74) 0.29 0.20 0.58 Median 0.61	1 (0.99-1) - - 1	VERY LOW

(a) Risk of bias mainly due to lack of information on interval between tests and a lack of blinding.
(b) Wide variation in sensitivity value.
(c) Precision not evaluable.

9.5.4 Hospital imaging: cardiac tamponade

No studies were found that evaluated diagnostic measures of cardiac tamponade in this population.

9.5.5 Hospital imaging: pulmonary contusion

Five adult studies[12,15,68,120,132] evaluated the diagnostic accuracy of methods to diagnose pulmonary contusion (Table 33).

- Three of these adult studies[68,120,132] assessed the diagnostic accuracy of US. This was an insufficient number of studies for a meta-analysis and so a narrative review has been undertaken (Table 34). Four adult studies[12,15,120,132] assessed the diagnostic accuracy of X-ray. This was an insufficient number of studies for a meta-analysis and so a narrative review has been undertaken (Table 35)
- The positioning of patients for X-ray was believed to be an important covariate. These studies were all believed to have carried out X-rays in supine, and this was based on an explicit description, or, if this were absent, based on the majority of patients in the study having blunt trauma, who are usually, in contrast to some penetrating trauma patients, kept in a supine position.

Table 33: Summary of studies included in the review

Study	Population	Index test(s)	Reference test	Comments
Barrios 2010[11,12]	Patients at level 1 trauma unit; n=374	X-ray	CT	No blinding; no raw data provided or able to be extracted, and only sensitivity yielded.
Blasinska—Przerwa 2013[15]	Patients with chest trauma; n=30	X-ray	CT	Retrospective. No blinding reported.
Hyacinth 2012[68,68]	Patients with mainly blunt trauma with indication for thoracic CT scan; n=119	US	CT	Prospective
Rocco 2008[120,120]	Trauma patients with acute respiratory failure; n=15	US and X-ray	CT	No blinding reported. No raw data reported
Soldati 2006[132,132]	Patients with isolated blunt chest trauma and injury severity score >15; n=88	US and X-ray	CT	Retrospective

US to detect pulmonary contusion

Table 34: Diagnostic accuracy profile for the use of US to detect pulmonary contusion

Number and name of studies	Number of patients	Risk of bias	Inconsistency	Indirectness	Imprecision	Sensitivity (95% CI) (in study order)	Specificity (95% CI)	Quality
Diagnostic accuracy for the use of US to detect pulmonary contusion (with CT as gold standard) in adults								
3	119 88 15	Very serious[a]	Serious[b]	None	NA[c]	0.61(0.53-0.69) 0.95 (0.82-0.99) 0.89 Median 0.89	0.80 (0.70-0.88) 0.96 (0.87-1) 0.89 Median 0.89	LOW

(a) Risk of bias mainly due to lack of information on interval between tests and a lack of blinding.
(b) Some variation in sensitivity values.
(c) Precision not evaluable.

X-ray to detect pulmonary contusion

Table 35: Diagnostic accuracy profile for the use of X-ray to detect pulmonary contusion

Number and name of studies	Number of patients	Risk of bias	Inconsistency	Indirectness	Imprecision	Sensitivity (95% CI) (in study order)	Specificity (95% CI)	Quality
Diagnostic accuracy for the use of X-ray to detect pulmonary contusion (with CT as gold standard) in adults								
4	30 88 374 15	Very serious[a]	Very serious[b]	None	NA[c]	0.727 0.27 (0.14-0.44) 0.44 0.39 Median 0.42	1 0.98(0.90-1) - 0.89 Median 0.89	VERY LOW

(a) Risk of bias mainly due to lack of information on interval between tests and a lack of blinding.
(b) Wide variation in sensitivity values.
1. Precision not evaluable.

9.5.6 Hospital imaging: flail chest

No studies were found that evaluated diagnostic measures of flail chest in this population.

9.5.7 Hospital imaging: aortic injury

Nine adult studies[12,21,24,44,53,89,104,110 125,125] were found that evaluated the diagnostic accuracy of methods to detect aortic injury (Table 36). Seven other studies were found but were excluded because they used single slice CT, which is not representative of current practice.

- Seven of these adult studies[21,21,44,44,53,89,104,110 125,125] assessed the diagnostic accuracy of CT, all of which provided sufficient data for meta-analysis (Table 37 and Figure 10).
- Three adult studies[12,21,24] assessed the diagnostic accuracy of X-ray. This was an insufficient number of studies for a meta-analysis and so a narrative review has been undertaken (Table 38). The positioning of patients for X-ray was believed to be an important covariate. These studies were all believed to have carried out X-rays in supine, and this was based on an explicit description, or, if this were absent, based on the majority of patients in the study having blunt trauma, who are usually, in contrast to some penetrating trauma patients, kept in a supine position.

Table 36: Summary of studies included in the review

Study	Population	Index test(s)	Reference test	Comments
Barrios 2010[11,12]	Patients at level 1 trauma unit; n=374	X-ray	CT	No blinding; no raw data provided or able to be extracted, and only sensitivity yielded.
Bruckner 2006[21,21]	Patients with suspicious mechanisms of injury, or widened mediastinum on chest X-ray; n=856	CT and X-ray	Aortography	Retrospective; no blinding reported
Cook 2001[24,24]	Consecutive patients with blunt trauma and suspected aortic laceration; n=188	chest X-ray	Aortography/ emergent thoracotomy	Retrospective; unclear if gold standard reading blinded
Fishman 1999[44,44]	Patients at level 1 trauma centre with clinical indications of blunt chest trauma; n=40	CT	Aortography	Retrospective; no blinding reported
Gavant 1995[53,53]	Patients with non-trivial blunt chest trauma; n=127	CT	Later surgical/clinical outcome	Blinding done
Mirvis 1998[88,89]	Blunt trauma patients with abnormal mediastinal contours on admission chest X-rays; n=1104	CT	Aortography	No blinding reported
Ng 2006[104,104]	Patients with deceleration injury mechanisms and radiographic findings of mediastinal hematoma; n=53	CT	Arteriography and/or later surgical findings	Index test used consensus between 2 examiners. This may reduce external validity

Study	Population	Index test(s)	Reference test	Comments
Parker 2001[110,110]	Patients with blunt trauma and potential thoracic trauma on X-ray; needed to have bot CT and aortography; n=142	CT	Aortography	Rigorous study but gold standard poorly described
Scaglione 2001[125,125]	Patients with major blunt trauma; n=1419	CT	Thoracotomy, or, for most, later clinical and radiographic findings	Retrospective; no blinding reported

CT for detection of aortic injury

Table 37: Diagnostic accuracy profile for CT detection of aortic injury

Number of studies	Number of patients	Risk of bias	Inconsistency	Indirectness	Imprecision	Pooled Sensitivity (95% CI)	Pooled Specificity (95% CI)	Quality
CT for detecting aortic injury (with aortography/later clinical or surgical findings as the gold standard) in adults								
7	3741	Very serious[a]	Serious[b]	None	Serious[c]	0.951(0.892 to 0.986)[d]	0.944 (0.744 to 0.997)	VERY LOW

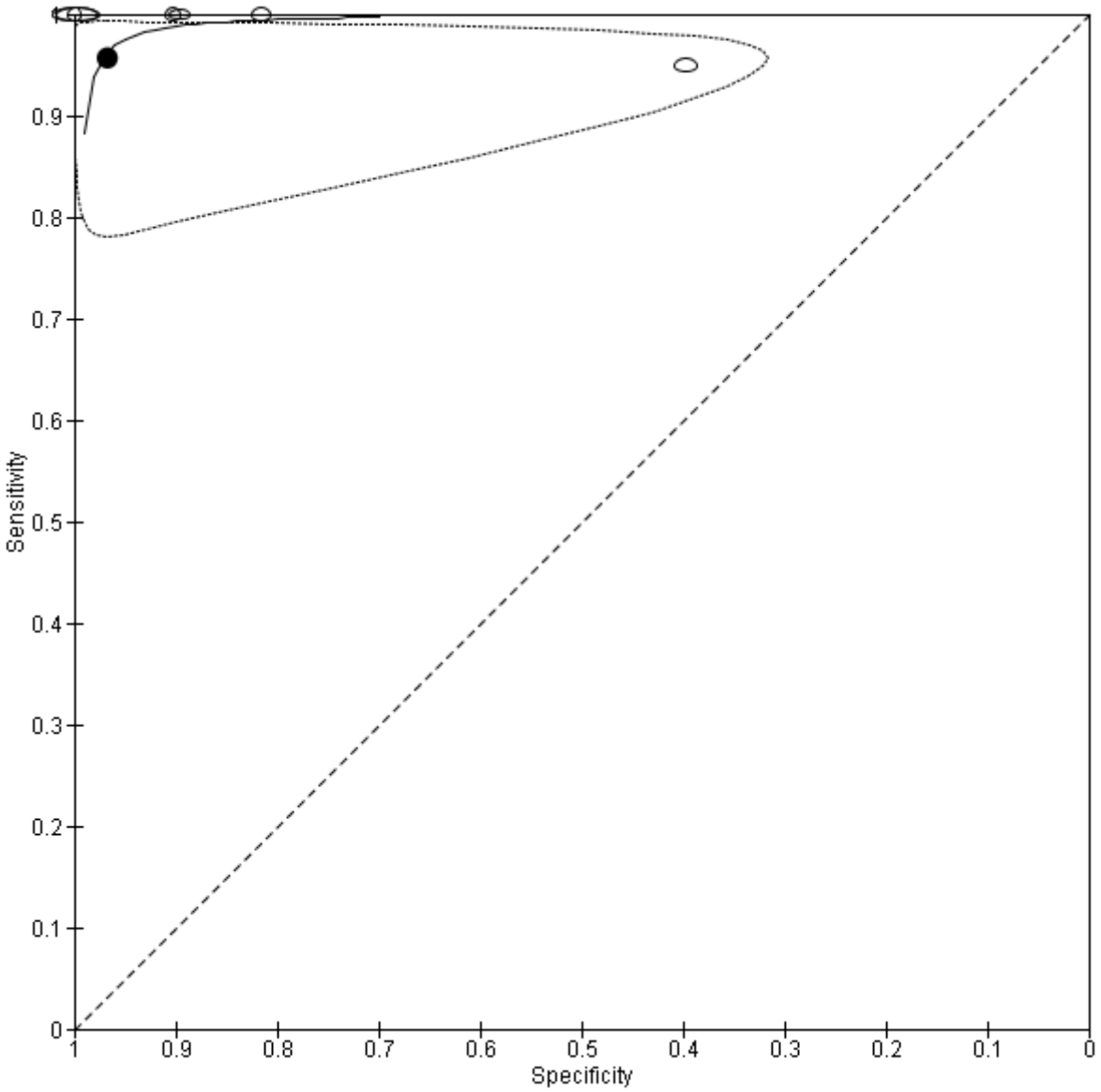
(a) Risk of bias mainly due to lack of information on interval between tests and a lack of blinding.

(b) Some lack of overlap of CIs on forest plot.

(c) Precision of sensitivity good, but a higher range in specificity.

(d) This is a conservative estimate. The WinBugs software[84] used to calculate the pooled sensitivity and specificity (and parameters for calculation of the 95% CIs) does not function when zeroes are present in the raw diagnostic data set. Hence where there were zero false negatives, or zero false positives, the zero had to be converted to the value of 1. This had the effect of creating less favourable sensitivity and specificity estimates than otherwise.

Figure 10: Diagnostic meta-analysis for CT in detecting aortic injury (gold standard=aortography)



Note: The solid black circle represents the pooled value of sensitivity and specificity. The dotted curve drawn around this point represents the 95% CIs around this point. The open circles represent the results of individual studies, and their area is proportional to the study size.

X-ray for detection of aortic injury

Table 38: Diagnostic accuracy profile for X-ray in detecting aortic injury (gold standard=aortography) in studies with insufficient data for meta-analysis

Number of studies	Number of patients	Risk of bias	Inconsistency	Indirectness	Imprecision	Sensitivity (95% CI) (in study order)	Specificity (95% CI)	Quality
X-ray for detecting aortic injury (with aortography as the gold standard) in adults								
3	374 188 856	Very serious[a]	Very serious[b]	None	NA[c]	0 1 0.9(0.74-0.98) Median 0.9 (0.74 to 0.98)	- 0.05 0.38 (0.35-0.41) Median 0.05	VERY LOW

(a) Risk of bias mainly due to lack of information on interval between tests and a lack of blinding.
(b) Wide variation in sensitivity values.
(c) Precision not evaluable.

9.6 Economic evidence

Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow chart in Appendix E.

Unit costs

Table 39: Diagnostic modality costs[37]

Imaging modality	Description	Cost
X-ray	Direct access plain film	£28
US scan	US scan, less than 20 minutes	£59
	US scan, 20 minutes and over	£40
FAST scan	US cost as a proxy	
CT	CT scan, one area, no contrast, 19 years and over	£60
	CT scan, one area, with post contrast only, 19 years and over	£71

Note: These costs are sourced from NHS reference costs 2012/13. Further detail on the cost,s such as the ranges and number of submissions, can be found in Appendix O.

9.7 Evidence statements

Clinical

Adults

Diagnostic accuracy of eFAST for tension pneumothorax

Very low quality evidence from 1 study comprising 345 adults showed that eFAST performed in hospital has a low and variable sensitivity of 0.40 (95% CI, 0.28 to 0.52) and a high specificity of 1.00 (95% CI 0.97 to 1.00) for diagnosing tension pneumothorax only.

Diagnostic accuracy of X-ray for tension pneumothorax

Very low quality evidence from 1 study comprising 345 adults showed that X-ray performed in hospital has a low and variable sensitivity of 0.24 (95% CI, 0.14 to 0.35) and a high specificity of 1.00 (95% CI: 0.99 to 1.00) for diagnosing tension pneumothorax only.

Diagnostic accuracy of US for pneumothorax

When diagnostic meta-analysis was conducted very low quality evidence from 10 diagnostic accuracy studies comprising 1921 adults showed that US has a pooled sensitivity of 0.845 (95% CI, 0.676 to 0.953) and a pooled specificity of 0.986 (95% CI, 0.974 to 0.994) at diagnosing pneumothoraces.

Diagnostic accuracy of chest X-ray for pneumothorax

When diagnostic meta-analysis was conducted very low quality evidence from 10 diagnostic accuracy studies comprising 1983 adults showed that chest X-ray has a pooled sensitivity of 0.5435 (95% CI, 0.299 to 0.775) and a pooled specificity of 0.991 (95% CI, 0.980 to 0.997) at diagnosing pneumothoraces.

Very low quality unpooled evidence from 4 studies comprising 1002 adults showed that chest X-ray has a median sensitivity of 0.52 and a median specificity of 1 (range 1-1) at diagnosing pneumothoraces.

Diagnostic accuracy of US for haemothorax

Moderate quality evidence from 1 study comprising 237 adults showed that US has a sensitivity of 0.37 (95% CI, 0.21 to 0.55) and a specificity of 0.96 (95% CI, 0.92 to 0.98) for diagnosing haemothorax.

Diagnostic accuracy of chest X-ray for haemothorax

Very low quality unpooled evidence from 4 studies comprising 903 adults showed that chest X-ray has a median sensitivity of 0.61 and a median specificity of 1 for diagnosing haemothorax.

Diagnostic accuracy of US for pulmonary contusion

Low quality unpooled evidence from 3 studies comprising 222 adults showed that US has a median sensitivity of 0.89 and a median specificity of 0.89 for diagnosing pulmonary contusion.

Diagnostic accuracy of chest X-ray for pulmonary contusion

Very low quality unpooled evidence from 4 diagnostic accuracy studies comprising 507 adults showed that chest X-ray has a median sensitivity of 0.42 and a median specificity of 0.89 at diagnosing pulmonary contusion, in relation to the gold standard of CT.

Diagnostic accuracy of CT for aortic injury

When diagnostic meta-analysis was conducted Very low quality evidence from 7 diagnostic accuracy studies comprising 3741 adults showed that CT has a pooled sensitivity of 0.951 (95% CI, 0.892 to 0.986) and a pooled specificity of 0.944 (95% CI, 0.944 to 0.997)at diagnosing aortic injury.

Diagnostic accuracy of chest X-ray for aortic injury

Very low quality unpooled evidence from 3 studies comprising 1418 adults showed that chest X-ray has a median sensitivity of 0.9 (95%CI, 0.74 to 0.98) and a median specificity of 0.05 at diagnosing aortic injury.

Children

Diagnostic accuracy of chest X-ray for pneumothorax

Low quality evidence from 1 diagnostic accuracy study comprising 200 children showed that chest X-ray has a sensitivity of 0 (95% CIs not estimable) at diagnosing pneumothoraces. Specificity was not measured in this study.

Economic

No relevant economic evaluations were identified.

9.8 Recommendations and link to evidence

Recommendations	**13. Imaging for haemorrhage in patients with suspected haemorrhage should be performed urgently, and the images should be interpreted immediately by a healthcare professional with training and skills in this area.** **14. Consider immediate chest X-ray and/or eFAST (extended focused assessment with sonography for trauma) as part of the primary survey to assess chest trauma in adults (16 or over) with severe respiratory compromise.** **15. Consider immediate CT for adults (16 or over) with suspected chest trauma without severe respiratory compromise who are responding to resuscitation or whose haemodynamic status is normal (see also recommendation 50 on whole-body CT).** **16. Consider chest X-ray and/or ultrasound for first-line imaging to assess chest trauma in children (under 16s).** **17. Do not routinely use CT for first-line imaging to assess chest trauma in children (under 16s).**
Relative values of different outcomes	The outcomes for this diagnostic review question are sensitivity and specificity of the index tests relative to a reference test (which is assumed to give the 'true' diagnosis). Sensitivity is an important outcome, because poor sensitivity may result in people with potentially serious chest trauma being undiagnosed and therefore, untreated. In contrast, low specificity, leading to incorrect positive diagnoses, will lead to unnecessary treatments. Though carrying a risk of unnecessary adverse events and higher costs, such additional treatments secondary to misdiagnoses are unlikely to be as much of a risk to the patient as missed diagnoses.
Trade-off between clinical benefits and harms	Although this review question concerns the overall entity of chest trauma, it is not possible to have a single diagnostic test for all kinds of chest trauma. The accuracy of each investigation varies according to the type of injury. The trade-off between clinical benefits and harms will, therefore, be described for each type of injury separately below. US (used here to denote the equipment, which can also be used to undertake eFAST) and X-ray can be performed relatively rapidly in the ED. US is not associated with any adverse events but X-ray carries a lifetime cancer risk which varies according to age. CT has a significantly higher radiation risk than X-ray, again depending on age, and increases time to diagnosis. While diagnostic cohort studies can tell us about the relative accuracy of a diagnostic test compared with a reference standard, they do not tell us whether adopting a particular diagnostic strategy improves patient outcomes. Evidence on patient outcomes is only available from diagnostic RCTs which compare two diagnostic interventions with identical subsequent treatment as indicated by the diagnostic test. No such evidence was identified.

	Tension pneumothorax: One adult study reported the diagnostic accuracy of eFAST and X-ray compared with CT for the diagnosis of traumatic pneumothorax requiring urgent decompression. eFAST had better sensitivity than X-ray, and would therefore, lead to less missed diagnoses. Specificity was equally good for both US and X-ray. **Pneumothorax**: Fifteen adult studies reported on the diagnostic accuracy of US and/or X-ray for pneumothorax. US had better sensitivity than X-ray, and would therefore, lead to less missed diagnoses. Specificity was equally good for both US and X-ray. **Haemothorax:** Four adult studies reported on the diagnostic accuracy of X-ray and one study of US for the diagnosis of haemothorax. It was unclear whether US or X-ray had better sensitivity, as both modalities had low sensitivity and there was a high level of heterogeneity within the X-ray evidence. Specificity was similar for both modalities. **Cardiac tamponade/flail chest** No evidence was identified. **Pulmonary contusion:** Five adult studies reported on the diagnostic accuracy of X-ray/US for pulmonary contusion. US had better sensitivity than X-ray and would therefore, lead to less missed diagnoses. Specificity was similar between the two techniques. **Aortic injury:** Nine adult studies reported on the diagnostic accuracy of X-ray/CT for aortic injury. CT had a pooled sensitivity which was far more accurate than that observed with X-ray. The GDG felt that the most important consideration for adults with potential chest trauma was whether they had severe respiratory compromise. In this group of patients the ability to rapidly perform X-ray and/or eFAST in the emergency department was considered to outweigh the additional benefit in terms of diagnostic accuracy to CT when the difficulties of performing a CT in this patient group are taken into consideration. In haemodynamically normal or unstable patients but responding to resuscitation, the benefits of CT with respect to diagnostic accuracy outweigh the risks of increased time to imaging and the difficulties monitoring these patients during scanning. In children, the GDG highlighted the radiation risks associated with CT and therefore, recommended X-ray and/or US as the first-line of investigation**.** For aortic injury, the previous gold standard of catheter angiography was regarded by the GDG as too invasive, too slow and misses some injuries which are visible on CT to consider for a recommendation in such a high-risk group.
Trade-off between net health benefits and resource use	There was no published economic evidence to inform this question. The GDG took into account the intervention cost of each diagnostic modality, and assessed each modality for each type of chest condition as outlined in the methods section in their deliberations (that is, taking into account the prevalence, predictive powers, the consequences of each diagnostic outcome in terms of potential net clinical benefit and cost of onward management, and potential incidental findings). See Appendix O for more detail on this.

	The GDG were presented with the costs of the different diagnostic modalities; X-ray had the lowest unit cost (£28), followed by US (with the US cost being used as a proxy for FAST) and CT had the highest unit cost (£71 – one area post contrast, £60 without contrast).[37] The main trade off in this question is around the accuracy of the modalities being considered versus the time taken to image using different modalities. It was noted that US machines may be less available in current practice than X-ray, and training may be required. Further accuracy of interpretation (and therefore cost effectiveness) of US was operator-dependent and may be improved with experience and in settings when presentation of the particular injury is common. A recommendation in favour of US could carry a cost impact, not least due to potential training costs in its operation. This, however, should not influence cost effectiveness deliberations, as the NHS reference cost of US is inclusive of staff and equipment costs. eFAST, which uses the same equipment, was felt to be less costly than US because it is performed by a member of the trauma team and is relatively quick. Given the lack of evidence for some of the index conditions and the general low quality of the evidence, a consensus was reached that the modalities more immediately available than CT, X-ray and eFAST do have a role to play and can be of benefit, particularly in the unstable patients where time is critical and CT is more time intensive, and X-ray can pick up other findings and assist in treatment (for example, tube placement). X-ray also has benefit in children where it can pick up other findings, such as rib fractures, and because sending children straight to CT is also a concern due to radiation risk. Combining X-ray and eFAST/US was not felt to add any more time to the assessment. The incremental cost of CT versus other modalities will most likely be offset by its accuracy. The small additional cost of CT was considered against the potential high benefits; in fact CT is considered the gold standard and has a high sensitivity and specificity. This is likely to generate fewer false positives and false negatives compared with other imaging strategies, consequently ensuring the right people receive the right treatment in a timely manner. This would save unnecessary costs further down the line and increase survival and therefore QALYs. Therefore, when considering both the costs and health benefits of different modalities, it is likely that CT is cost effective. As CT is the gold standard, the GDG felt that this should always be the first-line for stable patients, as in many instances, CT will already be indicated for a condition other than the suspected chest trauma, in which case it would not be cost effective to undertake other imaging prior to CT as they would not add value to the CT findings. The time versus accuracy trade-off is important here because unstable patients may have their survival compromised in the time it takes to CT them, therefore, the quicker modalities are recommended for unstable patients, and also for children due to the radiation concern.
Quality of evidence	The evidence retrieved was of low or very low quality. Chief limitations were a lack of blinding between examiners carrying out the index and reference tests; knowledge of the result in one might influence measurement in the other, which would tend to artificially improve diagnostic accuracy. There was also some unexplained inconsistency between studies which reduced confidence in the findings. Only one study was found in children.

	Economics NHS reference costs Costs for the diagnostic modalities were sourced from NHS reference costs [37]. Whether these costs are reflective of the true cost of the test is dependent on the number of submissions from hospitals. The cost of US was of particular concern to the GDG as the cost of US for less than 20 minutes was higher than the cost of US for more than 20 minutes. There were only submissions from 3 hospitals with a total of 13 units of activity for US more than 20 minutes, compared with 5 submissions with a total of 1,977 units of activity for US less than 20 minutes. This could be implying that the cost for US more than 20 minutes are slightly skewed as there are not enough units of activity to generate a nationally representative average cost. It would be assumed that a longer scan would cost more due to more staff time for example. However, there may be other reasons for the costs being higher for a shorter duration of US, such as more highly qualified or senior staff taking less time to do the US. CT also did not have many submissions (for no contrast: 4, with 70 units of activity; for post contrast: 1 submission, with 10 units of activity). X-ray had the most with 153 submissions and over 5 million units of activity. Additionally, it has been agreed with the GDG that the US cost can be used as a proxy for FAST, however, the actual cost was felt to be lower because FAST is most commonly carried out by a member of the trauma team rather than a radiologist (usually CT4 or above) and takes about 5 minutes. The US machine is in the resuscitation room and is actually usually a much more basic and cheaper machine than used in radiology. Given that the clinical review was not able to meta-analyse all the results, that some injuries had no clinical review data, the prevalence of the condition or index of suspicion of the imaged population is uncertain and that the implications of diagnostics were not fully considered (that is, the management/treatment of each type of injury and who is correctly/incorrectly receiving this based on the clinical data), conclusions regarding the cost effectiveness of a diagnostic strategy remain tentative.
Other considerations	Although US is the equipment that is also used to undertake FAST/eFAST, FAST/eFAST is usually carried out by a member of the trauma team, rather than a sonographer or radiographer who would usually carry out an US. For adults, eFAST, to look for fluid in the chest and abdomen, would be the modality used in the ED by the trauma team. However, for children, the term used in the recommendation is US as in the child population this modality would most likely be undertaken by a sonographer or radiographer. It was acknowledged that the interpretation of the different diagnostic modalities as well as their availability are considerations, as US is not always as readily available as X-ray, as well as the interpretation being entirely down to the operator of the machine, whereas an X-ray can be interpreted by a number of people. Thus, considerations relating to skill level of the clinician interpreting the scan were discussed and the potential need for training for US. Immediate CT for haemodynamic compromise: all the listed chest trauma will make the patient unstable so unsuitable for CT (heart rate up, blood pressure down, shock index up, so will not fulfil criteria for CT) at that particular time. The GDG acknowledged that for elderly patients the index of suspicion for severity of thoracic injury needs to be lower.

10 Assessment and management of haemorrhage

10.1 Control of external haemorrhage

10.1.1 Use of haemostatic dressings

Introduction

Uncontrolled haemorrhage is one of the leading causes of death after injury. In the pre-hospital setting it is important to have effective interventions to control haemorrhage before definitive treatment in hospital. Haemostatic dressings are novel treatments developed for the military setting that are now being considered for civilian use. They can be broadly categorised into three classes based on their method of haemorrhage control. Factor concentrators promote clotting through the rapid absorption of the water content of blood. Mucoadhesives act by adhering to tissue and physically sealing bleeding wounds. Procoagulants either activate the clotting cascade or provide clotting factors, such as fibrinogen and thrombin, to the wound site.

Review question: Are haemostatic dressings clinically and cost effective in improving outcomes in patients with haemorrhage in major trauma?

For full details see review protocol in Appendix C.

Table 40: PICO characteristics of review question

Population	Children and adults with haemorrhage after experiencing a traumatic incident.
Intervention(s)	Haemostatic dressings
Comparison(s)	A comparison of the above Standard dressings (with no active ingredients)

Outcomes	Critical:
	• Mortality at 24 hours, 30 days/1month and 12 months
	• Health-related quality of life
	• Adverse effects
	  ○ skin burns
	  ○ delayed wound healing
	  ○ necrosis
	  ○ surgical complications
	• Length of ICU stay
	• Blood product use
	
	Important:
	• Patient reported outcomes (psychological wellbeing)

Study design	RCTs or systematic reviews of RCTs; cohort/case control studies if RCT evidence is insufficient. Only cohort/case control studies accounting for important confounding factors will be considered (severity of shock, severity of injury, degree of head injury, age)

Clinical evidence

No relevant clinical studies were identified.

Economic evidence

Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow chart in Appendix E.

Unit costs

A range of the haemostatic agents available are presented below for illustration of costs.

Table 41: Intervention costs

Product	Cost	Source
Factor concentrators		
Quikclot ACS	£34.95	SP services
Mucoadhesive agents		
HemCon ChitoFlex	£160.95	SP services
HemCon ChitoGauze	£39.95	SP services
Celox Gauze (CEL)	£37	SP services
Procoagulant supplementor		
QuikClot Combat Gauze XL	£39.95	SP services

Note: SP services is a supplier used by the East Midlands Ambulance Service.

Evidence statements

Clinical

No relevant clinical studies were identified.

Economic

No relevant economic evaluations were identified.

Recommendations and link to evidence

Recommendations	18. Use simple dressings with direct pressure to control external haemorrhage.
Relative values of different outcomes	The critical outcomes for decision making were mortality health-related quality of life, skin burns, delayed wound healing, necrosis, surgical complications, length of ICU stay and blood product use. The GDG considered patient-reported outcomes such as psychological wellbeing to be important outcomes.
Trade-off between clinical benefits and harms	No clinical evidence was found to evaluate the trade-off between clinical benefits and harms of haemostatic dressings for control of haemorrhage. The potential benefits of haemostatic dressing are rapid control of bleeding and therefore, better patient outcomes, although, side effects, have been reported.
Trade-off between net health benefits and resource use	No economic evidence was identified for this question. Haemostatic dressings are designed as pre-hospital tools to control bleeding in situations where there is non-compressible bleeding. They can be classified into

	3 groups by mechanism of action: factor concentrators, mucoadhesive agents and procoagulant supplementors. Haemostatic dressings are more expensive than standard dressings and can vary from £30 to £160 depending on the type. Some types can have side effects.. Poor control of bleeding could also lead to longer hospital/ICU stay and more use of blood components. Any additional benefit has to be weighed up against the cost and potential adverse events. The population that will benefit from haemostatic dressings in a civilian population is likely to be very small, and additionally, the products also have an expiry date meaning it can be costly to replace them even if they have not been used. They are unlikely to stop uncompressible active arterial bleeding, and therefore, may be used in combination with other interventions to control bleeding, such as tourniquets applied to a limb. However, where these dressings may be useful, if effective, is when the injury is in a location in which it is difficult to apply a tourniquet. The GDG felt that given the small population that they will be used on and the resource impact in purchasing them (which can be expensive and then replacing them [used or unused]), as well as there being no evidence to suggest benefit above standard dressings and direct pressure – a recommendation to use simple dressings and direct pressure was considered appropriate. This could lead to cost savings. Haemostatic dressings are even less likely to be used in the paediatric population where penetrating injury to peripheral vasculature is extremely rare.
Quality of evidence	No relevant clinical studies were identified.
Other considerations	Haemostatic dressings are most commonly used in the military environment where they can be utilised almost immediately after injury. The GDG agreed that a key difference between the civilian and military settings is that the administration of haemostatic dressings will be on average much more delayed in the civilian setting. The GDG considered that this may mean an unproven treatment in the military setting is less effective in the civilian setting. The GDG indicated that currently haemostatic dressings are rarely used by ambulance trusts and there is limited knowledge around their correct use. This, combined with a high cost and limited shelf life, led the GDG to agree that there is no reason to recommend these products. In the absence of any evidence in favour of haemostatic dressings, the GDG did not believe that they offered any improvement over and above standard dressings with direct pressure. The GDG did not identify any considerations specific to children.

10.1.2 Use of tourniquets in major trauma

Introduction

The utility and safety of using pneumatic or mechanical tourniquets in a civilian trauma situation is widely debated and, at times, controversially supported predominately by anecdotal military evidence. While the preservation of life often takes precedence over the potential expense of a limb, there are many potential complications (morbidity, disability and amputation) resulting from inappropriately applied tourniquets or tourniquets left on for excessive amounts of time, when perhaps manual direct pressure would have sufficed to stem the bleeding. This review attempts to identify evidence on the use of mechanical or pneumatic tourniquets in comparison with each other (to find which may work best) or in comparison with no tourniquet or direct pressure (to find out if their use should be supported at all).

Review question: Is the use of pneumatic or mechanical tourniquets clinically and cost effective in improving outcomes in patients with haemorrhage in major trauma?

For full details see review protocol in Appendix C.

Table 42: PICO characteristics of review question

Objective	To determine the optimal type of tourniquet to use in patients with limb trauma haemorrhage in the emergency department.
Population	Children, young people and adults who have experienced a traumatic limb injury.
Intervention(s)	Pneumatic tourniquets Mechanical tourniquets
Comparison(s)	Each other No tourniquet/direct pressure
Outcomes	Critical • Mortality at 24 hours, 30 days/1 month and 12 months • Health-related quality of life • Blood product use (RBCs, platelets, plasma, cryoprecipitate) • Length of ICU stay • Adverse effects: amputation, nerve palsies, renal failure. Important • Time to definitive control of haemorrhage • Patient reported outcomes (psychological wellbeing)
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

Clinical evidence

No relevant clinical studies were identified.

Economic evidence

Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow chart in Appendix E.

Unit costs

Tourniquets can come in the form of mechanical or pneumatic:

- All mechanical tourniquets are single use. It is possible that they may be re-used if appropriately sterilised, however, given the nature of their use, they often come into contact with blood and are therefore generally disposed of and replaced within clinical practice.
- Pneumatic tourniquets, although involve a much larger upfront cost, are re-usable, and therefore, the cost per use is likely to be minimal, however, this is dependent upon whether re-usable or disposable cuffs are used, which can be expensive.

Table 43: Tourniquet costs

Product category	Product	Cost	Cost per use	Source
Mechanical tourniquets	SOFTT Special Operations Forces Tactical Tourniquet	£24.95	£24.95	SP services[a]
	Combat application tourniquet	£20.95	£20.95	SP services
	Mechanical application tourniquet	£28.95	£28.95	SP services
Pneumatic tourniquets	ATS 3000 tourniquet system Disposable cuff	£6,906.80 £241.24	£242.62[b] Depends whether cuffs are disposable or re-usable	NHS Supply Chain [3]
	Braun SCT 2x2 C/W Timers and 4 and 7 bar air lead Disposable cuff	£1,721[c] £300	£300.34[d] Depends whether cuffs are disposable or re-usable	Through GDG contact (personal communication – 20/03/2014)

(a) A supplier used by East Midlands Ambulance Service. This is the supplier cost and does not include any discounts. Assuming can be used 5,000 times, plus disposable cuff cost. The cost per use will depend upon how many people the device can be used on over its lifetime, as well as any ongoing costs that have to be factored in such as disposable cuffs which are single use, and maintenance of the device.

(b) The tourniquet has a one-off cost of £1,565 plus an additional pipe line was purchased at £156.

(c) Assuming can be used 5,000 times, plus disposable cuff cost. Disposable cuffs can vary in price but are around £300 (one of the higher estimates to be conservative), taken from the Braun catalogue.

Potential adverse events from tourniquets can include amputation of limbs, renal failure and nerve palsies. As further information, the cost of treating these adverse events can be found in Appendix O.

As a brief summary:

Table 44: Summary of adverse event costs

Adverse event	Cost detail	Cost per patient
Renal failure	ICU cost per day (1 organ being supported)	£852[b]
	Acute kidney injury cost (weighted for complications and comorbidities)	£4,257[b]
Amputations[a]	Major shoulder and upper arm procedures for trauma (weighted for complications, comorbidities, and excess bed days)	£5,295[b]
	Major knee procedures for trauma (weighted for	£6,921[b]

Adverse event	Cost detail	Cost per patient
	complications, comorbidities, and excess bed days)	
Nerve palsies	Treatment dependent on the extent of the injury. Could include: physiotherapy, splints, and in very rare cases nerve transfer surgery Cost of a physiotherapy session per hour	 £32[c]

(a) The amputation costs only include the acute procedure costs. Additional costs which have not currently been taken account here include the potential need for physiotherapy, and prosthetic limbs.
(b) NHS reference costs 2012-13 [37]
(c) Source: PSSRU 2013[29,30]

Evidence statements

Clinical

No relevant clinical evidence was identified.

Economic

No relevant economic evaluations were identified.

Recommendations and link to evidence

Recommendations	19. In patients with major limb trauma use a tourniquet if direct pressure has failed to control life-threatening haemorrhage.
Relative values of different outcomes	The GDG agreed the following critical outcomes to inform decision making: mortality, health-related quality of life, adverse effects, blood product use and length of intensive care stay. Time to definitive haemorrhage control and patient-reported outcomes such as psychological wellbeing were identified as important outcomes. Mortality was considered the most important outcome. If effective tourniquet use resulted in living with a reduced quality of life due to an adverse effect caused by tourniquet reducing blood flow to a limb (for example, nerve palsies), this was considered preferable to death from uncontrolled bleeding.
Trade-off between clinical benefits and harms	The GDG discussed the harms and benefits of tourniquets versus standard dressings overall, as well as mechanical versus pneumatic. Control of catastrophic haemorrhage should be the first stage of assessment and resuscitation of a critically injured person. Whereas, immediate haemorrhage control can be achieved by direct pressure, the decision of when direct pressure should be used over tourniquets was considered controversial as the GDG tried to weigh up the risk and cost of placing a tourniquet on a person who did not require it compared with those that do. If applied incorrectly, tourniquets can result in adverse effects associated with reduced blood flow (amputation, nerve palsies and renal failure) as well as result in increased venous bleeding. The GDG debated whether the harms associated with incorrect application could possibly outweigh the clinical benefit of avoiding mortality and agreed that a reduced quality of life due to an adverse effect was preferable to death. Hence, to be effective, tourniquets need to be appropriately placed proximal to the wound and applied tightly enough to stop bleeding. Tourniquets in the UK are now available on many UK ambulances, but the GDG did not consider there to be a

	question about which type of tourniquet should be used in the pre-hospital settings, as they felt it was standard practice to use mechanical tourniquets (improvised by police or bystanders, or commercially available varieties from first response personnel). It was agreed that when tourniquets are needed, early application would be appropriate and it was acknowledged that ideally they should be readily available close to the incident, for instance in first aid kits and potentially in kit dumps at important strategic sites, such as railway stations and airports. In hospital departments, pneumatic and mechanical tourniquets are both available. There is no evidence to compare one against the other. On a cost basis, pneumatic tourniquets may be more costly.
Trade-off between net health benefits and resource use	No economic evidence was identified comparing tourniquets with no tourniquet, direct pressure or each other (mechanical versus pneumatic). Pneumatic tourniquets can range in costs from a few pounds to a few hundred pounds per person, depending on how many people they can be used on over their lifetime, and also depending on whether the cuffs are re-usable or disposable, which can increase the cost dramatically. Mechanical tourniquets cost around £20–£30 for a disposable mechanical tourniquet, some can be re-used which would lower the cost per patient. Tourniquets can also lead to adverse events which will have associated health and resource implications. A lack of clinical evidence meant that data on the benefit (or lack of) of a tourniquet in controlling bleeding, as well as an estimate of the rate of adverse events, was not available. The GDG felt that it was more important to be able to save lives even if this meant there would be a risk of adverse events in a small proportion of patients. The main trade-off around the use of a tourniquet is that an effective tourniquet will control blood loss; however, this must be traded off against the possibility of adverse events from reducing blood flow. These can include amputation of the limb, renal failure and nerve palsies which would cause downstream resource and health implications. The incidence of adverse events from a tourniquet was estimated to be less than 10% by the GDG, with transient nerve palsy being the most reported of the three adverse events. If a tourniquet does not adequately control bleeding then the risk of mortality from this is likely to outweigh the risk of adverse events. As no evidence was identified, there is uncertainty as to the relative benefit of a tourniquet compared with direct pressure, however, use of direct pressure would not be associated with the adverse events associated with a tourniquet, but may not be as effective at controlling blood loss. The timing of application of the tourniquet is also an important factor. For the different types of tourniquets compared with each other, it is unclear whether the more expensive pneumatic tourniquets would be more effective than the mechanical tourniquets. Additionally no evidence was identified on the difference in adverse events between the two types. Thus, the cost effectiveness of tourniquets both in general (compared with no tourniquet or direct pressure) and compared with each other remains uncertain. However, the GDG felt mechanical tourniquets were standard practice pre-hospital. The GDG felt that in practice, tourniquets do provide benefit if used on the right

	people, however, they tend to be over-used and not necessarily used in the right circumstances, which is having a substantial cost impact to the NHS. The incidence of major trauma's where a tourniquet would be applicable was discussed, as their presence on ambulances have stemmed from their use in war, where the incidence of such injuries requiring a tourniquet would be much larger. It was decided that in order to tailor the use of tourniquets to the applicable population that would benefit most from them, a recommendation suggesting who they should be used on would be helpful for clinicians.
Quality of evidence	No evidence was retrieved which compared the clinical effectiveness of the different types of tourniquets.
Other considerations	It was noted in GDG discussion that much of the anecdotal support for tourniquet use is based on military experience. In the military context, tourniquet application takes place immediately or extremely soon after the injury, compared with the civilian context where tourniquet use is comparatively slower due to travel time of the first response personnel. It was suggested that those who would most benefit from tourniquet application in the civilian context usually die from uncontrolled haemorrhage before arrival of emergency personnel. The prevalence of injuries that would benefit from a tourniquet in a civilian setting would also be very small compared with a military setting. It was noted that current stocking of emergency response vehicles with tourniquets is a disproportionately large allocation of resource in relation to the dearth of evidence for their clinical and cost effectiveness. While this lack of evidence does not suggest that tourniquet use is harmful, it does highlight that spending limited NHS resources on their widespread use, given the small population they might be used on, is questionable. The GDG did not identify any considerations specific to children.

10.2 Pelvic binders

10.2.1 Introduction

Pelvic fractures are a life-threatening orthopaedic emergency; therefore, achieving pelvic stability is an early and critical goal in order to decrease bleeding, decrease pain, improve mobility and allow for transfers. The overall mortality rate for patients with pelvic fractures is between 10 and 20 percent. That rate jumps to 38 percent if the patient is hypotensive on admission and to 50 percent if the patient has an open pelvic fracture.The pelvic binder is used for the emergency stabilisation of pelvic fractures and haemorrhage control before definitive treatment. Current practice is to give any patient suspected of having a pelvic fracture a pelvic binder at the pre-hospital stage. The suspicion of a pelvic fracture is usually based on the mechanism of injury and so is very non-specific. If a patient has a pelvic fracture they will usually benefit from a pelvic binder, as the binder will stabilise the pelvis, reducing pain and blood loss, which will likely outweigh any adverse effects, such as pressure sores. A pelvic binder is considered to be a safe and non-invasive method of pre-hospital stabilisation that may not cause harm to the individual patient if applied correctly. However over-use will incur the costs of equipment, possible transfer to inappropriate locations or unnecessary investigations with no corresponding benefit in outcome.

10.2.2 Review question: Is the application of pelvic binders pre-hospital in patients suspected of pelvic fracture clinically and cost effective in improving outcomes?

Table 45: PICO characteristics of review question

Population	Children, young people and adults who are suspected of a pelvic fracture following a

	traumatic incident.
Intervention(s)	Pelvic binders
Comparison(s)	No treatment/standard care
Outcomes	Critical: • Mortality at 24 hours, 30 days/1 month and 12 months • Volume of blood components • Health-related quality of life • Adverse effects (unnecessary imaging) Important: • Patient-reported outcomes (pain/discomfort). • Improvement in haemodynamics (blood pressure and heart rate)
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.

10.2.3 Clinical evidence

No randomised studies were identified that met the inclusion criteria for our protocol. Two cohort studies were, therefore, included in the review; [47,47] [55] these are summarised in Table 46 below. Evidence from these studies is summarised in the clinical evidence summary below (Table 47). See also the study selection flow chart in Appendix D study evidence tables in Appendix G, forest plots in Appendix J, GRADE tables in Appendix I and excluded studies list in Appendix K.

All studies included only participants whose pelvic fracture had already been confirmed with imaging. While Krieg et al [76,76] investigated the use of pre-hospital pelvic binders on this population, the other two studies investigated the use, or otherwise, of pelvic binders while in hospital.

Table 46: Summary of studies included in the review

Study	Intervention/comparison	Population	Outcomes	Comments
Fu 2013[47,47]	**Intervention:** Any non-invasive pelvic circumferential compression device including pelvic binder and improvised 'sheet binder' prior to transfer to level 1 centre; n=153 **Comparison:** No binder n=432	All patients with any pelvic fracture (both stable and unstable) transferred to a level 1 trauma centre from other hospitals. Taiwan	• Mortality • Volume of blood transfusion	Patients who received interventional radiology or surgery in first presenting hospital were excluded. The patients were similar as baseline for age, shock, GCS and injury severity.
Ghaemmaghami 2007[55]	**Intervention:** 18-inch wide circumferential woven cloth binder with string pulley (recruited 2003-2006); n=118 **Comparison:** Historic control with no	All patients with pelvic fracture and either an unstable fracture pattern and/or aged >55 years and/or a systolic BP <90 mmHg.	• Mortality • Requirement for massive transfusion (>6 units in 24 hours)	Suggestion that prior to introducing pelvic binder protocol there was occasional use of improvised binder.

Study	Intervention/comparison	Population	Outcomes	Comments
	binder (2002-2003) n=119	USA		

Table 47: Clinical evidence summary: pelvic binder versus no binder

Outcome	Number of studies (no. of participants)	Imprecision	GRADE rating	Absolute difference	Control event rate (per 1000)	Control event rate for continuous outcomes
Mortality	1 (n=585)	Very serious	VERY LOW	7 fewer per 1000 (from 9 fewer to 13 more)	9 per 1000	-
Mortality (adjusted data)	1 (n=237)	Very serious	VERY LOW	OR 0.9 (0.31 to 2.6)	-	-
Volume of blood (packed red blood cell [pRBC]) transfused	1 (n=135, unstable and n=450, stable)	No serious imprecision	VERY LOW	Unstable MD 0.11 lower (0.16 lower to 0.66 higher Stable MD 1.56 lower (1.67 lower to 1.44 lower)	-	0.231 1.9545
Need for massive transfusion (>6 units pRBC in 24 hours)	1 (n=237)	Very serious	VERY LOW	OR 1.4 (0.58 to 3.38)	-	-

10.2.4 Economic evidence

Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow chart in Appendix E.

Unit costs

Pelvic binders can come in the form of:

- Improvised pelvic binders (made from a bed sheet for example), which will not have any costs associated with them to the NHS as the materials were already available.
- Purpose made pelvic binders.

The costs of a sample of purpose made pelvic binders used in practice are provided below to aid the consideration of cost effectiveness. The costs are the unit costs from the supplier of the product. However, each ambulance service can negotiate individual discounts with suppliers.

Also note that these costs are per patient. Although it may be possible to re-use some of the pelvic binders if disinfected appropriately, generally they are treated as single use in practice.

Table 48: Costs of purpose made pelvic binders

Product	Cost[a]	Source
SAM Pelvic Sling™ II – Single	£54.95	SP services[b]
T-Pod	£79	The Air Ambulance Service – through GDG contact (personal communication – 22/04/2014)
Prometheus pelvic splint	£29.50	GDG member

(a) These costs are the unit cost from the suppliers and are not inclusive of any discounts
(b) A supplier used by the East Midlands Ambulance Service

As additional information, cost per unit of packed red blood cells is £122.[105]

10.2.5 Evidence statements

Clinical

Very low quality evidence from one cohort study comprising 585 participants showed that pelvic binders were clinically effective compared with no binder in terms of reducing mortality, with very serious imprecision.

Very low quality evidence from one cohort study comprising 585 participants showed pelvic binders resulted in a clinically important reduction in total blood product use compared with no binder, with serious imprecision. This effect was greater in the stable patient group.

Very low quality evidence from one cohort study comprising 237 participants demonstrated a clinically important reduction in pRBC use for pelvic binders when compared with no binder, with very serious imprecision.

Economic

No relevant economic evaluations were identified.

10.2.6 Recommendations and link to evidence

Recommendations	**20. If active bleeding is suspected from a pelvic fracture after blunt high-energy trauma:** • **apply a purpose-made pelvic binder or** • **consider an improvised pelvic binder, but only if a purpose-made binder does not fit.**
	In addition to the major trauma GDG reviewing the clinical and cost effectiveness of pelvic binders, the complex fractures GDG reviewed the accuracy of risk tools for the use of pelvic binders (Complex fractures Clinical guideline see section 7.3) . These recommendations were developed and supported by both of the evidence reviews addressing pelvic binders. **Developing the recommendations** The pelvic binder recommendations were developed across the two guidelines by all members of both GDGs. Evidence reviews were completed for all the guidelines and the separate GDGs reviewed the evidence and drafted recommendations. The overall guideline population of patients with pelvic bleeding meant that similarities and duplication between the draft recommendations were inevitable. The recommendations were taken to the project executive team (PET) for coherence and consistency checking, the PET also had the advantage of identifying gaps in the separate guidelines that had been addressed in another guideline. The PET agreed on a core set of draft recommendations. The core set of recommendations were taken back to each of the separate GDGs for review and agreement. The GDG had access to both evidence reviews.
Relative values of different outcomes	The GDG agreed the following critical outcomes to inform decision making: mortality, health-related quality of life, adverse effects and blood product use. Haemodynamic improvement and patient-reported outcomes, such as psychological wellbeing, were identified as important outcomes.
Trade-off between clinical benefits and harms	Two retrospective cohort studies were identified. Both studies included only participants whose pelvic fracture had already been confirmed with imaging. One study investigated the use of pelvic binder pre-hospital, and one study investigated the use of pelvic binders in hospital. Two studies reported pelvic binders to be associated with a clinically beneficial reduction in mortality but with very serious imprecision. The evidence also indicated that pelvic binders were associated with a clinically important reduction in blood product transfusion (no imprecision to serious imprecision). One study reported more patients with a pelvic binder requiring massive transfusion compared with no pelvic binder but with very serious imprecision. The GDG noted that both studies were conducted with patients with confirmed pelvic fractures. As pelvic binders will be applied pre-hospital for patients with a suspected pelvic fracture, the evidence, therefore, only represents a sub-population of patients that will receive a pelvic binder. As a consequence, the GDG felt that pelvic binders should only be applied for patients with strong suspicion of pelvic fracture. However, as the GDG noted that there is currently no accurate method of identifying patients with pelvic fracture pre-hospital, the GDG chose to limit their recommendation to patients with suspected active bleeding following blunt high

	energy trauma to the pelvis. The GDG felt that this patient group are the patients that are most likely to have a pelvic fracture and most likely to benefit from a pelvic binder. The GDG also noted that this recommendation is supported by the clinical evidence that demonstrated a benefit from pelvic binders in a population with major pelvic fracture and associated haemodynamic instability or shock (except for the patients with stable pelvic fractures included in the Fu study) (that is, not avulsion injuries or fractured pubic rami). No evidence was identified to evaluate the risk of adverse effects when using pelvic binders. The GDG noted that this may include reduced quality of life due to the binder reducing blood flow to a limb (for example, nerve palsies). However, the GDG felt that the clinical benefit of the pelvic binder in avoiding mortality due to the effective control of bleeding was considered to outweigh the possible harm of adverse effects. It was noted that, in general, the pelvic binder used should always be proprietary and not improvised due to the risks of adverse events associated with inappropriate force used in the application of improvised 'sheet' binders. However, the GDG noted that are pelvic binders available to fit large adults and small children but they may not be available, and therefore, an improvised binder may in these cases be better than no intervention. The GDG discussed the possibility that, because they are non-invasive and generally perceived as safe, pelvic binders may be applied unnecessarily in some patients with a low index of suspicion for a pelvic fracture as staff choose to 'err on the side of caution'. The GDG confirmed that the only function of a pelvic binder is to control bleeding. The GDG felt that the over-use of pelvic binders may not cause any harm to the individual patient, but that the NHS would incur the costs of equipment, possible transfer to inappropriate locations or unnecessary investigations with no corresponding benefit in outcome.
Trade-off between net health benefits and resource use	No economic evidence was identified comparing pelvic binders with no treatment/standard care. Pelvic binders can come in the form of improvised binders (using a bed sheet for example) or purpose-made binders. Improvised binders would have no cost to the NHS whereas purpose-made binders can vary from £30-£80. The accuracy of the pre-hospital assessment in identifying suspected pelvic fracture will determine how many pelvic binders are used. Over-use of pelvic binders is likely to have an impact on hospital imaging because those who come into hospital wearing a pelvic binder will probably be imaged (this may be negated if the patients are multiply injured and would have been imaged anyway, but our population is not just polytrauma), when actually only a small proportion of them may turn out to have a pelvic fracture. Additionally, a suspected pelvic fracture will affect the triaging decision and the transfer destination as a suspected pelvic fracture can trigger a major trauma call using some current triaging protocols, and result in transfer to a major trauma centre. A more effective binder is assumed to lead to lower downstream resource use in terms of blood components, adverse events and potentially length of stay. Two studies were identified comparing pelvic binders with no pelvic binders: Both studies showed that mortality is likely to be lower in the pelvic binder group. The results were somewhat conflicting with regards to resource use as one study (Fu 2013) identified that the pelvic binder group used less blood whereas one study

	(Ghaemmaghami 2007) identified that the pelvic binder group needed more massive transfusions (more than 6 units of pRBCs in 24 hours, an odds ratio of 1.4). If a pelvic binder does reduce downstream resource use, such as blood components, then it is possible that using less blood components also reduces the risk of transfusion or over-transfusion-related adverse events. It is important to note, however, that both studies were in patients who already had a confirmed pelvic fracture, whereas pre-hospital, not all patients applied a binder will turn out to have a fracture, and it is the benefit of the binder in this entire 'suspected' group that has not been identified. The likelihood of having a clinically relevant pelvic fracture (and therefore really needing to have a pelvic binder) is critical in determining whether routine application of a pelvic binder as a preventative measure is cost effective. If the incidence of pelvic fracture is really low, it is unlikely that the costs involved in routinely applying the binder (plus imaging) will justify the potential health gains or savings of blood components (for which there is conflicting low quality evidence). It was mentioned that open book fractures (which are a type of fracture that would benefit from the use of a binder) have a prevalence of less than 1% in adults, and even less for children. The GDG agreed that when used in the right population, pelvic binders do have a benefit and particularly purpose-made binders over improvised binders. Currently in practice, pelvic binders are being applied to a large population, most of whom may not benefit and therefore, this is a costly practice. The GDG decided to limit the use of pelvic binders to those patients who are suspected of active bleeding, as this is the group most likely to benefit from a binder.
Quality of evidence	The quality of the evidence was very low for each outcome reported due to risk of bias, imprecision and indirectness as the study populations were patients with confirmed pelvic fractures. This can be considered an indirect population as the question was focusing on whether the pre-hospital application of binders is clinically and cost effective, and this question remains unanswered because it involves including all the groups this would be applied to; those who do not turn out to have a fracture and have a binder, as well as those who do have a fracture and have a binder. Thus focusing on just the latter group (who are more likely to benefit from the binder) may be over estimating both clinical and cost effectiveness.
Other considerations	The GDG noted that pre-hospital health professionals and clinicians need to be trained to recognise and monitor for the signs of active bleeding. The importance of dispatching the correct personnel to major trauma incidents was also highlighted.

10.3 Haemostatic agents

10.3.1 Introduction

Uncontrolled haemorrhage is a major cause of death in major trauma. Haemostatic agents prevent, stop or control bleeding and have been shown to improve outcomes in patients following surgery and they may also be effective in major trauma patients.

10.3.2 Review question: Is the use of systemic haemostatic agents clinically and cost effective in improving outcomes in patients with confirmed or suspected haemorrhage in major trauma?

For full details see review protocol in Appendix C.

Table 49: PICO characteristics of review question

Population	Children, young people and adults who have a suspected haemorrhage following a

	traumatic incident.
Intervention(s)	Factor 7 (recombinant activated factor VII) Tranexamic acid Fibrinogen concentrate Prothrombin complex concentrates Other anti-fibrinolytic agents
Comparison(s)	Nothing A comparison of the above In combination In addition to standard care (Blood components [plasma, RBCs, platelets])
Outcomes	Critical: • Mortality at 24 hours, 30 days/1 month and 12 months • Health-related quality of life • Adverse effects ○ venous thromboembolism ○ thrombotic events (myocardial infarction [MI]/stroke, pulmonary embolism) ○ over-transfusion related morbidity ○ infections • Blood product use: ○ Red blood cells (RBCs) ○ platelets ○ plasma ○ cryoprecipitate Important: • Time to definitive control of haemorrhage • Patient-reported outcomes (psychological wellbeing).
Study design	RCTs or systematic reviews of RCTs

10.3.3 Clinical evidence

A relevant Cochrane review[118,119] was identified but additional outcomes were specified in this protocol to that reported in the review. The review was checked for included studies. Four studies were included in this review[127,127]; [16,16]; [61,61]; [41,42] . Two papers reported on two parallel RCTs each (blunt and penetrating trauma populations) [16,16]; [61,61]. The included studies are summarised in Table 50 below. Evidence from these studies is summarised in the clinical evidence summary tables below (Table 51 and Table 52). See also the study selection flow chart in Appendix D study evidence tables in Appendix G, forest plots in Appendix J, GRADE tables in Appendix I and excluded studies list in Appendix K.

Summary of included studies:

Table 50: Summary of studies included in the review

Study	Intervention/comparison	Population	Outcomes	Comments
Tranexamic acid versus placebo				
CRASH-2[127,127]	Intervention: Loading dose of 1 g over 10 minutes followed by an infusion of 1 g over 8 hours; n=10,096 Comparison: Placebo	Adult trauma patients with significant haemorrhage (systolic blood pressure	• Morality • MI/Stroke • Pulmonary embolus • Deep vein	Multiple countries

Study	Intervention/comparison	Population	Outcomes	Comments
	n=10,115	<90 mmHg or heart rate >110 beats per minute, or both), or who were considered at risk of significant haemorrhage and who were within 8 hours of injury	thrombosis • Blood components transfused	
Recombinant factor VIIa versus placebo				
Boffard 2005[16,16]	Intervention: 200 micrograms/kg administered after the eighth unit of RBCs. Followed by two 100 micrograms/kg one and three hours after the initial dose. Blunt, n=69; penetrating, n=70 Comparison: Placebo. Blunt, n=74; penetrating, n=64	Patients with severe blunt and/or penetrating trauma. Severe trauma was defined as those suffering from physical injury requiring 6 units of RBCs within 4 hours of admission. Aged 16-65 years	• Mortality • MI/Stroke • Venous thromboembolism • Pulmonary embolism • Thrombotic adverse events • RBCs • Platelets • Fresh frozen plasma (FFP) • Cryoprecipitate • Sepsis	Multiple countries 2 parallel RCTs (blunt or penetrating trauma)
CONTROL[61,61]; [41,42]	Intervention: 200 micrograms/kg administered after the eighth unit of RBCs. Followed by two 100 micrograms/kg one and three hours after the initial dose. Blunt, n=221; penetrating, n=46 Comparison: Placebo. Blunt, n=247; penetrating, n=40	Patients with active haemorrhage caused by trauma who had already received 4 units of RBCs but had not yet completed an eighth unit. Aged 18-70 years	Mortality Cerebral infarct • RBCs • FFP • Cryoprecipitate • Sepsis • Thrombotic adverse events • Venous thromboembolic adverse events • Pulmonary embolism	2 parallel RCTs (blunt or penetrating trauma)

Table 51: Clinical evidence summary: Tranexamic acid versus standard care

Outcome	No. of studies (no of participants)	Imprecision	GRADE rating	Absolute difference	Control event rate (per 1000)	Control event rate for continuous outcomes
Mortality 28 days	1 (n=10115)	No serious imprecision	HIGH	14 fewer per 1000 (from 5 fewer to 24 fewer)	160	-
MI/stroke (follow-up 28 days)	1 (n=10115)	Serious	MODERATE	3 fewer per 1000 (from 5 fewer to 0 more)	2	-
Pulmonary embolus (follow-up 28 days)	1 (n=10115)	Very serious	LOW	0 more per 1000 (from 2 fewer to 3 more)	7	-
Deep vein thrombosis (follow-up 28 days)	1 (n=10115)	Very serious	LOW	0 fewer per 1000 (from 1 fewer to 2 more)	4	-
Blood components transfusion (follow-up 28 days)	1 (n=10115)	No serious imprecision	HIGH	10 fewer per 1000 (from 21 fewer to 5 more)	513	-

Table 52: Clinical evidence summary: Recombinant factor VIIa versus standard care

No of studies	No. of studies (no of participants)	Imprecision	GRADE rating	Absolute difference	Control event rate (per 1000)	Control event rate for continuous outcomes
Mortality (follow-up mean 30 days)	2 (n=819)	Very serious	VERY LOW	10 fewer per 1000 (from 62 fewer to 58 more)	206	-
MI/Stroke (follow-up mean 90 days)	1 (n=560)	Very serious	LOW	1 more per 1000 (from 12 fewer to 45 more)	17	-
Venous thromboembolic AEs - Blunt (follow-up mean 90 days)	1 (n=474)	Serious	MODERATE	34 more per 1000 (from 18 fewer to 120 more)	96	-
Venous thromboembolic AEs - Penetrating (follow-up 90 days)	1 (n=86)	Serious	MODERATE	100 fewer (from 200 fewer to 0 more)	100	-
Pulmonary embolism (follow-up mean 90 days)	1 (n=560)	Very serious	LOW	6 more per 1000 (from 15 fewer to 59 more)	28	-
Thrombotic AEs (follow-up 30-90 days)	2 (n=837)	Very serious	LOW	7 more per 1000 (from 19 fewer to 46 more)	73	-

No of studies	No. of studies (no of participants)	Imprecision	GRADE rating	Absolute difference	Control event rate (per 1000)	Control event rate for continuous outcomes
RBCs	1 (n=554)	Serious	MODERATE	MD 1.45 lower (3.11 lower to 0.21 higher)	-	8
Platelets	1 (n=554)	Serious	MODERATE	MD 0.46 lower (1.58 lower to 0.66 higher)	-	3.3
FFP	1 (n=554)	No serious imprecision	HIGH	MD 2.66 lower (4.02 to 1.29 lower)	-	7.3
Cryoprecipitate	1 (n=554)	Serious	MODERATE	MD 0.49 lower (1.15 lower to 0.18 higher)	-	1.7
Sepsis	1 (n=560)	Very serious	LOW	16 fewer per 1000 (from 48 fewer to 32 more)	115	-

Narrative review

There was no statistically significant difference between tranexamic acid and placebo for the median units of blood product transfused (tranexamic acid 3 [IQR2-6] versus placebo 3 [2-6]; p=0.59) [127,127].

In patients with blunt trauma, recombinant factor VIIa reduced 48 hour RBC requirements by 2.6 units compared with the placebo (p=0.02). There was no difference in patients with penetrating trauma (RBC reduction 1.0 unit; p=0.10) [16,16]. No significant differences were observed in either trauma population with respect to administration of FFP, platelets or cryoprecipitate [16,16].

10.3.4 Economic evidence

Published literature

Four economic evaluations were identified with the relevant comparison and have been included in this review.[93,113,117,122]

One cost effectiveness analysis compared tranexamic acid with placebo and was based on the CRASH-2 trial. [117,119] Three cost utility analyses compared Factor VIIa with placebo and were based on the Boffard trial.

These are summarised in the economic evidence profiles below (Table 53 and Table 54) and the economic evidence tables in Appendix H. [93,113,122]

One economic evaluation relating to this review question was identified but was excluded due to limited applicability and the availability of more applicable evidence.[75,75] This is summarised in Appendix L, with reasons for exclusion given.

See also the economic article selection flow chart in Appendix E.

Table 53: Economic evidence profile: Tranexamic acid versus placebo

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Roberts 2013[117,119] (UK)	Partially applicable[a]	Potentially serious limitations[b]	Markov model estimating the gain in life years of a cohort of trauma patients with haemorrhage who receive tranexamic acid (TXA) compared with placebo. Mortality data from CRASH-2 trial.	£31	0.755 life years	£42 per life year gained	80% probability of being cost-effectiveness at a threshold of £65 per life year gained.[c]

(a) Appropriate population and treatment comparison in a UK NHS setting with discounting of life years (costs not discounted they are incurred in the first year only). However, the main health outcome is life years gained rather than QALYs.

(b) The model does not consider any adverse events of the intervention. Additionally, the only costs included were those of the intervention and non-ICU stay days. Does not use QALYs. Does not include long-term costs, therefore, does not take into account potential future health savings as CRASH-2 trial showed that a higher proportion of patients in TXA group reported no symptoms, therefore, TXA group potentially more likely to survive without disability.

(c) Study only looked at cost effectiveness from a willingness to pay threshold of £0 to £163 per life year gained.

Table 54: Economic evidence profile: Factor VIIa versus placebo

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Morris 2007[93] (UK)	Directly applicable[a]	Potentially serious limitations[b]	Lifetime model based on patient level data from two randomised placebo-controlled phase II trials[16,16]. Data was supplemented with additional UK data to estimate costs and benefits (mortality following the trial duration, and QoL).	£13,243	0.70 QALYs	£18,825 per QALY	52% (61%) probability of being cost effective at a threshold of £20,000 (£30,000).
Rossaint 2007 [121,122] (Germany)	Partially applicable[c]	Potentially serious limitations [d]	Lifetime model based on patient level data from two randomised placebo-controlled phase II trials[16,16]. Data was supplemented	£14,831	0.69	£21,613 per QALY	48% (60%) probability of being cost effective at a threshold of £20,000 (£30,000)[h]

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
			with additional German data to estimate costs and benefits (mortality following the trial duration, and QoL).				
Pohar 2009 [113,113](Canada)	Partially applicable[e]	Potentially serious limitations[f]	Decision tree model based on patient level data from two randomised placebo-controlled phase II trials[16,16]., supplemented by further sources for costing, utilities and in extrapolation technique to estimate long-term survival estimates.	£20,342[g]	1.68 QALYs[g]	£12,108 per QALY[g]	36% (52%) probability of being cost effective at a threshold of £20,000 (£30,000)[h]

Abbreviations: NR, not reported; QoL, quality of life; QALYs, quality-adjusted life years

(a) Appropriate population (blunt severe trauma who are bleeding or at risk of bleeding), intervention and comparison, in a UK setting with costs and benefits discounted at 3.5%.

(b) Adverse events not included (from the interventions and consequences of blood transfusions). The trial that the economic evaluation is based on is stated to be underpowered to detect mortality and comprised of a sample of 143 patients. Potential conflict of interest from the authors and funders (study funded by drug manufacturer). First two authors have received fees from the company and third and fourth authors are employees of the company. No information given on the structure of the model. Extrapolation methods used to predict probability of survival post 30 days are not explained enough to identify whether there may be any issues such as the previous stage in the 3 stage process are having an impact on the probability derived for later stages. Also the populations compared within the TARN database are stated to be older and less severely injured than the patients in the Boffard trial.

(c) Appropriate population (blunt severe trauma who are bleeding or at risk of bleeding), intervention and comparison. Costs from a German third party payer perspective (social insurance). Costs and effects discounted at 5%.

(d) Adverse events not included (from the interventions and consequences of blood transfusions). The trial that the economic evaluation is based on is stated to be underpowered to detect mortality and comprised of a sample of 143 patients. Potential conflict of interest from the authors and funders (original trial funded by drug manufacturer and most of the authors have received fees from Novo Nordisk). Limitations in trial data used to estimate of mortality in first 30 days may carry through in limiting the estimation of longer term mortality, thus limiting the lifetime horizon estimates

(e) Appropriate population (blunt severe trauma who are bleeding or at risk of bleeding), intervention and comparison. Costs from the Canadian perspective. Does not report the discounted QALYs or ICER despite reporting that discounted values were calculated. Benefits discounted at 5%, costs not discounted as only include first year costs.

(f) No adverse events considered. Costs beyond one year were not considered. Not possible to work out a discounted ICER as mean discounted QALYs not reported. So ICER estimated in table above using the undiscounted QALYs reported. The trial that the economic evaluation is based on is stated to be underpowered to detect mortality and comprised of a sample of 143 patients. Estimation of mortality post 30 days used data from the Rossaint paper (please see limitations described in footnote (d) above).

(g) Only undiscounted values reported. Mean discounted QALY not reported, however, confidence interval for discounted incremental QALY reported to be -1.50 to 2.95 ICER presented was calculated by NCGC using undiscounted mean values.

(h) From inspection of cost-effectiveness acceptability curve

The Pohar study does not report discounted QALYs, and therefore, the ICER reported in the table has been estimated based on the undiscounted QALYs reported which further limits the applicability of the findings. The incomplete reporting may also be seen as a limitation, as it is uncertain where the mean incremental discounted QALY may lie within the reported confidence interval of -1.50 to 2.95. The benefit of this paper in terms of usefulness for decision making is that it is funded by the Canadian Government (as it is a Canadian Health Technology Assessment) and is, therefore, likely to be more impartial compared with the Morris and Rossaint papers whose authors have conflicts of interest.

Unit costs

Table 55: Intervention costs

Intervention	Cost	Unit	Source
Factor 7 (recombinant activated factor VII)	£667		Blood products, band 1 (factor VIIa [recombinant]) (mean cost per episode of care where used). NHS reference cost 2012-1013. Health Resource Groups code XD05Z [37]
Tranexamic acid	£1.55	500 mg	BNF [73]
Fibrinogen concentrate	£500	1-mg vial	GDG contact
Prothrombin complex concentrates	£600	1000 international units	Manufacturer website

Dosing is dependent on weight and extent of bleeding, thus costs presented above are per unit and may not be representative of the total dose of intervention needed to treat the patient. Doses will also be re-evaluated post coagulation testing.

The success of the haemostatic agents could also be measured by the amount of blood components used. An estimate of these resources involved can be seen below. Again the units used per patient can vary.

Table 56: Blood product costs

Resource	Cost	Unit	Source
Packed RBCs	£122	1 pack 220-300 ml per pack	NHS Blood and transplant price list 2014/15[105]
FFP	£28	1 pack Mean: 271 ml per pack (240-280 is common)	NHS Blood and transplant price list 2014/15
Platelets	£197	1 adult therapeutic dose	NHS Blood and transplant price list 2014/15
Cryoprecipitate	£181	Pooled cryoprecipitate (5 pack) Mean: 199ml in pooled pack	NHS Blood and transplant price list 2014/15

Note: Unit information sourced from GDG contact and internet.

Note that for children, the costs of FFP and cryoprecipitate are substantially larger due to the Department of Health recommendations for those born after 01.01.96 should use particular types of

FFP and cryoprecipitate that have undergone additional reduction procedures to reduce the risk of viruses. Please see chapter 10.4.4 for more detail on this.

10.3.5 Evidence statements

Clinical

Tranexamic acid

High quality evidence from 1 RCT comprising 10,115 participants showed that tranexamic acid was clinically effective compared with placebo in terms of mortality, with no imprecision.

Moderate quality evidence from 1 RCT comprising 10,115 participants showed that no difference in clinical effectiveness between tranexamic acid and placebo in terms of MI/stroke, with serious imprecision.

Low quality evidence from 1 RCT comprising 10,115 participants showed that no difference in clinical harm between tranexamic acid and placebo in terms of pulmonary embolism or deep vein thrombosis, with very serious imprecision.

High quality evidence from 1 RCT comprising 10,115 participants showed that no difference in clinical effectiveness between tranexamic acid and placebo in terms of blood components transfused, with no serious imprecision.

Recombinant factor VIIa

Very low quality evidence from 2 RCTs comprising 819 participants showed that recombinant factor VIIa was clinically effective compared with placebo in terms of mortality, with very serious imprecision.

Low quality evidence from 1 RCT comprising 560 participants showed there was no difference in clinical effectiveness between recombinant factor VIIa and placebo in terms of MI/stroke, with very serious imprecision.

Moderate quality evidence from 1 RCT comprising 474 participants (blunt trauma) showed there was no difference in clinical effectiveness between recombinant factor VIIa and placebo in terms of venous thromboembolism, with serious imprecision.

Moderate quality evidence from 1 RCT comprising 86 participants (penetrating trauma) showed that recombinant factor VIIa was clinically harmful compared with placebo in terms of venous thromboembolism, with serious imprecision.

Low quality evidence from 1 RCT comprising 560 participants showed there was no difference in clinical harm between recombinant factor VIIa and placebo in terms of pulmonary embolism, with very serious imprecision.

Low quality evidence from 1 RCT comprising 837 participants showed there was no difference in clinical harm between recombinant factor VIIa and placebo in terms of thrombotic adverse events, with very serious imprecision.

Moderate quality evidence from 1 RCTs comprising 554 participants showed that recombinant factor VIIa was associated with clinically important reduction compared with placebo in terms of RBCs use, with serious imprecision.

Moderate quality evidence from 1 RCT comprising 554 participants showed that there was no clinical difference between recombinant factor VIIa and placebo in terms of platelets and cryoprecipitate use, with serious imprecision.

High quality evidence from 1 RCT comprising 554 participants showed that recombinant factor VIIa was associated with clinically important reduction compared with placebo in terms of FFP use, with no serious imprecision.

Low quality evidence from 1 RCT comprising 560 participants showed there was no difference in clinical effectiveness between recombinant factor VIIa and placebo in terms of sepsis, with very serious imprecision.

Economic

One cost effectiveness analysis found that tranexamic acid had a cost per life year gained of £42 compared with placebo in bleeding patients. This study was assessed as partially applicable with potentially serious limitations.

One cost utility analysis found that recombinant activated factor VII was cost effective compared with placebo at a threshold of £20,000 (ICER of £18,825 per QALY) in bleeding patients. This study was assessed as directly applicable with potentially serious limitations.

One cost utility analysis found that recombinant activated factor VII was not cost effective compared with placebo at a threshold of £20,000 (ICER of £21,613 per QALY) in bleeding patients. This study was assessed as partially applicable with potentially serious limitations.

One cost utility study found that recombinant activated factor VII was more costly than placebo (£20,342 more per patient) with incremental QALYs calculated but not reported. This study was assessed as partially applicable with potentially serious limitations.

10.3.6 Recommendations and link to evidence

Recommendations	**21. Use intravenous tranexamic acid[a] as soon as possible in patients with major trauma and active or suspected active bleeding.** **22. Do not use intravenous tranexamic acid[a] more than 3 hours after injury in patients with major trauma unless there is evidence of hyperfibrinolysis.**
Relative values of different outcomes	Critical outcomes for decision making were mortality, health related quality of life, adverse events (venous thromboembolism, thrombotic events [MI/stroke, pulmonary embolism], over-transfusion-related morbidity and infections) and blood product. Important outcomes were time to definitive control of haemorrhage and patient-reported outcomes. For tranexamic acid there was no clinical evidence for mortality (24 hours, 12 months), health-related quality of life, venous thromboembolism, over transfusion-related morbidity, infections, blood product use (RBCs, platelets, plasma, cryoprecipitate), time to definitive control of haemorrhage and patient-reported outcomes. For recombinant factor VIIa there was no clinical evidence for mortality (24 hours, 12 months), health-related quality of life,

a At the time of publication (February 2016), tranexamic acid did not have a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

	over-transfusion-related morbidity, time to definitive control of haemorrhage and patient-reported outcomes
Trade-off between clinical benefits and harms	Tranexamic acid resulted in a clinically important reduction in mortality (high quality) compared with placebo. The GDG noted that the control event rate was lower than in the major trauma population that could potentially be treated with tranexamic acid and the mortality benefits of the drug would be higher than that reported in the trial. There was no data on quality of life. There were no clinically important harms reported in the trial. A post-hoc sub-group analysis (not reported here) suggested clinical harm if tranexamic acid is administered after three hours. The GDG noted that empiric administration of tranexamic acid should be avoided if the patient presented more than three hours after injury. However, patients could still benefit from tranexamic acid after three hours if there was diagnostic evidence of continued hyperfibrinolysis. The GDG did not recommend factor VIIa because, although there was an observed reduction in mortality, the confidence intervals were consistent with both benefit and harm (very low quality). There were clinically more venous thromboembolic events in the patient with blunt trauma. There was a reduction in RBCs (serious imprecision) and FFP associated with recombinant factor VIIa. The GDG felt that the potential for increased thromboembolism reported in non-trauma populations without obvious improvement in survival meant that recombinant factor VIIa could not be recommended.
Trade-off between net health benefits and resource use	One economic evaluation comparing tranexamic acid with standard care, and three economic evaluations comparing recombinant factor VIIa with standard care were identified. For tranexamic acid, the outcome of the study was cost per life year gained rather than cost per QALY, and as such, cannot be assessed using the £20,000 cost per QALY decision rule. This paper was assessed as partially applicable with potentially serious limitations. The economic evidence identified showed that particularly for recombinant factor VIIa, cost effectiveness is uncertain, as two studies identified comparing recombinant factor VIIa with placebo generally found that the ICER is just as likely to be under £20,000 as over £20,000[93,122] (these papers were assessed as being directly applicable and partially applicable respectively, and both had potentially serious limitations), and one study suggested that it was less likely to be cost effective [113,113] (this paper was assessed as partially applicable with potentially serious limitations). Tranexamic acid has a substantially lower cost compared with factor VIIa, and the clinical evidence showed a higher risk of adverse events for factor VIIa. The use of tranexamic acid is common practice; therefore, a recommendation in favour of tranexamic acid is not expected to have a large cost impact.
Quality of evidence	One RCT was identified comparing tranexamic acid with standard care. The RCT was a very large multicentre trial with low risk of bias. Outcomes were graded from high to low quality. Three studies reporting on two RCTs (2x2 parallel RCTs in the blunt and penetrating trauma populations) were identified comparing recombinant factor VIIa with standard care. One RCT was at high risk of bias (Boffard) and one at low risk of bias (Hauser). Outcomes were graded from high to low quality. **Economic evidence** The health economic evidence was based on the CRASH-2 trial in the case of

	evaluating TXA [117,119] and the Boffard trial [16,16] in the case of recombinant factor VIIa. As such, the evaluations suffer from the same limitations of the evidence as outlined above. Furthermore, two of the studies on recombinant factor VIIa had conflict of interest [93,122] and no study considered adverse events. Most studies were graded as partially applicable (except Morris 2007 which was directly applicable) and with potentially serious limitations.
Other considerations	The CRASH-2 trial was in adults, but the GDG felt that the results could be extrapolated to children. Tranexamic acid has been used in non-traumatic paediatric populations with a low incidence of adverse events. The GDG noted that the evidence on tranexamic acid was in patients with or at risk of significant haemorrhage and emphasised that the importance of pre-hospital personnel recognising the signs of active bleeding or people who at risk of active bleeding.

10.4 Anticoagulation reversal

10.4.1 Introduction

Anticoagulant medicines are most commonly prescribed for people who are at elevated risk of developing blood clots in veins or arteries, and work to prevent this. People who experience a traumatic injury are at increased risk of getting coagulopathy, a condition in which the blood's ability to clot is impaired. When people on pre-existing anticoagulant medication experience a traumatic injury their coagulopathy is exacerbated by the medication and chance of dying increased. Consequently, mortality can be reduced by reversing the effects of any pre-existing anticoagulant medication. There are varying mechanisms by which anticoagulants work and each class of drug requires its own reversal regimen. This clinical question focuses on reversal of four anticoagulant classes: coumarins and phenindione, direct thrombin inhibitors, anti-platelet agents and low molecular weight heparins. Warfarin, the most prescribed anticoagulant, sits within the coumarin and phenindione class.

10.4.2 Review question: What is the most clinically and cost effective regimen for reversal of pre-existing therapeutic anticoagulation (laboratory effect) in major trauma?

For full details see review protocol in Appendix C.

Table 57: PICO characteristics of review question

Population	Children, young people and adults who have experienced a traumatic incident and who are on pre-existing therapeutic anticoagulation therapy.

Intervention(s)	• Reversal agents
	  ○ fibrinogen concentrate
	  ○ cryoprecipitate
	  ○ platelets
	• Vitamin K (phytonadione)
	• Fresh frozen plasma (FFP)
	• Prothrombin complex concentrates (PCCs)
	• Recombinant factor VIIa

Comparison(s)	To each other
Outcomes	Critical: • Mortality at 24 hours, 30 days/1month and 12 months • Health-related quality of life

	• Adverse events:
	  ○ stroke
	  ○ myocardial infarction (MI)
	  ○ thromboembolism (PA and venous)
	• Reversal of anti-coagulation as measured by laboratory assessment
	• Neurological outcome (brain injured patients)
	• Blood product use
	
	Important:
	• Patient reported outcomes (pain/discomfort, return to normal activities, psychological wellbeing)

Study design	RCTs or systematic reviews of RCTs

10.4.3 Clinical evidence

No relevant clinical studies were identified.

10.4.4 Economic evidence

Published literature

One economic evaluation was identified with the relevant comparison and has been included in this review. [57,57] This is summarised in the economic evidence profile below (Table 58) and the economic evidence tables in Appendix H.

See also the economic article selection flow chart in Appendix E.

Table 58: Economic evidence profile: PCC versus FFP

Study	Applicability	Limitations	Other comments	Incremental cost	Incremental effects	Cost effectiveness	Uncertainty
Guest 2010[57,57] (UK)	Partially applicable[a]	Potentially/ very serious limitations[b]	Probabilistic decision tree with a lifetime horizon comparing PCCs with FFP for three different types of haemorrhage: intracranial, gastrointestinal and retroperitoneal in patients receiving anti-coagulant therapy using warfarin.[c]	Intracranial £3,246 Gastrointestinal £401 Retroperitoneal £534	Intracranial 2.1 QALYs Gastrointestinal 0.14 QALYs Retroperitoneal 0.71 QALYs	Intracranial £1,600 per QALY Gastrointestinal £2,900 per QALY Retroperitoneal £800 per QALY	PSA with 10,000 iterations was performed, with variation in probabilities, utilities, unit costs and resource use in the model. The probability of PCC being cost-effective was ≥ 90% at a threshold of £10,000 per QALY for all types of haemorrhage. Deterministic sensitivity analyses were also performed. All sensitivities for all types of haemorrhage resulted in a cost per QALY of ≤ £16,000 for treatment with PCC.

(a) Appropriate intervention and comparator assessed from a UK NHS perspective with health outcomes measured in quality adjusted life-years using utilities from two systematic reviews. However, the population is not specific to trauma and no discounting is reported for costs or outcomes. Time horizon uncertain.

(b) Resource use based on assumptions from a group of doctors. Mortality for gastrointestinal and retroperitoneal haemorrhages for PCC based on assumptions. Methodology is not always clear (for example, with regards to the time horizon). Mortality from the treatments taken from various sources (RCT's and observational studies) with varying, but mostly small, sample sizes. No discounting reported. A probabilistic sensitivity analysis used an arbitrary standard deviation of 10% in the distribution of probabilities. Potential conflict of interest as funded by manufacturer of PCC

(c) Dosages: FFP – 3 units plus 10 mg vitamin K; PCC– 30 units/kg plus 5 mg vitamin K.

This study was assessed as partially applicable due to the population not being specific to trauma patients and no discounting being reported. There may be a difference in mortality rates for haemorrhage in a trauma population due to the severity of the haemorrhage, which could change the conclusions of cost-effectiveness. The intracranial bleeding population was felt to be most similar to a trauma haemorrhage population.

A lack of discounting would overestimate the cost of stroke rehabilitation only, since all other costs were assumed to occur in the first year following haemorrhage. However, all QALYs beyond the first year will be overestimated without discounting, which could also change the conclusions about cost-effectiveness. Additionally, as trauma patients are at risk of coagulopathy, this in combination with the anticoagulants increases mortality further, thus the interventions ability to be able to reverse this may have a different level of success, lead to different mortality rates and different resource use to that of the population considered in the paper. Therefore, all these factors could impact the cost effectiveness and reduce the applicability of this paper to the population of this clinical question.

This study has been assessed as having potentially serious limitations due to the lack of evidence for resource use, the small sample sizes for mortality rate estimates and the lack of weighting to calculate the mean mortality rate as well as the assumptions made where evidence is unavailable. Resource use and probabilities of successful reversal were elicited from a group of consultant physicians and so are based on assumptions. There is, therefore, a large amount of uncertainty around these estimates. The uncertainty around mortality rate estimates following PCC treatment has been taken into account by sensitivity analyses; however, the range of values used for gastrointestinal and retroperitoneal haemorrhage, where values were assumed, may not reflect the true uncertainty in mortality. For the mortality estimates following FFP treatment, sensitivity analyses were not performed and there is uncertainty, especially for gastrointestinal haemorrhage, due to the small number of studies found. For the probability distributions in the probabilistic sensitivity analysis, an arbitrary standard deviation of 10% was used for probabilities, which may not reflect the true magnitude of the uncertainty given that these probabilities were based on assumptions. NHS costs were only included in the first year because the authors thought that the costs incurred after this time would be equally likely for both treatments and therefore, the differences would be negligible. However, this does not consider the difference in the number of survivors following treatment, which could cause a greater difference in costs. These limitations could change the conclusion of cost-effectiveness and therefore, must be judged as having potentially serious limitations.

Unit costs

Table 59: Cost of interventions and resources

Resource	Cost	Unit	Source
Fibrinogen concentrate	£500	1-mg vial	GDG contact
Cryoprecipitate	£181	Pooled cryoprecipitate (5 pack) Mean: 199 ml per pooled pack	NHS Blood and transplant price list 2014/15[105]
Platelets	£197	1 adult therapeutic dose	NHS Blood and transplant price list 2014/15
Vitamin K	£0.38	10 mg vial	BNF [73]
FFP	£28	1 pack Mean: 271 ml per pack (240-280 is common)	NHS Blood and transplant price list 2014/15

Resource	Cost	Unit	Source
PCC	£600	1000 International Units	Manufacturer website
Factor VIIa	£667		Blood Products, Band 1 (Factor VIIa (recombinant)) (Mean cost per episode of care where used). NHS reference cost 2012-2013. Health Resource Groups code XD05Z [37]
Additional blood product resources			
Red blood cells	£122	1 pack 220-300 ml per pack	NHS Blood and transplant price list 2014/15 [105]

Source: Unit information sourced from GDG contact and internet.

The costs expressed above are per unit. Dosing can vary depending on, for example; the weight of the patient, if the patient is severely bleeding they may need more products. Therefore, the costs above may not be indicative of the actual volume of a particular product needed.

As well as the costs of the products themselves, additional costs would be involved in the handling and administration of the products, which would apply each time a product is issued, and could vary depending on the type of product (see more in section 10.8.4).

For children, Department of Health recommendations [39] state that children should use particular types of FFP and cryoprecipitate that have undergone additional reduction procedures to reduce the risk of viruses. Any patient born after 01.01.1996 should receive methylene blue (MB)-treated FFP. The MB treatment is a viral inactivation phase and the plasma is sourced abroad. Cryoprecipitate also follows the same rule as FFP for children. An alternative to MB-treated FFP is Octaplas; a solvent detergent treated plasma that undergoes a prion reduction step. Octaplas can be used on adults and children.

MB-treated FFP for children is over 6 times more expensive than standard FPP, and pooled MB-treated cryoprecipitate is over £1000 as the plasma is non-UK sourced, as per the Department of Health recommendation (plasma from outside the UK is known to have lower risk of transfusion transmitted Creutzfeldt Jakob disease [vCJD]). However, the supply of these products is limited due to the difficulty in sourcing sufficient plasma from countries with a lower prevalence of vCJD as they are very few in number and tend not to have available capacity to supply the UK.

The costs of these products can be seen below.

Table 60: Intervention costs for children and young people

Resource	Cost	Unit	Source
FFP			
Paediatric MBFFP (Non-UK Sourced)	£178	1 pack Mean: 226 ml per bag Range: 200 -320 ml	NHS Blood and transplant price list 2014/15 [105]
Octaplas LG	£64	1 pack 200 ml	GDG contact
Cryoprecipitate			
MB cryoprecipitate-pooled (non-UK sourced)	£1,080	Pooled cryoprecipitate (6 pack) Mean: 275 ml per pooled pack	NHS Blood and transplant price list 2014/15

10.4.5 Evidence statements

Clinical

No clinical evidence identified

Economic

One cost-utility analysis found that PCC was cost-effective compared with FFP for emergency warfarin reversal (ICER: £3000 or less per QALY gained for each type of haemorrhage). The paper was assessed as partially applicable with potentially serious limitations.

10.4.6 Recommendations and link to evidence

Recommendations	**23. Rapidly reverse anticoagulation in patients who have major trauma with haemorrhage.** **24. Hospital trusts that admit patients with major trauma should have a protocol for the rapid identification of patients who are taking anticoagulants and the reversal of anticoagulation agents.** **25. Use prothrombin complex concentrate immediately in adults (16 or over) with major trauma who have active bleeding and need emergency reversal of a vitamin K antagonist.** **26. Do not use plasma to reverse a vitamin K antagonist in patients with major trauma.** **27. Consult a haematologist immediately for advice on adults (16 or over) who have active bleeding and need reversal of any anticoagulant agent other than a vitamin K antagonist.** **28. Consult a haematologist immediately for advice on children (under 16s) with major trauma who have active bleeding and may need reversal of any anticoagulant agent.** **29. Do not reverse anticoagulation in patients who do not have active or suspected bleeding.**
Relative values of different outcomes	The critical outcomes for decision making were mortality, health-related quality of life, stroke, MI, thromboembolism, reversal of anticoagulation, neurological outcome and blood product use. Important outcomes were patient-reported outcomes, such as pain/discomfort, return to normal activities and psychological wellbeing.
Trade-off between clinical benefits and harms	No clinical evidence was found to evaluate the trade-off between clinical benefits and harms of reversal regimens for people on pre-existing therapeutic anticoagulant therapy. The GDG stated that in patients with haemorrhage, effective and immediate reversal of anticoagulant medication is essential. Delays in reversal are associated with an increase in poor outcomes. As such, the GDG agreed it was imperative that anticoagulant reversal is prioritised in actively bleeding patients without necessarily waiting for laboratory results. To ensure this is standard practice in hospitals receiving trauma patients, the GDG considered it important that all hospitals have a policy for the rapid identification and reversal of oral anticoagulant agents.

	The GDG recommended PCC because in their opinion it provides rapid effective specific reversal of a vitamin K antagonist compared with other reversal therapies. It is better than plasma because it is comprised of pooled plasma products that have higher levels of coagulation factors and therefore leads to the much more rapid normalisation of INR. PCCs also have the advantage that, in contrast to plasma, they may be held in emergency departments; their volume of infusion is small and not associated with volume-associated sequelae from fluid overload. Furthermore, faster normalisation of INR is possible with PCCs as due to faster preparation (no thawing required) and faster infusion of the product. The GDG could not recommend PCC for reversal of other causes of anticoagulation in trauma patients as its safety and efficacy is less known. Reversal of anticoagulation therapy can result in significant adverse effects; including stroke, MI and thromboembolism, and it is important it is not used in patients that are not actively bleeding.
Trade-off between net health benefits and resource use	One economic evaluation was identified comparing PCC with FFP (Guest 2010). The study was a decision tree model capturing the success of reversal of warfarin for three types of haemorrhage (intracranial, gastrointestinal and retroperitoneal), and the probability of requiring an additional warfarin reversal treatment when the initial attempt is unsuccessful. The population was not major trauma patients, instead they were bleeding because of the therapeutic over-anticoagulation (warfarin). The study showed that PCC was cost effective in all three patient groups. Limitations of the study included a conflict of interest (the study is funded by the manufacturers of PCC), resource use and some mortality based on assumptions, and methodology not always clear. This study was rated as partially applicable with very serious limitations. Intracranial haemorrhage was felt to be the most similar population to a trauma population, however, the resource use would be significantly different, such as admission longer than 2 days (most likely weeks), and more than 5% would require an operation. This may have an impact on the conclusions as for those that survive the reversal, the resource use will then be more costly, however, this would be weighed up against the QALYs that are being accrued from those patients still alive. The effect of this on the overall cost effectiveness is therefore uncertain. Initially, the study was presented to the GDG as having potentially serious/very serious limitations. The group felt that, although the interventions were relevant, it was discussed how the population groups included in the paper were not directly applicable to trauma, with the most applicable being intracranial haemorrhage as discussed above. This along with the limitations meant it was downgraded to very serious limitations. The GDG also agreed that the conclusions of the study were feasible and in line with what they expected. Costs of the interventions were also presented to the GDG and it was highlighted that notably PCC is expensive, with a typical dose (30 units/kg for a 75 kg person – considered to be a relatively high dose) costing around £1,350. Factor VIIa is also expensive at several hundred pounds, whereas FFP is not as expensive. FFP is a blood product and has to be de-thawed which adds time, and issues of wastage and time spent cross-matching to blood arise (to note; for children, FFP is more expensive because a special type has to be used that goes through a reduction step to reduce

	viruses). Whereas, PCC can be administered immediately and does not have the timing issues and risks associated with FFP because it does not need to be matched to blood type. Note that, as well as the costs of the products, there will also be administration costs related to handling, and laboratory costs. Although there is a large population that are on anticoagulants, notably a proportion of the elderly, the number of patients who have had a trauma and are on anticoagulants is likely to be small. The GDG acknowledged the limitations of the included study and based their recommendation of PCC as opposed to FFP on other considerations such as its rapid effect and fewer complications. Since there is less certainty on its effectiveness in other populations, this intervention was recommended only for people with major trauma who have active bleeding and need emergency reversal of a vitamin K antagonist. PCC is used in current practice to reverse anticoagulation of warfarin; therefore, this recommendation is not expected to have a cost impact.
Quality of evidence	No relevant clinical studies were identified. **Economic evidence** The health economic evidence was based on the single paper identified. The population was an indirect population of which intracranial haemorrhage was felt to be the most applicable to a trauma population. The study had many limitations, such as a conflict of interest, many assumptions were made and no adverse events considered. It was rated as partially applicable with very serious limitations.
Other considerations	The GDG stated that there are currently no clear strategies for reversing novel oral anticoagulants (including apixaban, dabigatran etexilate and rivaroxaban) or direct thrombin inhibitors and these patients should be discussed immediately with a haematologist. There was no clinical evidence evaluating treatments for reversing anticoagulants in children and the GDG discussed the possibility of duplicating the advice for adults. The GDG agreed that while treatment for children could be the same as for adults because of the very small numbers of involved and the potential to do harm (for example, children with replacement heart valves), it was important that any treatment is discussed immediately with a consultant haematologist.

10.5 Haemorrhage shock prediction/risk tools

10.5.1 Introduction

Haemorrhagic shock is associated with high mortality. The early detection of haemorrhagic shock and patients requiring massive transfusion by the application of a risk tool could substantially improve patient outcomes.

10.5.2 Review question: What is the most accurate risk tool to predict the need for massive transfusion in patients with major trauma (pre-hospital and hospital)?

For full details see review protocol in Appendix C.

Table 61: PICO characteristics of review question

Population	Children, young people and adults who have experienced a traumatic incident.

Target condition	Haemorrhagic shock
Index test(s)/comparator(s)	Pre-hospital and hospital: • Clinical risk scores • ABC score • TASH score • PWH score • McLaughlin score • Emergency transfusion score • Shock Index • Shock Classification (part of ATLS protocols)
Reference standard(s)	Massive transfusion
Statistical measure/outcomes	Diagnostic accuracy Outcomes from false positive/false negative results, adverse effects
Study design	Observational studies

10.5.3 Clinical evidence

Nine studies were included in the review[18,18]; [22,22]; [26,27]; [77,77]; [86,86]; [90,92]; [109,109]; [114,114]; [137,137] these are summarised in Table 62 below. Evidence from these studies is summarised in the GRADE clinical evidence profile below. See also the study selection flow chart in Appendix D study evidence tables in Appendix G, forest plots in Appendix J, GRADE tables in Appendix I and excluded studies list in Appendix K.

All of the studies were retrospective cohort studies in the adult hospital population. Two of the studies were in military populations[22,22]; [86,86] with the rest of the studies in the civilian population.

In the Brockamp study[18,18] in order to compare the clinical risk tools, the area under the receiver operating characteristic curves (AUCs) were calculated and the cut-off (threshold) with the best relationship between sensitivity and specificity was used to recalculate sensitivity and specificity for each tools.

10.5.3.1 Summary of included studies

Table 62: Summary of studies included in the review

Clinical risk tool	Study	Prevalence% (no. of patients undergoing massive transfusion)	Risk predicted	Setting	Comments
ABC Penetrating mechanism, systolic blood pressure ≤ 90 mmHg on ER arrival, heart rate ≥120 bpm on emergency department arrival and positive focused assessment sonography for	Brockamp 2012[18,18] Cotton 2010[26,27] Krumrei 2012[77,77] Mitra[90,92] Poon 2012[114,114]	Brockamp – 5.6 Cotton – 14-15 Krumrei – 10 Mitra – 17.2 Poon – 2.6	Brockamp: ≥10 units packed red blood cells between arrival to the emergency room and the intensive care unit. Cotton, Krumrei, Poon: 10 units or more of red blood cells in the first 24 hours Mitra: ≥5 units of packed red blood	Civilian	Pooled meta-analysis except Brockamp reported separately threshold ≥0.5

Clinical risk tool	Study	Prevalence% (no. of patients undergoing massive transfusion)	Risk predicted	Setting	Comments
trauma (FAST) examination. Threshold ≥ 2.			cells in the first 4 hours since presentation		
Larson score Heart rate, systolic blood pressure, haemoglobin and base deficit. Threshold ≥ 1.5	Brockamp 2012[18,18]	5.6	As above	Military	
McLaughlin Heart rate > 105 bpm, Systolic blood pressure <110 mmHg, pH <7.25, haematocrit <32% Equation: log (p/[1-p]) = 1.576 + (0.825 x SBP) + (0.826 x HE) + (1.044 x Hct) + (0.462 x pH), where the variables have the value of 0 or 1 based on whether or not the value is classed as predictive	Krumrei 2012[77,77] McLaughlin 2008[86,86] Nunez 2009[109,109]	Krumrei – 10 McLaughlin Not reported Nunez – 12.6	Krumrei as above McLaughlin - ≥10 units of blood in the initial 24 hours after admission Nunez - Ten units of packed red blood cell transfusion within 24 hours	Civilian (Krumrei and Nunez) Military (McLaughlin)	Nunez 2x2 table could not be calculated McLaughlin (threshold not specified)
Modified Field Triage Score GCS (total), systolic arterial pressure, haemoglobin	Cancio 2008[22,22]	Not reported	Ten units of packed red blood cell transfusion within 24 hours	Military	Threshold not specified 2x2 table could not be calculated
Prince of Wales (PWH)/Rainer score Heart rate ≥120 bpm, systolic blood pressure ≤90 mmHg, Glasgow Coma	Brockamp 2012[18,18] Mitra 2012[90,92] Poon 2012[114,114]	Brockamp – 5.6 Mitra – 17.2 Poon – 2.6	As above	Civilian	Brockamp threshold ≥2.5

Clinical risk tool	Study	Prevalence% (no. of patients undergoing massive transfusion)	Risk predicted	Setting	Comments
Scale ≤8, displaced pelvic fracture, CT scan or FAST positive for fluid, base deficit >5 mmol/litre, haemoglobin ≤7 g/dl, and haemoglobin 7.1 to 10.0 g/dl. Threshold ≥6					
Revised Trauma Score (RTS) GCS, SBP and Respiration rate RTS=0.9368*GCS_{code}+ 0.7326*SBP_{code} + 0.2908*RR_{code}	Cancio 2008[22,22]	Not reported	As above	Military	Threshold not specified
Schreiber score (derived from military) Haemoglobin, INR and penetrating mechanism of injury Threshold ≥0.5	Brockamp 2012[18,18]	5.6	As above	Civilian	
Trauma-associated severe haemorrhage (TASH) Weighted variables: Systolic blood pressure, sex, haemoglobin, FAST, heart rate, base excess, and extremity or pelvic fractures. Range 0 to 28. Threshold ≥16 or 18. The TASH score in	Krumrei 2012[77,77] Mitra [90,92] Nunez 2009[109,109] Poon 2012[114,114]	Krumrei - 10 Mitra – 17.2 Nunez – 12.6 Poon – 2.6	As above	Civilian	Original TASH Krumrei used a cut-off of 80% risk of massive transfusion Nunez threshold not specified Modified TASH Poon threshold 16 Mitra threshold of 18

Clinical risk tool	Study	Prevalence% (no. of patients undergoing massive transfusion)	Risk predicted	Setting	Comments
transformed into a probability for massive transfusion using the following logistic function: (p= 1/(1 + exp (4.9-0.3*TASH))) Modified TASH (p= 1/(1 + exp (5.4-0.3*TASH)))					
Vandromme score Blood lactate ≥5 mmol/litre, heart rate >105 bpm, INR 1.5, haemoglobin ≤11 g/dl and systolic blood pressure <110 mmHg. Threshold ≥3	Brockamp 2012[18,18] Vandromme 2011[137,137]	Brockamp – 5.6 Vandromme not reported	Vandromme - 10 units or more of packed red blood cells within 24 hours of admission	Civilian	Brockamp threshold ≥1.5

Table 63: Diagnostic evidence profile: Haemorrhagic shock risk prediction

Clinical risk tool and threshold (if applicable)	No. of studies	n	Risk of bias	Inconsistency	Indirectness	Imprecision	Pooled sensitivity/ median (95%CI)	Pooled specificity/ median (95CI)	Area under curve (range)	Quality
ABC										
ABC	4[a]	3553	Serious[b]	Very serious inconsistency[3]	No indirectness	Very serious imprecision[d]	0.72 (0.45 to 0.91)	0.88 (0.76 to 0.95)	-	VERY LOW
ABC threshold ≥0.5	1	5147	Very serious[b]	No inconsistency	No indirectness	Serious imprecision	0.76 (0.71 to 0.81)	70 (69 to 72)	0.76 (0.73 to 0.79)	VERY LOW
Larson										
Larson	1	5147	Very serious[b]	No inconsistency	No indirectness	Serious imprecision	71 (65 to 76)	0.80 (0.79 to 0.81)	0.82 (0.80 to 0.85)	VERY LOW
McLaughlin										
McLaughlin	1	372	Serious[b]	No inconsistency	No indirectness	Very serious imprecision[d]	0.16 (0.6 to 0.31)	0.98 (0.96 to 0.99)	-	VERY LOW
	1	396	Serious[b]	No inconsistency	No indirectness	Imprecision could not be assessed[d]	0.59	0.77	0.75	LOW
	1	596	Serious[b]	No inconsistency	No indirectness	Imprecision could not be assessed[d]	-	-	0.76	LOW
Modified Field Triage Score										
Modified Field Triage Score	1	536	Very serious[b]	No inconsistency	No indirectness	Serious imprecision[c]	-	-	0.62 (0.57 to 0.67)	VERY LOW
PWH/Rainer										
PWH/ Rainer	2	2164	Very serious[b]	No inconsistency	No indirectness	Very serious imprecision[d]	0.37 (0.30 to 0.44) 0.33 (0.17 to 0.54)	0.97 (0.96 to 0.98) 0.98 (0.97 to 0.99)	-	VERY LOW
PWH/Rainer threshold ≥	1	5147	Very	No	No	No	0.81 (0.76 to	0.78 (0.77	0.86 (0.84 to	LOW

Clinical risk tool and threshold (if applicable)	No. of studies	n	Risk of bias	Inconsistency	Indirectness	Imprecision	Pooled sensitivity/ median (95%CI)	Pooled specificity/ median (95CI)	Area under curve (range)	Quality
2.5			serious[b]	inconsistency	indirectness	imprecision	0.85)	to 0.79)	0.99)	
RTS										
RTS	1	536	Serious[b]	No inconsistency	No indirectness	No imprecision	-	-	0.64 (0.59 to 0.69)	MODERATE
Schreiber										
Schreiber	1	5147	Very serious[b]	No inconsistency	No indirectness	No imprecision	0.86 (0.81 to 0.90)	0.62 (0.61 to 0.63)	-	LOW
TASH										
TASH 80% threshold	1	382	Serious[b]	No inconsistency	No indirectness	Very serious imprecision[d]	0.26 (0.13 to 0.43)	1.0 (0.98 to 1.0)	-	VERY LOW
TASH threshold not specified	1	596	Serious[b]	No inconsistency	No indirectness	Imprecision could not be assessed[d]	-	-	84	LOW
Modified TASH threshold 16	1	1030	Serious[b]	No inconsistency	No indirectness	Very serious imprecision[d]	0.26 (0.11 to 0.46)	0.99 (0.98 to 1.0)	-	VERY LOW
Modified TASH threshold 18	1	1134	Very serious[b]	No inconsistency	No indirectness	Serious imprecision[d]	0.25 (0.19 to 0.32)	1.0 (0.99 to 1.0)	-	VERY LOW
Vandromme										
Vandromme threshold ≥ 1.5	1	5147	Very serious[b]	No inconsistency	No indirectness	No imprecision	0.79 (0.74 to 0.83)	0.76 (0.75 to 0.77)	84 (82 to 86)	MODERATE
Vandromme threshold ≥ 3	1	208	Serious[b]	No inconsistency	No indirectness	Imprecision could not be assessed[d]	0.61	0.96	-	LOW

Note: GRADE was conducted with emphasis on test sensitivity as this was the primary outcome for decision making

(a) There were n=6 data sets.

(b) Studies were downgraded by one increment for limitations in one risk of bias domain or by two increments for risk of bias in two or more domains. Studies were assessed using the QUADAS –II criteria. Risk of bias domains: patient selection, index test, reference standard, flow and timing.

(c) Inconsistency was assessed by inspection of the sensitivity/specificity RevMan 5 plots. Difference in prevalence rates may account for any observed inconsistency.

(d) The judgement of precision for sensitivity and specificity separately was based on visual inspection of the confidence region in the diagnostic meta-analysis, where diagnostic meta-analysis has not been conducted imprecision was assessed using the confidence interval of the median sensitivity value. For studies with only AUC data precision was based on the corresponding 95% CI. Downgrading by one increment was applied for confidence intervals 10-20% or by two increments for confidence intervals > 20%. If no variance data was available (imprecision could not be assessed) the studies were downgraded by one increment.

10.5.4 Economic evidence

Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow chart in Appendix E.

10.5.5 Evidence statements

Clinical

ABC

When diagnostic meta-analysis was conducted on Very low quality evidence from 4 studies (6 validation data sets) with 3553 participants pooled sensitivity (95% CI) and specificity (95% CI) of the ABC were 0.72 (0.45 to 0.91) and 0.88 (0.76 to 0.95), respectively.

Very low quality evidence from 1 study of 5147 participants showed that the sensitivity (95% CI), specificity (95%CI) and area under curve (95% CI) of the ABC score with a threshold of 0.5 or more was 0.76 (0.71 to 0.81), 0.70 (0.69 to 0.72) and 0.76 (0.73 to 0.79), respectively.

Larson

Very low quality evidence from 1 study with 5147 participants showed the sensitivity (95% CI), specificity (95% CI) and area under curve (95% CI)of the Larson score was 0.71 (0.65 to 0.76), 0.80 (0.79 to 0.81) and 0.82 (0.80 to 0.85), respectively.

McLaughlin

Very low quality evidence from one study with 372 participants showed the sensitivity (95% CI) and specificity (95% CI) of the McLaughlin score was 0.16 (0.6 to 0.31) and 0.98 (0.96 to 0 99).

Low quality evidence from one study with 396 participants showed the sensitivity, specificity and area under curve of the McLaughlin score was 0.59, 0.77 and 0.75.

Low quality evidence from one study of 596 participants showed that the area under curve of the McLaughlin score was 0.76.

Modified Field Triage Score

Very low quality evidence from 1 study of 536 participants showed that the area under curve (95% CI) of the modified Triage Score was 0.62 (0.57 to 0.67).

Prince of Wales/Rainer

Very low quality evidence from 2 studies of 2164 participants showed that the sensitivity (95% CI) Prince of Wales/Rainer score was 0.37 (0.30 to 0.44) and 0.33 (0.17 to 0.54) and the specificity (95% CI) was 0.97 (0.96 to 0.98) and 0.98 (0.97 to 0.99), respectively.

Low quality evidence from 1 study of 5147 participants showed that the sensitivity (95% CI), specificity (95% CI) and area under curve (95% CI) was 0 81 (0.76 to 0.85), 0.78 (0.77 to 0.79) and 0.86 (0.84 to 0.99), respectively.

RTS

Moderate quality evidence from 1 study of 536 participants showed that area under curve (95% CI) of the RTS score was 0.64 (0.59 to 0.69).

Schreiber

Low quality evidence from 1 study of 5147 participants showed that the sensitivity (95% CI) and specificity (95% CI) of the Schreiber score was 0.86 (0.81 to 0.90) and 0.62 (0.61 to 0.63), respectively.

TASH

Very low quality evidence from 1 study of 382 participants showed that the sensitivity (95% CI) and specificity (95% CI) of the TASH score with a threshold of 80% was 0.26 (0.13 to 0.43) and 1.0 (0.98 to 1.0), respectively.

Low quality evidence from 1 study of 596 participants showed that the area under curve of the TASH score with an unspecified threshold was 0. 84.

Very low quality evidence from 1 studies of 1030 participants showed that sensitivity (95% CI) and specificity (95% CI) of the modified TASH score with a threshold of 16 was 0.26 (0.11 to 0.46) and 0.99 (0.98 to 1.0) respectively.

Very low quality evidence from 1 study of 1134 participants showed that the sensitivity (95% CI) and specificity (95% CI) of the modified TASH score with a threshold of 18 was 0.25 (0.19 to 0.32) and 1.0 (0.99 to 1.0).

Vandromme

Low quality evidence from 1 study of 5147 participants showed that the sensitivity (95% CI), specificity (95% CI) and area under curve (95% CI) of the Vandromme score with a threshold of 1.5 or more was 0.79 (0.74 to 0.83), 0.76 (0.75 to 0.77) and 0.84 (0.82 to 0.86), respectively.

Low quality evidence from 1 study of 208 participants showed that the sensitivity and specificity of the Vandromme score with a threshold of 3 or more was 0.61 and 0.96, respectively.

Economic

No relevant economic evaluations were identified.

10.5.6 Recommendations and link to evidence

Recommendations	**30. Use physiological criteria that include the patient's haemodynamic status and their response to immediate volume resuscitation to activate the major haemorrhage protocol.** **31. Do not rely on a haemorrhagic risk tool applied at a single time point to determine the need for major haemorrhage protocol activation.**
Relative values of different outcomes	The outcomes for this diagnostic review question are sensitivity and specificity of the clinical risk tools relative to a reference standard (patients receiving massive transfusion). Sensitivity is an important outcome, because poor sensitivity may result in people with potentially serious haemorrhage being undiagnosed and therefore, untreated. In contrast, low specificity, leading to incorrect positive diagnoses, will lead to unnecessary treatments (blood transfusion).
Trade-off between clinical benefits and harms	The clinical risk tools resulted in low sensitivity and higher specificity. The GDG noted that the sensitivity and specificity of the tools were too low to be used to identify patients in need of massive transfusion. The GDG discussed the importance of clinicians having a clear set of indicators that supported them in identifying patients

	with life-threatening bleeding and the risks of using current risk tools .The tools need to reflect changes over time in a patient's status clearly showing responses to management rather than measuring status at a single time point. Some of the scores weight the variables which may make calculation difficult in the emergency room setting. Some of the parameters, for example laboratory analysis, may not be available within appropriate time frames. The GDG noted the important criteria (physiological criteria, including the patient's haemodynamic status and their response to immediate volume resuscitation) in the risk tools and made a recommendation highlighting the importance of using this.
Trade-off between net health benefits and resource use	No published economic evidence was identified for this review. Most risk scores would not necessarily have any costs associated with them directly; however, time involved in undertaking the assessment to use the score involves staff costs. Some of the scores also contain imaging or tests which would take time and involve resources. In current practice, the tools are not commonly used and where risk tools are used, there is variation in their selection as it is felt there is no current 'gold standard' for predicting transfusion. This is in part due to lack of confidence in their accuracy, as well as some being difficult/time intensive to use due to the factors that need to be assessed as part of the tools. Therefore, clinical judgement tends to be used based on presenting factors, such as physiology, mechanism of injury and observation of pattern of deterioration over time (as time itself is a good diagnostic indicator). The benefit of a risk score comes from being able to correctly stratify people (or predict outcome) to get them the right treatment. So just like a diagnostic test, there may be false negatives and positives, with people being missed or inappropriately categorised to need treatment. For the false negatives, these patients will deteriorate further, possibly leading to mortality or longer ICU stay as they are treated later when they are potentially more severe. Length of ICU stay is commonly seen as a marker of the success of strategies in predicting/identifying haemorrhage. A day in ICU for example (assuming no organs being supported) costs £619 and can increase to nearly £2000 depending on the number of organs being supported. No clinical net benefit in using the tools was suggested by the evidence. Therefore, it is unlikely that use of any tool is cost-effective.
Quality of evidence	Nine studies reported data on nine clinical risk tools. Only studies reporting an external validation of a risk tool were included. All of the studies were retrospective cohort studies. Some of the studies had a high proportion of missing of data and many studies had wide confidence intervals. One diagnostic meta-analysis was conducted on the ABC score. This was graded as very low quality and had very serious inconsistency. 2x2 tables could not be calculated for a number of the studies and some only reported the area under the curve.
Other considerations	In the Brockamp study, in order to compare the clinical risk tools, the AUCs were calculated and the cut-off (threshold) with the best relationship between sensitivity and specificity was used to recalculate sensitivity and specificity for each tools. This resulted in higher sensitivities than for the studies using pre-specified cut-offs. The reference standard of massive transfusion is based on physician discretion rather than biologic or laboratory outcome. Massive transfusion may have been initiated but not warranted. The GDG did not identifying any considerations specific to children.

10.6 Intraosseous (IO)/intravenous (IV) access

10.6.1 Introduction

In trauma patients where intravenous access to provide fluids and medication is neither available nor feasible IO infusion, that is, the direct injection into the bone marrow, may be used to provide a non-collapsible entry point into the systemic venous system. It has been argued that due to the critical nature of traumatic incidences, IO access ought to be attempted in the first instance. This is because attempts at gaining peripheral access are likely to fail which can lead to a delay in treatment.

The GDG sought to identify the optimal technique for circulatory access in adults, young people and children with major trauma.

10.6.2 Review question: What is the most clinically and cost effective technique for circulatory access in patients with major trauma, including following a failed attempt at initial peripheral access?

For full details see review protocol in Appendix C.

The objectives of the clinical questions were to determine whether:

Table 64: PICO characteristics of review question

Population	Children, young people and adults who have experienced a traumatic incident.
Intervention(s)	IO
Comparison(s)	IV (central and peripheral)
Outcomes	Critical: • Mortality at 24 hours, 30 days/1 month and 12 months • Health-related quality of life • Adverse effects: pain, infection, thrombosis, multiple access failures, compartment syndrome, fracture • Time to establish access Important: • Patient-reported outcomes (psychological wellbeing).
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

10.6.3 Clinical evidence

Summary of included studies

One within-patient cohort study was included in the review [80,81]; the details of which are summarised in Table 65 below. Evidence from this study is summarised in the clinical evidence summary (Table 66). See also the study selection flow chart in Appendix D study evidence tables in Appendix G, forest plots in Appendix J, GRADE tables in Appendix I and excluded studies list in Appendix K.

No RCTs were identified to meet the criteria for inclusion in this review. The included study was a non-randomised within-subject design study and compares IO vascular access with central venous catheterisation in patients who had failed 3 attempts at peripheral intravenous access. No comparative studies were identified for the population of patients without failed peripheral access.

Table 65: Summary of studies included in the review

Study	Intervention/comparison	Population	Outcomes	Comments
Leidel 2012 [80,81] Within-subject design	IO cannulation versus central venous catheterisation	n=40 Severely injured or critically ill adult patients having had three failed attempts of peripheral large bore cannula insertion over a maximum of 2 minutes	• Success rate for access • Procedure time • Adverse effects	Within subject design - simultaneous access by both methods in the same patient therefore interpretation of patient outcomes (aside from local effects) not possible

Table 66: Clinical evidence summary: IO access versus central IV access

Outcome	Number of studies	Imprecision	GRADE rating	Absolute difference	Control event rate (per 1000)	Control event rate for continuous outcomes
Time to establish access	1	Serious imprecision	VERY LOW	MD 6.5 lower (10.97 to 2.03 lower)	-	8.5
Adverse effects – failure to establish access	1	Serious imprecision	VERY LOW	248 fewer per 1000 (from 56 fewer to 336 fewer)	400	-

10.6.4 Economic evidence

Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow chart in Appendix E.

Unit costs

Below are estimates of the costs of the different methods of access. These are based on a micro costing approach of the equipment that would be needed for each type of access, based on GDG opinion.

Table 67: Resources and costs of interventions

Method of access	Equipment needed	Cost	Cost per patient	Source[a]
IO	EZ-IO Driver	£220.00 (one-off cost)	£0.44[b]	The Air Ambulance Service[c]
	EZ-IO Needles (sizes 45 mm, 25 mm and 15 mm)	£345.00 (box of 5)	£69	The Air Ambulance Service[c]
	Alcohol prep pad - Medi-Prep	£2.57 (box of 500)	£0.01	The Air Ambulance Service[d]
	10 ml syringe green 21 gauge x 1.5-inch needle	£26.30 (box of 100)	£0.26	NHS Supply chain [3]
			Total = £69.71	
IV (peripheral)	Alcohol prep pad - Medi-Prep	£2.57 (box of 500)	£0.01	The Air Ambulance Service[d]
	cannulas (22-14G)	£42.00 (box of 50)	£0.84	The Air Ambulance Service[d]
	Tegaderm Film	£28.82 (box of 100)	£0.29	The Air Ambulance Service[d]
	10ml syringe green 21 gauge x 1.5-inch needle (x2)	£26.30 Box of 100	£0.53	NHS Supply chain
	10 ml sodium chloride	£3.36 (10 per pack)	£0.34	Drug tariff [106]
			Total = £2	
IV (central)	EPIC antimicrobial triple lumen central venous catheterisation pack 7fr 16 cm	£686.25 (box of 15)	£45.75	NHS Supply Chain
	US to guide insertion	£59 US scan, less than 20 minutes	This will include the time of the attending physician and the equipment/ machinery cost for	NHS reference costs 2012/13 [37]

			the US[e]	

(a) Details on costs from The Air Ambulance Service.
(b) Based on the manufacturers guide of approximately 500 insertions.
(c) Products supplier is Vidacare.
(d) Supplier is through the NHS Supply Chain.
(e) It will be the doctor inserting the central IV line who will be undertaking the US. Therefore, using a cost from NHS reference costs for US is likely to be an overestimate, as this will include costs such as radiologist/sonographer which are not applicable to this scenario.

Economic considerations

The study identified from the clinical review showed that the IO method takes less time to undertake, as well as leading to fewer failed attempts (a clinically important difference), thus requiring less staff time.

The difference in staff costs due to IO taking less time is shown in the table below. Only the difference in cost based on a consultant is shown here as it would be a doctor who inserts a central IV line.

Table 68: Difference in staff costs due to time taken (IO versus central IV access)

Staff level	IO cost	IV cost	Difference in cost	Source of staff cost
Consultant	£4.63	£19.69	£15.06	PSSRU 2013 [29,30]

Note: Using the data for the time taken for each method from the clinical review (IO, 2 minutes; central IV, 8.5 minutes). Consultant cost is £2.32 per minute (based on £139 per hour including qualification costs)

10.6.5 Evidence statements

Clinical

Very low quality evidence from 1 non-randomised within-subject design study comprising 80 participants showed there were fewer failures to establish access in the IO access group compared with the central venous access group, with serious imprecision.

Very low quality evidence from 1 non-randomised within-subject design study comprising 80 participants showed that IO cannulation was clinically effective in terms of reducing the time to achieve vascular access, with serious imprecision.

One non-randomised within-subject design study comprising 80 participants reported no occurrence of other adverse effects, so the quality of this outcome could not be assessed.

No evidence was reported for the outcomes mortality, health-related quality of life and patient-reported outcomes (psychological wellbeing).

Economic

No relevant economic evaluations were identified.

10.6.6 Recommendations and link to evidence

Recommendations	**Circulatory access in pre-hospital settings** **32. For circulatory access in patients with major trauma in pre-hospital settings:** • **use peripheral intravenous access or**

	• **if peripheral intravenous access fails, consider intra-osseous access.** **33. For circulatory access in children (under 16s) with major trauma, consider intra-osseous access as first-line access if peripheral access is anticipated to be difficult.** **Circulatory access in hospital settings** **34. For circulatory access in patients with major trauma in hospital settings:** • **use peripheral intravenous access or** • **if peripheral intravenous access fails, consider intra-osseous access while central access is being achieved.**
Relative values of different outcomes	The critical outcomes to inform decision making for this review were agreed to be mortality, health-related quality of life, time to establish access and the following adverse events; pain, infection, thrombosis, multiple access failures, compartment syndrome, fracture. These specific adverse events were chosen as the most common or potentially harmful effects of the methods of circulatory access investigated. Time to establish circulatory access was considered a critical outcome as an accepted and well established surrogate for survival in resuscitation. Although patient-reported outcomes, such as psychological wellbeing, including depression and anxiety, were felt to be important they were not critical to the decision making.
Trade-off between clinical benefits and harms	The GDG agreed that the evidence in adults was quite clear in demonstrating that IO access is likely to be more rapid to achieve circulatory access for patients in whom obtaining peripheral access is not possible. It was discussed, however, that the IO route does not provide the same rate of fluid administration or drug action as large bore peripheral or central access, though no data on final outcomes was identified to support this. Despite the lack of evidence for quality of each route of vascular access, there was consensus across the GDG that the IO route, while not sufficient for definitive circulatory access, is useful as a 'bridging' access technique while definitive venous access is achieved. The benefits in using the IO route as an intermediate or 'bridging' route include the time to achieve access, and the minimal skill required to perform the procedure. Central venous access requires significant skill and training, however, provides definitive vascular access permitting rapid infusion of fluids and drugs. In the absence of evidence of adverse events the GDG agreed that, in their clinical experience, adverse events from peripheral venous cannulation are not immediately life threatening. This was seen to be the case for IO access also; however, this is more painful and has additional complications associated with failed attempts (such as fracture, epiphyseal injury in children). Potential harms of central venous access were agreed to be more serious than of peripheral and IO (including haemorrhage and pneumothorax). In view of the potential harms, it was agreed that peripheral IV access should always be considered first regardless of the age of the patient. However, there may be occasions where achieving peripheral access may be difficult (such as in infants), where IO access may be preferred as a first-line treatment. In children, IV access takes more time and can be more difficult, and the GDG felt that time is an

	important factor and the type of access method used should not induce delays in transfer. It was also noted that for central access a large bore device, such as 'swan sheath/pulmonary artery flotation catheter introducer' is the device that should be used in patients with major trauma as they permit greater speed of fluid administration than standard central venous catheters.
Trade-off between net health benefits and resource use	No economic evidence was identified comparing IV access with IO access. The GDG were presented with the costs of the different methods of access. For central IV access, the costs of the staff time and equipment involved in undertaking an US to guide insertion of the central IV line have not been included. It was also noted that there is no additional staff cost involved in performing the US as the same member of staff administering the line would also do this. And so all that would be involved would be the opportunity cost of the doctor's time and the equipment. It was also highlighted that IO access is only used as a bridging method, with the ultimate goal being central IV access. Adverse events were also discussed and should be considered within the trade-off. These include pain being a big factor for IO access in conscious patients, not just for insertion of the needle but also while fluids are being inserted. Additional adverse events can include fracture. For IV access adverse events can include infection and misplacement. The clinical review data showed that IO access takes less time to perform, and also leads to fewer failed attempts (clinically significant difference), although the study was unclear as to what categorised as a 'failed attempt'. The data was also of a low quality. The GDG felt that the difference in time taken between the two methods was a clinically-relevant factor in a time critical situation when you are trying to get fluids into a patient as quickly as possible for resuscitation purposes. As mentioned above, the US staff time costs and equipment have not been included; therefore, it is unclear if central IV access is likely to be more expensive than IO access. However, given that IO is used as a bridging method for inserting fluids until central IV access can be performed, then IO access is the more expensive option as this will include the IO access followed by central IV access. Using IO access while central access is being achieved was considered cost effective as it would ensure quicker access. The GDG felt that time is an important factor and the type of access method used should not induce delays in transfer, as time is a critical factor in major trauma patients and delay can impact patient outcomes.
Quality of evidence	One single study was identified comparing IV with IO access. The study population was seriously ill or critically injured adult patients (requiring fluid resuscitation) who had received three failed attempts at peripheral large-bore cannula insertion. It was unclear precisely whether this population was entirely a trauma population, therefore, the evidence was somewhat indirect. The design of this study was non-randomised within-patient, which, while eliminating the bias arising from baseline differences, also made any meaningful comparison of the effect of the equipment impossible. The only outcomes reported were time to achieve access and unsuccessful attempts. Given the small size of the study sample, there was large variation and so considerable uncertainty around the effect estimate, for which the quality of the

	evidence was downgraded accordingly.
Other considerations	The GDG noted that if achieving peripheral access is difficult, further attempts should not delay transport to hospital. IV access is often not absolutely required. If circulatory access is required, IO access is rapid and where appropriate should be recommended in the pre-hospital environment. Circulatory access in children (particularly infants and patients who are cold) may be more difficult. In the pre-hospital environment, IO access, where appropriate, may be the first-line preferred method for circulatory access.

10.7 Volume resuscitation

10.7.1 Introduction

Uncontrolled bleeding remains the leading cause of preventable death following major trauma and requires early detection and prompt action to resuscitate the patient with fluid and achieve a stable hemodynamic status. Traditionally, fluid resuscitation of an actively bleeding patient has emphasised the maintenance of normal circulation in order to maintain organ perfusion. However, studies have indicated that limiting the amount of fluids administered using permissive hypotension during the initial resuscitation period may improve trauma outcomes. However, the evidence for the practice remains limited and practice may differ depending on type of injury (penetrating or blunt). Moreover, much of the evidence was made before the use of haemostatic resuscitation and clear guidance on resuscitation strategy is still required.

10.7.2 Review question: What are the most clinically and cost effective fluid resuscitation strategies in the major trauma patient (hypotensive versus normotensive)?

For full details see review protocol in Appendix C.

Table 69: PICO characteristics of review question

Population	Children, young people and adults experiencing a traumatic incident with acute haemorrhage.
Intervention:	Combination of permissive hypotension and normotension Permissive hypotension
Comparison	Resuscitation with normotension as aim
Outcomes	Critical: • Mortality at 24 hours, 30 days/1 month, and 12 months • Health-related quality of life • Neurological outcome • Length of intensive care stay • Blood product use Important: • Multi-organ failure • Time to definitive control of haemorrhage • Patient-reported outcomes: pain/discomfort return to normal activities psychological wellbeing)
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

10.7.3 Clinical evidence

Two studies were included in the review; [13,41] these are summarised in Table 70 below. Evidence from these studies is summarised in the clinical evidence summary. See also the study selection flow chart in Appendix D study evidence tables in Appendix G, forest plots in Appendix J, GRADE tables in Appendix I and excluded studies list in Appendix K.

Bickell[13] considered fluid resuscitation strategies in the pre-hospital and Dutton[41]/ within hospital population. Studies were also stratified by mechanism of injury with two studies [13] analysed for penetrating trauma. No studies were found in populations with an exclusively blunt mechanism of injury and in children and young people.

Table 70: Summary of studies included in the review

Study	Intervention/comparison	Population	Outcomes	Comments
Bickell 1994 [13]	Randomised 1:1- 598 Patients Immediate fluid resuscitation (normotension as aim) vs. delayed resuscitation (permissive hypotension)	Adults with penetrating injury treated pre-hospital	Mortality at 30 days; days in ICU; multi-organ failure.	
Dutton 2002 [41]	Randomised 1:1- 110 Patients Fluid administration titrated to systolic blood pressure SBP >100 mm Hg (normotension as aim) vs. SBP >70 mm Hg as aim (permissive hypotension)	Adults with a mix of blunt and penetrating injuries treated in the Emergency Room	Mortality at 24 hours; mortality at 30 days; time to definitive haemorrhage control	

Table 71: Clinical evidence summary: Permissive Hypotension versus Resuscitation with normotension as aim – Pre-hospital

Outcome	Number of studies (no. of participants)	Imprecision	GRADE rating	Absolute difference	Control event rate (per 1000)	Control event rate for continuous outcomes
Mortality at 30 days	1 (n=309)	Serious	MODERATE	79 fewer per 1000 (from 139 fewer to 0 more)	375	-
Length of ICU Stay - days	1 (n=465)	No serious	HIGH	MD 1 lower (3.51 lower to 1.51 higher)	-	8
Multi-organ failure	1 (n=465)	Serious	LOW	73 fewer per 1000 (from 134 fewer to 9 more)	304	-

Table 72: Clinical evidence summary: Permissive Hypotension versus Resuscitation with normotension as aim – In-hospital

Outcome	Number of studies (no. of participants)	Imprecision	GRADE rating	Absolute difference	Control event rate (per 1000)	Control event rate for continuous outcomes
Mortality at 24 hours	1 (n=110)	Very Serious	LOW	18 more per 1000 (from 27 fewer to 275 more)	36	-
Mortality at 30 days	1 (n=110)	Very serious	LOW	6 fewer per 1000 (from 54 fewer to 204 more)	73	-
Time to definitive haemorrhage control - hours	1 (n=105)	Serious	MODERATE	MD 0.4 lower (1.02 lower to 0.22 higher)	-	2.97

Table 73: Clinical evidence summary: Permissive Hypotension versus Resuscitation with normotension as aim – In-hospital (Combined)

Outcome	Number of studies (no. of participants)	Imprecision	GRADE rating	Absolute difference	Control event rate (per 1000)	Control event rate for continuous outcomes
Mortality at 24 hours	2 (n=708)	Serious	VERY LOW	72 fewer per 1000 (from 16 fewer to 113 more)	231	-
Mortality at 28 days	2 (n=708)	Serious	VERY LOW	66 fewer per 1000 (from	330	

Outcome	Number of studies (no. of participants)	Imprecision	GRADE rating	Absolute difference	Control event rate (per 1000)	Control event rate for continuous outcomes
				119 fewer to 0 more)		
Length of ICU Stay - days	1 (n=465)	No serious	HIGH	MD 1 lower (3.51 lower to 1.51 higher)	-	8
Multi-organ failure	1 (n=465)	Serious	LOW	73 fewer per 1000 (from 134 fewer to 9 more)	304	-
Time to definitive haemorrhage control - hours	1 (n=105)	Serious	MODERATE	MD 0.4 lower (1.02 lower to 0.22 higher)	-	2.97

Table 74: Clinical evidence summary: Permissive Hypotension versus Resuscitation with normotension as aim – Penetrating Injury

Outcome	Number of studies (no. of participants)	Imprecision	GRADE rating	Absolute difference	Control event rate (per 1000)	Control event rate for continuous outcomes
Mortality at 30 days	1 (n=598)	Serious	MODERATE	79 fewer per 1000 (from 139 fewer to 0 more)	375	-
Length of ICU Stay - days	1 (n=465)	No serious	HIGH	MD 1 lower (3.51 lower to 1.51 higher)	-	8
Multi-organ failure	1 (n=465)	Serious	LOW	73 fewer per 1000 (from 134 fewer to 9 more)	304	-

10.7.4 Economic evidence

Published literature

One economic evaluation relating to this review question was identified but excluded due to a combination of limited applicability and methodological limitations.[136,136] This is listed in Appendix L, with reasons for exclusion given.

See also the economic article selection flow chart in Appendix E.

Unit costs

Below are the costs of the various fluid and blood products available, to aid consideration of cost effectiveness.

Table 75: Fluid and blood product costs

Resource	Cost	Source
Crystalloids: • 0.9% Sodium Chloride (1000-ml bag) • Hartmann's Solution (1000-ml bag) • Plasmalyte M (1000-ml bag) Ringer's • Lactate (500-ml bag)	 £0.70 £0.85 £0.91 £1.25	IV fluid guideline
Packed red blood cells	£122	NHS Blood and Transplant price list 2014/15 [105]
Fresh frozen plasma[a]	£28	NHS Blood and Transplant price list 2014/15
Platelets	£197	NHS Blood and Transplant price list 2014/15
Pooled cryoprecipitate (5 packs)[a]	£181	NHS Blood and Transplant price list 2014/15

(a) Can be considerably more expensive if the methylene blue versions of these products are used for children.

As well as the costs of the products themselves, additional costs would be involved in the handling and administration of the products, which would apply each time a product is issued, and could vary depending on the type of product (see more in section 10.8.4).

10.7.5 Evidence statements

Clinical

Permissive Hypotension versus normotension – Pre-hospital

Moderate quality evidence from a 1 RCT comprising of 598 participants demonstrated a clinical benefit of permissive hypotension over normotension for mortality at 30 days, with serious imprecision.

High quality evidence from 1 RCT with 598 participants demonstrated no clinical difference between permissive hypotension and normotension for length of ICU stay, with no serious imprecision.

Low quality evidence from 1 RCT comprising of 598 participants demonstrated a clinical benefit of permissive hypotension over normotension for multi-organ failure at 30 days, with serious imprecision.

Permissive Hypotension versus normotension – In hospital

Low quality evidence from 1 RCT comprising of 110 participants demonstrated no clinical difference between permissive hypotension and normotension for mortality at 24 hours, with very serious imprecision.

Low quality evidence from 1 RCT comprising of 110 participants demonstrated no clinical difference between permissive hypotension and normotension for mortality at 30 days, with very serious imprecision.

Moderate quality evidence from 1 RCT comprising of 110 participants demonstrated no clinical difference between permissive hypotension and normotension for time to definitive control of haemorrhage, with serious imprecision.

Permissive Hypotension versus normotension – In hospital (Combined)

Very low quality evidence from 2 RCTs with 708 participants demonstrated a clinical benefit of permissive hypotension over normotension for mortality at 24 hours, with serious imprecision.

Very low quality evidence from 2 RCTs with 708 participants demonstrated a clinical benefit of permissive hypotension over normotension for mortality at 30 days, with serious imprecision.

High quality evidence from 1 RCT with 598 participants demonstrated no clinical difference between permissive hypotension and normotension for ICU length of stay, with no imprecision.

Low quality evidence from 1 RCT comprising of 598 participants demonstrated a clinical benefit of permissive hypotension over normotension for multi-organ failure at 30 days, with serious imprecision.

Moderate quality evidence from 1 RCT comprising of 110 participants demonstrated no clinical difference between permissive hypotension and normotension for time to definitive control of haemorrhage, with serious imprecision.

Permissive Hypotension versus Normotension – Penetrating Injury

Moderate quality evidence from 1 RCT comprising of 598 participants demonstrated a clinical benefit of permissive hypotension over normotension for Mortality at 24 hours, with serious imprecision.

High quality evidence from 1 RCT with 598 participants demonstrated no clinical difference between permissive hypotension and normotension for length of ICU stay, with no imprecision.

Low quality evidence from 1 RCT comprising of 598 participants demonstrated a clinical benefit of permissive hypotension over normotension for multi-organ failure at 30 days, with serious imprecision.

Economic

No economic evidence identified

10.7.6 Recommendations and link to evidence

Recommendations	**35. For patients with active bleeding use a restrictive approach to volume resuscitation until definitive early control of bleeding has been achieved.** **36. In pre-hospital settings, titrate volume resuscitation to maintain a palpable central pulse (carotid or femoral).**

	37. In hospital settings, move rapidly to haemorrhage control, titrating volume resuscitation to maintain central circulation until control is achieved. **38. For patients who have haemorrhagic shock and a traumatic brain injury:** • **if haemorrhagic shock is the dominant condition, continue restrictive volume resuscitation or** • **if traumatic brain injury is the dominant condition, use a less restrictive volume resuscitation approach to maintain cerebral perfusion.**
Relative values of different outcomes	Mortality, health-related quality of life, length of intensive care stay, neurological complications and blood product use were critical outcomes. Multi-organ failure, time to definitive control of haemorrhage, patients reported outcomes, return to normal activities and psychological wellbeing were important outcomes. The selection of outcomes reflects both short-term and long-term sequelae of fluid replacement therapy.
Trade-off between clinical benefits and harms	**Pre-hospital** Pre-hospital evidence from a single study on adults indicated that a permissive hypotension strategy was associated with reduced mortality at 30 days and multi-organ failure. The GDG discussed the concept of permissive hypotension and noted that the majority of evidence supporting this practice has been conducted in animal studies and demonstrated that liberal fluid resuscitation reduces in vivo coagulation. Based on the evidence, their clinical experience and the fact that a restrictive approach to fluid administration in patients with trauma (particularly those who are actively bleeding) is the current practice, the GDG recommended a restrictive approach to fluid administration (that is, small boluses of crystalloid or blood components). The GDG then discussed how to titrate resuscitation to a specific target (that is, 50 mmHg arterial pressure for permissive hypotension). The GDG noted that identification of active bleeding and shock is difficult. Moreover, recordings of blood pressure may be inaccurate in the critically ill patient and measurement difficulties are intensified in the pre-hospital setting. The GDG discussed the various indicators of shock, but felt that a simple assessment tool, such as assessment of central pulse (carotid or femoral), would be more reliable for the pre-hospital clinician and allow patients to be transported quicker for definitive care. The GDG also discussed the measurement of radial pulse, but felt a central indicator of pulse matched the blood pressure targets used in the clinical studies (pre and hospital). The central pulse is also easier to palpate than a radial pulse. The GDG also noted that the patients response following initial fluid bolus, would provide the best information if this patient is shocked and ongoing management should be based on this (that is, a patient who does not respond to initial volume resuscitation is likely to be actively bleeding). **In hospital** The GDG discussed the evidence for in-hospital resuscitation from a small

	single study in adults. The study demonstrated no difference between normotension and permissive hypotension for mortality and time to definitive control of haemorrhage. However, it was felt that the study by Bickell et al. could be combined with this study (as the intervention is also carried out in hospital). When combined, the evidence suggested a benefit of a permissive strategy (systolic blood pressure titrated to 70 mmHg and delayed resuscitation) for mortality at 24 hours and 28 days. The GDG noted the benefits of permissive hypotension in the emergency department and physiological rationale, which was similar to the pre-hospital. However, the GDG felt this should be governed by a rapid protocol to definitively stop the source haemorrhage, as this is a critical factor for improved patient outcome. The GDG discussed titration of the resuscitation strategy to a set BP, but the evidence from both studies demonstrated this to be difficult. The GDG, therefore, agreed that this should be titrated against maintenance of central circulation, as there would be risk of organ failure and death if central circulation was unable to maintain vital organ perfusion. The measurement of blood pressure may be more reliable (for example, with the placement of an arterial line) in hospital. **Head injury** The GDG discussed a subpopulation of patients with traumatic brain injury in which hypotension may be associated with worse outcome. No clinical evidence was presented for patients with combined head injury and active bleeding and the GDG noted that majority of practice in this area was based on animal studies. The GDG, therefore, made a recommendation on these patients using informal consensus. Assessment of severity of head injury is difficult in the pre-hospital setting. The GDG noted that patients with a severe brain injury may not benefit from a restrictive fluid approach and that maintenance of cerebral perfusion best reflects current practice. The GDG also noted that in patients who present with both traumatic brain injury and active bleeding, the physician should treat with an appropriate strategy for the most severe injury (that is, use a restrictive approach if active bleeding is the prevailing injury and brain injury secondary).
Trade-off between net health benefits and resource use	No economic evidence was identified for this question. Permissive hypotension involves delaying or restricting fluids in order to reach a defined endpoint – which is lower than normal blood pressure. Normotension as an aim involves giving fluids until the patients has reached the normal level of blood pressure (pre-injury levels). The types of fluids used would have an impact on costs, as blood is comparably more expensive than crystalloids. It would be assumed that the normotensive group would receive more fluids overall than the permissive group. There are various adverse events that could be associated with the different techniques and it is often unclear which method is the best. It is perceived that normotensive hypotension can lead to more bleeding and have a negative effect on the clotting process by raising blood pressure to a higher level. The clinical evidence tended to favour permissive hypotension, particularly the larger study (Bickell et al.), which reported lower mortality, length of stay, and

	fewer cases of multiple organ failure for the permissive group. Thus potentially a dominating strategy. This recommendation will lead to a change in practice as currently, clinicians are trained to follow an approach of early recognition and intervention. The recommendation may be cost saving as fewer units of fluids will be used.
Quality of evidence	The GDG noted that clinical data from well controlled, prospective trials applying the concept of permissive hypotension in trauma patients (as described in the protocol) was still missing. **Pre-hospital** The GDG noted that the single study comparing hypotension with normotension was a well conducted single centre RCT. However, the GDG noted that crystalloids were used, which are not recommended over haemostatic resuscitation agents in our guidance. The outcome of multi-organ failure was not reported clearly and said to be at an increased risk of bias. Overall, the outcomes were rated from high to low quality. The GDG noted that the objective of that study was the comparison between standard pre-hospital trauma fluid resuscitation versus delayed onset of fluid resuscitation (fluid not administered until patients reached the operating room). This did not directly compare a permissive hypotension strategy with normotension, but the GDG noted that the restrictive approach to fluid replacement (as described in the study) is commonly used in UK pre-hospital practice and detailed in consensus guidelines, such as the Joint Royal Colleges Ambulance Liaison Committee. Moreover, the GDG noted that only patients with penetrating trauma were included in the study and these patients would require a more conservative fluid management. **In hospital** The GDG noted that the small RCT was conducted in a mixed population with both blunt and penetrating injuries. The blood pressure following the intervention was similar and the subjects were not truly randomised to each respective arm. However, the GDG noted that this may due to physiological adaption. All outcomes were rated at a high risk of bias. The GDG also discussed that the Bickell et al. study could be interpreted to cover in-hospital and pre-hospital, but the overlap is not clear in the paper and presents an additional risk of bias. All outcomes combining both studies were rated a very high risk bias.
Other considerations	The GDG noted that there were varying interpretations of the meaning and goals of permissive hypotension and that the technique used to achieve permissive hypotension varied across the studies and in practice. The GDG also noted that local practice will be based on proximity to a trauma centre; whereby it is essential resuscitate a patient in shock if there is a prolonged travel time to definitive management. The GDG did not identify any considerations specific to children.

10.8 Fluid replacement

10.8.1 Introduction

The main purpose of volume replacement in traumatized patients is to re-establish tissue perfusion. There is not yet a consensus about which if any fluids should be used in trauma patients.

10.8.2 Review question: What is the best volume expansion fluid to use in the resuscitation of haemorrhagic shock?

For full details see review protocol in Appendix C.

Table 76: PICO characteristics of review question

Population	Children, young people and adults who have experienced a traumatic incident.
Intervention(s)	• Red blood cells (RBCs) • Fresh frozen plasma (FFP) • Liquid plasma • Crystalloids • Lyophilised plasma
Comparison(s)	A comparison or combination of the above (including different ratios)

Outcomes	Critical:
	• Mortality at 24 hours, 30 days/1 month and 12 months
	• Health-related quality of life
	• Length of intensive care stay
	• Acute transfusion reaction:
	  ○ haemolytic transfusion reaction – acute
	  ○ haemolytic transfusion reaction – delayed
	  ○ post-transfusion purpura
	  ○ previously uncategorised complications of transfusion
	  ○ transfusion-associated graft versus host disease
	  ○ transfusion-associated circulatory overload
	  ○ transfusion associated dyspnoea
	  ○ transfusion-related acute lung injury
	  ○ transfusion-transmitted infections
	
	Important:
	• Time to definitive control of haemorrhage
	• Patient-reported outcomes:
	  ○ return to normal activities
	  ○ psychological wellbeing

Study design	RCTs or systematic reviews of RCTs; cohorts if no RCTs retrieved (matched at baseline or adjusted for age, Glasgow coma scale [GCS], injury severity score and shock)

10.8.3 Clinical evidence

One RCT comparing plasma, platelet and RBCs in a ratio of 1:1:1 to 1:1:2[63,64] and one secondary analysis of a prospective cohort study was identified comparing different ratios of crystalloid with RBCs [102,103] and one RCT comparing two different crystalloids[143,144] were identified. The study comparing different ratios of plasma, platelet and RBCs was included even though one of the products was platelets because the GDG were confident that the addition of platelets to plasma and

RBCs was not likely to influence the ratio of plasma to RBCs used. Also, platelets are frequently given with volume expansion products to control coagulopathy. Both studies were in the civilian population. The study characteristics are summarised in Table 77 below. Evidence from these studies is summarised in the clinical evidence summary below (Table 78). See also the study selection flow chart in Appendix D study evidence tables in Appendix G, forest plots in Appendix J, GRADE tables in Appendix I and excluded studies list in Appendix K.

Only studies on patients undergoing massive transfusion were included.

Table 77: Summary of studies included in the review – Massive transfusion by risk of survivor bias

Study	Intervention/comparison	Population	Outcomes	Comments
FFP:platelets:RBCs				
Holcomb 2015[63,64]	FFP:platelets:packed RBC (pRBC)ratio: High 1:1:1 n=338 Low 1:1:2 n=342	Patients meeting the highest level of activation at 1 of 12 participating level 1 trauma centres. Estimated age 15 years or over. Inclusion: At least 1 unit of any blood product component transfused prior to hospital arrival or within 1 of admission and prediction by an American Assessment of Blood Consumption score of 2 or more or by physician judgement of the need for a massive transfusion (10 or more units of RBCS within 24 hours). Exclusion: Indirect transfers, required thoracotomy prior to randomised blood components. Median age 34.5 to 34 years. USA	Mortality at 24 hours, 30 days, ICU free days, GCS – Extended, Discharged home, transfusion related metabolic complication, transfusion related circulatory overload, achieved haemostasis	
Crystalloid:pRBC				
Neal 2012[102,103]	Crystalloid: pRBC ratio: <0.5:1 n=114	Patients receiving massive	Mortality (in-hospital)	Patients who died in the initial

	≥0.5:1 and <1.1 n=113 ≥1.1 and <1.5:1 n=111 ≥1.5:1 n=114	transfusion (≥10 units pRBC within the first 24 hours of admission). Blunt trauma only. Excluded patients <16 and >90 years. Mean age 42 years. USA	Nosocomial infection Multiple organ failure Acute respiratory distress syndrome	24 hours post injury were excluded. Analysis adjusted for age, gender, GCS, injury and shock severity, transfusion and resuscitation requirements, operative interventions and comorbidities. The effect of including FFP:pRBC ratio in the regression analysis for multiple organ failure and acute respiratory distress syndrome (note: not mortality). This had no effect on the results attributable to crystalloid: pRBC ratio >1/5:1
Crystalloid versus crystalloid				
Young 2014[143,144]	0.9% NaCl; n=24 Plasma-Lyte A; n=22	All patients received by a level 1 major trauma centre with severe acute injury. Patients were eligible if they were 18 years or over and were intubated transfused blood, or taken to an operating room or interventional radiology suite within 60 minutes of arrival	Mortality ICU length of stay Hospital length of stay	Intervention administered within hospital. Patients anticipated to die within 48 hours excluded.

Table 78: Clinical evidence summary: FFP: platelets: RBCs

Outcome	Number of studies (no. of participants)	Imprecision	GRADE rating	Absolute difference	Control event rate (per 1000)	Relative 1:1:1 vs. 1:1:2	Control event rate for continuous outcomes
Mortality (24 hours)	1 (n=680)	Serious	MODERATE	43 fewer (from 82 fewer to 14 more)	170	RR 0.75 (0.52 to 1.08)	-
Mortality (30 days)	1 (n=680)	Serious	MODERATE	39 fewer (from 91 fewer to 29 more)	260	RR 0.85 (0.65 to 1.11)	-
Transfusion-related metabolism complication	1 (n=680)	Very Serious	LOW	16 fewer (from 61 fewer to 48 more)	173	RR 0.91 (0.65 to 1.28)	-
Transfusion-associated circulatory overload	1 (n=680)	Very serious	VERY LOW	0 (from 10 fewer to 10 more)	0	Peto OR 7.48 (0.15 to 376.84)	-
Achieved haemostasis	1 (n=680)	None	HIGH	78 more (from 23 more to 141 more)	781	RR 1.1 (1.03 to 1.18)	-
Discharged home (at 30 days)	1 (n=680)	Serious	MODERATE	43 more (from 25 fewer to 126 more)	307	RR 1.14 (0.92 to 1.41)	-

Table 79: Clinical evidence summary: Crystalloid: RBCs

Outcome	Number of studies (no. of participants)	Imprecision	GRADE rating	Absolute difference	Control event rate (per 1000)	Relative High versus low	Control event rate for continuous outcomes
Mortality (in hospital)	1 (n=452)	Very serious	VERY LOW	GIV	No adjusted data presented	OR 0.9 (0.58 to 1.45)	-
Nosocomial infection	1 (n=452)	Very serious	VERY LOW	GIV	No adjusted data presented	OR 1.3 (0.68 to 2.5)	-
Multiple organ failure	1 (n=452)	Serious	VERY LOW	GIV	No adjusted data presented	OR 1.7 (1.2 to 2.6)	-
Acute respiratory distress syndrome	1 (n=452)	None	VERY LOW	GIV	No adjusted data presented	OR 2.2 (1.5 to 3.1)	-

Table 80: Clinical evidence summary: Crystalloid (0.9% NaCl) versus crystalloid (Plasma-Lyte A)

Outcome	Number of studies (no. of participants)	Imprecision	GRADE rating	Absolute difference	Control event rate (per 1000)	Relative 0.95 NaCl vs. Plasma-Lyte A	Control event rate for continuous outcomes
Mortality (in hospital)	1 (n=38)	Very serious	LOW	17 more per 1000 (from 154 fewer to 681 more)	214	RR 1.08 (0.28 to 4.18)	-

Narrative review

The study comparing plasma:platelets:RBCs 1:1:1 versus 1:1:2[63,64] reported the median (IQR) ICU-free days as 5 (0 to 11) versus 4 (0 to 10) (0=0.10). The median (IQR) GCS – Extended for 1:1 versus 1:1:2 was 4 (3 to 6) (n=30) versus 4.5 (3.5 to 7.0) (n=30) (p=0.11).

When a dose-response relationship was evaluated in the study comparing ratios of crystalloid:pRBC [102,103], regression analysis revealed that a crystalloid:pRBC ratio was associated with: multiple organ failure (OR 2.6; 95%CI 1.2 to 5.4, p=0.011) and acute respiratory distress syndrome (OR 2.5; 95%CI 1.2 to 4.9; p=0.010).

The study comparing 0.9% NaCl with Plasma-Lyte A [143,144]reported a median (IQR) hospital length of stay of 9 (4, 30) versus 12 (4, 21) days and an ICU length of stay of 4 (2, 13) versus 4 (1, 9) days.

10.8.4 Economic evidence

Published literature

No economic evidence identified.

See also the economic article selection flow chart in Appendix E.

Unit costs

Table 81: Blood product costs

Resource	Cost	Unit	Source
RBCs	£122	1 pack 220-300 ml per pack	NHS Blood and transplant price list 2014/15 [105]
FFP	£28	1 pack Mean: 271 ml (240-280 is common)	NHS Blood and transplant price list 2014/15
Crystalloids: • 0.9% Sodium Chloride • Hartmann's Solution • Plasmalyte M • Ringer's Lactate	 £0.70 £0.85 £0.91 £1.25	 1000-ml bag 1000-ml bag 1000-ml bag 500-ml bag	IV fluid guideline [98]

Source: Unit information sourced from GDG contact and internet.

Note that for children, FFP is substantially more expensive due to the Department of Health recommendations that those born after 01.01.96 should use particular types of FFP and cryoprecipitate that have undergone additional reduction procedures to reduce the risk of viruses. Please see chapter 10.4.4 for more detail on this.

Lyophilised plasma and liquid plasma are not as commonly used in practice as fresh frozen plasma. Costs could not be sourced for these interventions.

Issues of finite supply and wastage arise in the use of blood components. In order to avoid waiting for cross matching tests, patients are mostly given the universal donor blood type, which may be in short supply. This is relevant for both blood and plasma. Additionally with FFP, this takes time to thaw. Some major trauma centres may have a small amount of plasma pre-thawed which can save time in a time critical situation, however, pre-thawed plasma only has a shelf life of 24 hours, and thus, is wasted if a suitable patient is not identified to use it on.

As well as the costs of the products themselves, there are also administration costs involved from the hospital laboratory that must prepare and issue the products. For example, the following costs are from GDG member contact and illustrate the blood product handling and administration costs involved in providing the blood components:

Table 82: Blood product handling and administration costs

	Cost	Components
Cost of group and save	£7.76	These costs include, but are not limited to: • Staff to receive the components, book into stock and place in controlled storage. • The running costs, maintenance, monitoring, mapping and repair of controlled storage devices. • Cost of remote blood fridges in theatres • The cost of the blood group and save sample plus consumables and reagents • The cost of selecting the blood, cross-matching, issue and labelling plus consumables and reagents • The annual cost of blood tracking devices • Staff costs • Lab costs (general) • Support for point of care • Training for theatre staff to use blood tracking kit • Training for blood administration competencies
Cost of cross-match (per unit)	£7.58	
Cost of issue of FFP (per unit)	£4.18	
Cost of issue cryoprecipitate	£3.51	
Cost of issue of platelets	£6.83	

Note these costs are from one particular hospital and may not be representative of all hospitals

10.8.5 Evidence statements

Clinical

Plasma: platelets: RBCs

Moderate quality evidence from 1 RCT comprising 680 participants showed that a 1:1:1 ratio was clinically effective compared with 1:1:2 in terms of mortality (24 hours, 30 days), with serious imprecision.

Low and Very low quality evidence from 1 RCT comprising 680 participants showed there was no difference in clinical harm between a1:1:1 and a 1:1:2 ratio in terms transfusion-related metabolic complication and transfusion-associated circulator overload, with very serious imprecision.

High quality evidence from 1 RCT comprising 680 participants showed that a 1:1:1 ratio was clinically effective compared with 1:1:2 in terms of achieving haemostasis, with no imprecision.

Moderate quality evidence from 1 RCT comprising 680 participants showed that a 1:1:1 ratio was clinically effective compared with 1:1:2 in terms of discharged home, with serious imprecision.

Crystalloids: RBCs

Very low quality evidence from 1 cohort study comprising 452 participants showed there was no difference in clinical effectiveness between a high and a low ratio in terms mortality, with very serious imprecision.

Very low quality evidence from 1 cohort comprising 452 participants showed there was no difference in clinical harm between a high and a low ratio in terms nosocomial infection, with very serious imprecision.

Very low quality evidence from 1 cohort comprising 452 participants showed that a high ratio was clinically harmful compared with low in terms of multiple organ failure, with serious imprecision.

Very low quality evidence from 1 cohort comprising 452 participants showed that a high ratio was clinically harmful compared with low in terms of multiple acute respiratory distress syndrome, with no imprecision.

Economic

No economic evidence identified

10.8.6 Recommendations and link to evidence

Recommendations	**39. In pre-hospital settings only use crystalloids to replace fluid volume in patients with active bleeding if blood components are not available.** **40. In hospital settings do not use crystalloids for patients with active bleeding (See the section on resuscitation in the NICE guideline 'Intravenous fluid therapy in adults in hospital' and the section on fluid resuscitation in the NICE guideline 'Intravenous fluid therapy in children and young people in hospital' for advice on tetrastarches.** **41. For adults (16 or over) use a ratio of 1 unit of plasma to 1 unit of red blood cells to replace fluid volume.** **42. For children (under 16s) use a ratio of 1 part plasma to 1 part red blood cells, and base the volume on the child's weight.**
Relative values of different outcomes	Mortality, health-related quality of life, length of intensive care stay and transfusion-related complications were critical outcomes. Time to definitive control of haemorrhage, patient-reported outcomes, return to normal activities and psychological wellbeing were important outcomes. The selection of outcomes reflects both short-term and long-term sequelae of fluid replacement therapy. For the RCT comparing plasma:platelets:RBCs 1:1:1 versus 1:1:2 the only outcomes reported were in-hospital mortality, transfusion-related metabolic complications, transfusion-associated circulatory overload, achieved haemostasis and discharged home. For the study comparing high versus low ratio of crystalloids with RBCs, the only outcomes reported were in-hospital mortality, nosocomial infection, multiple organ failure and acute respiratory distress syndrome. For the RCT comparing two different types of crystalloids, the only outcome reported was mortality.
Trade-off between clinical benefits and harms	The RCT in adults comparing on FFP:platelets:RBCs reported of clinically important reduction in mortality at 24 hours and 30 days in favour of a 1:1:1 ratio compared with a 1:1:2 ratio but with serious imprecision. Clinically important benefits were also reported with 1:1:1 for the number of patients achieving haemostasis (with no imprecision) and the number of patients discharged home (with serious imprecision). No clinically important harms

	were associated with 1:1:1 (transfusion-related related metabolic complications and transfusion-related circulatory overload). One cohort study on adults evaluating different ratios of crystalloids with RBCs, reported no difference in in-hospital mortality, but there was evidence that higher ratios were associated with significant harms (nosocomial infection, multiple organ failure and acute respiratory distress syndrome). One RCT on adults compared two different types of crystalloid administered in-hospital. It reported a higher mortality rate with 0.9% NaCl compared with Plasma-Lyte A (but the difference was not considered to be clinically important), but with very serious imprecision. The GDG acknowledged that a recommendation to avoid using crystalloids and other clear fluids except in patients with profound haemorrhagic shock in the pre-hospital environment is a change in clinical practice. The GDG wanted to highlight that haemorrhage and other forms of shock (inadequate perfusion of end organs) in major trauma has a potential early and continued detrimental effect on clotting function ranging from an alteration in the complex systems involved in clotting itself to an absolute reduction in the body's raw materials required for creating adequate clot formation. Both crystalloids and colloids have an effect upon the complex clotting systems and their effective function in the patient who is severely injured. Additionally, continued and prolonged periods of shock have a detrimental effect upon outcome manifesting as inadequate perfusion of organs converting to organ failure and hence multi-organ dysfunction syndrome – so there is impact from the severity of the shock, the type of shock, the length of time that the patient is shocked for; this will affect the end organs and the clotting systems and both (for example, bone marrow and haematopoietic organs and their capability to manufacture essential ingredients for clot formation and replenishment of the circulating blood components and volume). The optimum management is fluid replacement with blood components. The GDG discussed the situation when a pre-hospital practitioner is treating a patient in profound haemorrhagic shock but does not have access to blood components. In this case small boluses of crystalloids would be appropriate.
Trade-off between net health benefits and resource use	No economic evidence was identified for this question. The different blood components can vary in price with blood being the most expensive of those currently used in practice (lyophilised plasma and liquid plasma are not commonly used in practice). Costs will also increase substantially if many units are used. The high ratio strategies will have a higher cost as there is more of the first product being used for every unit of the second (for example, 1:1 [high ratio] versus 1:2 [low ratio]). The cost effectiveness of the higher units is thus dependent on their effectiveness in resuscitating patients. Blood product wastage and the opportunity cost of not being able to use these blood components on others are also costs that need to be taken into account. Blood components also have administration costs associated with the handling and issuing of the products from the hospital laboratory. If blood was to be used pre-hospital then this would lead to additional costs of storage equipment and clinical systems and waste of unused blood if all pre-hospital services had to start carrying blood or blood components.

	There are various complications associated with transfusion which can lead to long-term morbidities or mortality. Although the risk of transfusion-related complications is likely to be low, infection and the immunological consequences are more common. For more information on these risks please see the latest SHOT report (ref), an extract of which can be found in Appendix O. The evidence showed that high ratios of FFP to blood are favoured (more FFP per unit of blood), and low ratios of crystalloids to blood are favoured (less crystalloids per unit of blood). Although, this evidence was of low quality. The GDG felt that recommending a balanced administration of FFP and RBCs, with a ratio of 1:1, was appropriate given the evidence. Current practice is variable with regards to ratios used, however, 1:1 is likely to be more common. The supply of FFP is a consideration here because a ratio of 1:1 in comparison to 1:2 means twice as much FFP will be needed per unit of blood. This creates additional pressure on the limited supply of the universal donor group AB, and also adds further pressure to have blood tests done earlier in order to match the plasma to the patients' blood type if group AB is not available. Wastage is also an issue because if more plasma needs to be used then having more plasma de-thawed which has only a 24-hour shelf life may lead to more wastage problems and high opportunity cost. FFP for children is over 6 times more expensive than that of adults because department of Health recommendations state that those born after 1996 must use specially treated FFP. Therefore, this recommendation is likely to have an effect on practice and a cost impact. A statement about crystalloids and other clear fluids was made, with awareness that blood may not be available pre-hospital. Avoiding the use of crystalloids pre-hospital is a change to current practice which could potentially result in cost savings if crystalloids are not used, however, these are relatively cheap, and this saving may be offset if this recommendation encourages blood use pre-hospital. In hospital, if clear fluids are avoided, this also increases the pressure to have blood available as soon as possible. No comment could be made on the other interventions in the protocol as no evidence was identified and also these are not commonly used in practice.
Quality of evidence	The RCT had no methodological limitations but evidence was downgraded for imprecision where appropriate. The quality of the evidence ranged from low to high quality. Only one study was identified comparing different ratios of crystalloids with RBCs and this had been adjusted for survivor bias by excluding patients who died within 24 hours' of admission. The outcomes were graded as very low quality due to study design and imprecision. The RCT comparing two different types of crystalloids reported one low quality outcome due to imprecision.

Other considerations	The GDG noted that the patients in the 1:1:1 arm received platelets first (6 units) followed by alternating RBCs and plasma. In comparison, in the 1:1:2 arms patients received two units of RBCs first and one unit of plasma. Platelets were not transfused until after nine units of other blood components. The total number of platelets received in the 1:1: arm was slightly higher than it should have been (if given in accordance with a 1:1:1 ratio) and slightly lower in the 1:1:2 arm. Despite the considerations above, the GDG felt that a 1:1 ratio of plasma to RBCs is beneficial especially in the absence of any clinical harm. This ratio is the most similar in composition to whole blood. The recommendation to administer small boluses of crystalloids and to avoid other clear fluids is specific to the major trauma patients who are actively bleeding. To note, the NICE guideline on intravenous fluid therapy in adults is specific to hospitalised patients and excluded the major trauma population. With the exception of adjusting dose to weight, the GDG identified no consideration specific to children. The GDG noted the there are people who refuse blood components based on religious beliefs. This was not a problem specific to Major Trauma and the issue occurs in other clinical situations. The GDG noted NG24 Blood transfusion includes recommendations that address this issue. The committee acknowledged there may be unique situations in Major trauma when a patient is unable to give consent (either they are unconscious or have reduced mental capacity) and these situations are dealt with on an individual basis.

11 Control of haemorrhage in hospital

11.1 Haemorrhage protocols

11.1.1 Introduction

Haemorrhage is one of the leading causes of preventable in-hospital death among trauma patients. Empiric transfusion protocols, such as those that deliver a fixed ratio of blood components, have been recently adopted by trauma centres worldwide to treat haemorrhaging patients. Where used, this strategy has replaced the use of targeted transfusion protocols, where patients receive blood components guided by laboratory or point of care findings. However, there is some inconsistency across centres in the strategy used. Furthermore, both strategies are associated with significant safety and resource implications. This review examines the clinical and cost effectiveness of both empiric and targeted haemorrhage protocols in treating haemorrhage in trauma patients.

11.1.2 Review question: What type of major haemorrhage protocol is the most clinically and cost effective for improving outcomes in patients with major trauma?

For full details see review protocol in Appendix C.

Table 83: PICO characteristics of review question

Population	Children, young people and adults who have experienced a traumatic incident.
Intervention(s)	Empiric haemorrhage/transfusion protocols Targeted (laboratory-guided, point of care [POC] guided) haemorrhage/transfusion protocols
Comparison(s)	A comparison of the above
Outcomes	Critical: • Mortality at 24 hours, 30 days/1 month, 12 months • Health-related quality of life • Blood product use (red blood cells [RBCs], platelets, plasma, cryoprecipitate) • Length of intensive care stay • Adverse effects: over-transfusion-related morbidity, thromboembolism, transfusion reactions and infections Important: • Patient reported outcomes (psychological wellbeing) • Blood product waste
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

11.1.3 Clinical evidence

One study was included in the review;[96,97], which is summarised in Table 84 below. A second paper[97,97], reporting the protocol for this study, was also consulted. These papers report a feasibility trial comparing the effects of a fixed ratio transfusion protocol with a laboratory-guided transfusion protocol. Evidence from this study is summarised in the clinical evidence summary below (Table 85).

Table 84: Summary of studies included in the review

Study	Intervention/comparison	Population	Outcomes	Comments

Study	Intervention/comparison	Population	Outcomes	Comments
TRFL trial: [96,97]	Fixed ratio (1:1:1) transfusion protocol (n=40) versus Laboratory-guided transfusion protocol (n=38)	Young people and adults (over 16 years)	• Mortality (all cause; exsanguination), • Thromboembolism • Blood product use (RBC, frozen plasma, platelets, cryoprecipitate) • Plasma wasted	

Table 85: Clinical evidence summary: [Fixed ratio transfusion protocol versus Laboratory-guided transfusion protocol]

Outcome	Number of studies (no. of participants)	Imprecision	GRADE rating	Absolute difference	Control event rate (per 1000)	Control event rate for continuous outcomes
Mortality (all cause) at 28 days	1 (n=38)	Serious	MODERATE	204 more per 1000 (from 3 fewer to 882 more)	94	-
Mortality (exsanguination) at 28 days	1 (n=38)	Very serious	LOW	123 more per 1000 (from 31 fewer to 655 more)	94	-
RBC units used (median)	1 (n=38)	Not assessed[a]	HIGH	MD 0 higher (from 5 fewer to 2.5 more[b]	-	Median units (IQR) = 7 (6-14)
Frozen plasma units used (median)	1 (n=38)	Not assessed[a]	HIGH	MD 2 higher (from 0 more to 4 more)[b]	-	Median units (IQR) = 4 (3-8)
Platelet units used (median)	1 (n=38)	Not assessed[a]	HIGH	MD 4 higher (from 3 fewer to 6 more)[b]	-	Median units (IQR) = 4 (0-8)
Cryoprecipitate units used (median)	1 (n=38)	Not assessed[a]	HIGH	MD = ns[b]	-	Median units (IQR) = 0 (0-10)
Deep vein thrombosis at 28 days	1 (n=38)	Very serious	LOW	81 more per 1000 (from 20 fewer to 182 more)	0	-
Plasma wasted at 12 hours	1 (n=38)	No serious imprecision	HIGH	116 more per 1000 (from 46 more to 222 more)	104	-

(a) Imprecision could not be assessed as raw data was reported as median and interquartile range.
(b) Median difference and confidence intervals estimated using bootstrapping (10,000 simulations) as reported by the study authors.

11.1.4 Economic evidence

Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow chart in Appendix E.

Unit costs

Table 86: Resource unit costs

Resource	Cost	Unit	Source
ICU stay[a]	£852	Per day	NHS reference costs 2012/13. Adult critical care unit costs [37]
Packed RBCs	£122	1 pack 220-300 ml per pack	NHS Blood and transplant price list 2014/15 [105]
Fresh frozen plasma (FFP)	£28	1 pack Mean: 271 ml (240-280 is common)	NHS Blood and transplant price list 2014/15
Platelets	£197	1 adult therapeutic dose	NHS Blood and transplant price list 2014/15
Cryoprecipitate	£181	Pooled cryoprecipitate (5 pack) Mean: 199 ml per pooled pack	NHS Blood and transplant price list 2014/15
Integrated Blood Services (lab work)	£2	Mean cost per episode of related care.	NHS reference cost 2012-2013[37]. Currency code DAPS03[b]

(a) This cost is for 1 organ being supported (conservative assumption that the haemorrhage is coming from a vital organ).
(b) See Appendix O for full details. Other laboratory services, such as clinical biochemistry, haematology, immunology, microbiology, phlebotomy, other range in cost from £1 to £7 per episode.

As well as the costs of the products themselves, additional costs would be involved in the handling and administration of the products, which would apply each time a product is issued, and could vary depending on the type of product (see more in section 10.8.4).

Product wastage is an important consideration due to the finite supply of blood components, particularly the universal donor type. This means the opportunity cost of blood components is high, and a haemorrhage protocol tailored to the needs of the patient based on laboratory findings is likely to use resources more efficiently.

11.1.5 Evidence statements

Clinical

Moderate quality evidence from 1 RCT comprising 38 participants demonstrated a clinical harm of a fixed ratio transfusion protocol when compared with a laboratory-guided protocol for all-cause mortality, with serious imprecision.

Low quality evidence from 1 RCT comprising 38 participants demonstrated a clinical harm of a fixed ratio transfusion protocol when compared with a laboratory-guided protocol for mortality due to exsanguination, with very serious imprecision.

High quality evidence from 1 RCT comprising 38 participants demonstrated no clinical difference between a fixed ratio transfusion protocol and a laboratory-guided protocol for units of red blood cells, platelets, frozen plasma or cryoprecipitate used, with no imprecision.

Low quality evidence from 1 RCT comprising 38 participants demonstrated a clinical harm of a fixed ratio transfusion protocol when compared with a laboratory-guided protocol for incidences of deep vein thrombosis, with very serious imprecision.

High quality evidence from 1 RCT 38 participants demonstrated a clinical harm of a fixed ratio transfusion protocol when compared with a laboratory-guided protocol for units of plasma wasted, with no imprecision.

Economic

No relevant economic evaluations were identified.

11.1.6 Recommendations and link to evidence

Recommendations	**43. Hospital trusts should have specific major haemorrhage protocols for adults (16 or over) and children (under 16s).** **44. For patients with active bleeding, start with a fixed-ratio protocol for blood components and change to a protocol guided by laboratory coagulation results at the earliest opportunity.**
Relative values of different outcomes	Critical outcomes for decision making were mortality, health-related quality of life, length of intensive care stay, blood product use and adverse effects. Patient psychological wellbeing and blood product use were also identified as important review outcomes. Only one study was included in the review question, which included mortality, incidence of deep vein thrombosis, and blood product use and plasma wastage as outcomes.
Trade-off between clinical benefits and harms	The evidence indicated that in adults, the use of a fixed ratio haemorrhage transfusion protocol was associated with a greater risk of mortality within 28 days (both all-cause mortality and death by exsanguination), greater risk of deep vein thrombosis within 28 days and greater use and waste of plasma within 12 hours when compared with a laboratory guided protocol. The data did not indicate any significant difference in use of RBCs, platelets or cryoprecipitate within 12 hours.
Trade-off between net health benefits and resource use	There was no published economic evidence to inform this recommendation. The GDG considered the resource use involved with implementing a fixed ratio protocol and a laboratory-guided protocol to guide blood product use. A fixed ratio protocol would not involve the same level of laboratory support as for a laboratory-guided protocol (a unit cost of laboratory support is approximately £2) and therefore, slightly less costly to implement. The use of a particular protocol is to guide blood product use for the individual. Blood components are costly and are in finite supply. Cost effectiveness of using a particular protocol will, therefore, be driven by ensuring these products are not wasted. The opportunity cost of not having blood components available to benefit another person was acknowledged alongside the financial opportunity cost.

	The unit costs of the blood components were thought to be under-representative of true cost as only related to the products themselves. Additional costs, for example, would involve the administration and handling of the products, such as, cross match testing and laboratory work (for example, £7.58 to cross match each unit of blood, and £4.18 to issue each unit of FFP, which can add up if many units are used.) The extent that plasma would be wasted also depends on the ability of the provider to be able to recycle. Pre-thawed plasma has a shelf life of 24 hours, thus, if another trauma case does not require the leftover plasma, this will be wasted and the hospital will bear the cost of this. It was also noted how children would use more expensive FFP and cryoprecipitate given Department of Health recommendations that children should use particular types of these products that have undergone additional reduction procedures to reduce the risk of viruses, in other words; pathogen inactivation steps to reduce the risk of pathogen transmission. Thus, methylene blue (MB)-treated FFP for children is over 6 times more expensive that standard FPP and pooled MB-treated cryoprecipitate is over £1000 as the plasma is non-UK sourced, as per the Department of Health recommendation. The clinical review inferred that it was likely that a fixed ratio protocol, used in isolation, will incur greater opportunity cost due to the potential for blood product waste, notably plasma, and therefore, be less cost effective than use of a laboratory-guided protocol for blood product use. Having said this, laboratory-based guided blood product use would only be possible once the findings of the laboratory were available, which could be up to 45 minutes after the patient's arrival. Where the laboratory is located in relation to the emergency department (ED) and also technology available in the ED to present findings in 'real time' would influence the extent of delay in implementing a laboratory-based protocol. How laboratory findings are delivered is variable according to local circumstances, and therefore, the GDG assumed whilst making the recommendations; that whilst laboratory services (involving at least three members of staff) would be available, there would be a delay (and as such, did not consider service delivery costs further). During the delay in retrieving laboratory findings, the clinician still needs to be guided in blood product use so that the clinical benefit of early blood transfusion was realised. Therefore, the GDG recommended that blood product use should be guided by laboratory findings as soon as possible; however, during the delay in retrieving results, a fixed ratio was necessary so that the benefit of prompt treatment could be realised.
Quality of evidence	The evidence in the review is high quality. However, the GDG noted that the evidence is taken from only one study, for which the sample size was relatively small (n=78). Furthermore, the evidence for mortality (all-cause and due to exsanguination) and deep vein thrombosis was downgraded for imprecision. There was no clinical evidence evaluating the use of empiric or point of care-based transfusion protocols in children with haemorrhage. The laboratory test cost that would be involved in the laboratory-guided protocol has been sourced from NHS reference costs. As this is a national average over many submissions, it is likely that this cost may be higher for certain tests that might be undertaken when checking a patient's coagulation. Additionally, costs can vary between hospitals due to individual hospital laboratory arrangements.
Other considerations	The evidence in this review is taken from one small RCT. While the study was high quality, there was some imprecision in the findings for the risk of mortality. The GDG further noted that the findings are in opposition to much

	of the previous, non-randomised evidence evaluating the clinical efficacy of empiric and laboratory-guided transfusion protocols. Given the increased risk of bias associated with non-randomised studies and the potential high risk of mortality associated with fixed-ratio transfusion protocols, the GDG decided to make a recommendation in favour of laboratory-guided transfusion protocols. The GDG noted that in current practice, clinicians may wait 30-45 minutes for laboratory findings to be available. The GDG expressed concern that a delay in waiting for the findings of laboratory tests may delay treatment for haemorrhage. The GDG felt that it was, therefore, important for patients to receive treatment for haemorrhage while waiting for laboratory results. As fixed ratio transfusion protocols are used in current practice, the GDG advised that this should be implemented for all patients with haemorrhage until laboratory results were available. The GDG stipulated that laboratory findings should be received and a laboratory-guided transfusion protocol should be initiated as soon as possible.

11.2 Haemorrhage imaging

11.2.1 Introduction

It is imperative that major trauma patients are diagnosed as accurately and as quickly as possible to avoid preventable death. Missed injuries and unrecognised haemorrhage are a major concern and the diagnostic work-up poses challenges for emergency department (ED) clinicians as evaluation needs to be rapid and reliable. While multi-detector CT scanning is widely recognised as the gold standard for investigations of suspected internal haemorrhage, it is important to know the diagnostic accuracy of other available imaging techniques that may be cheaper and faster to access. This review addresses the diagnostic accuracy of ultrasound for injured children, and X-ray and focussed assessment with sonography for trauma (FAST) or combinations of these imaging techniques for injured adults.

11.2.2 Review question: What are the most clinically and cost effective imaging strategies for detecting life threatening internal haemorrhage in major trauma patients?

Table 87: PICO characteristics of review question

Population	Children, young people and adults who have experienced a traumatic incident.
Intervention	Tests: • X-ray • FAST • CT scans • X-ray plus CT • FAST plus CT • X-ray plus FAST • X-ray plus FAST plus CT Possible treatments: • Initiate haemorrhage/transfusion protocol • Surgery • Interventional radiology • Observation/careful monitoring • Combination of the above

Comparison	A comparison of the above Surgical or interventional radiology findings
Outcomes	Critical: • Mortality (24 hours, 30 days/1 month and 1 year) • Health related quality of life • Blood product use: • RBCs • Platelets • Plasma • cryoprecipitate) • Length of intensive care stay Adverse events: • Infarction • Infection • surgical complications) Important: • Time to definitive control of haemorrhage • Patient reported outcomes: • Pain/discomfort • Return to normal activities • Psychological wellbeing) Population size and directness: • No limitations on sample size • Studies with indirect populations will not be considered.
Study design	RCTs or systematic reviews of RCTs or quasi-RCTs

11.2.3 Clinical evidence

No clinical evidence identified.

11.2.4 Review question: What is the diagnostic accuracy of imaging strategies for detecting life threatening internal haemorrhage in major trauma patients?

For full details see review protocol in Appendix C.

Table 88: PICO characteristics of review question

Population	Children, young people and adults who have experiences a traumatic incident suspected of having internal haemorrhage.
Index test(s)	• X-ray • FAST • X-ray and FAST • Ultrasound (children <12 years)
Reference standard(s)	• Surgical or interventional radiology findings • CT (for X-ray and FAST)
Outcomes	Diagnostic accuracy (including sensitivity, specificity, positive predictive value, negative predictive value).

Study design	Cohorts or case-controls

11.2.5 Clinical evidence

Thirteen studies were found that investigated the diagnostic accuracy of FAST in both adults and children. However, only two of these studies specified the type of CT used as reference standard (and in one it was not multi-detector so was therefore excluded). We attempted to contact the authors of the eleven other papers to request further information. We received seven responses which resulted in the inclusion of five studies and the exclusion of two others. The remaining four studies for which we did not receive an author response were excluded on the basis of not containing enough information to ensure they matched our review protocol.

Six studies were included in the review.[20,20,45,46,48,49,67,67,111,111,139,140] These are summarised in Table 89 below. Evidence from these studies is summarised in the clinical evidence summary below (Table 90). See also the study selection flow chart in Appendix D study evidence tables in Appendix G, forest plots in Appendix J, GRADE tables in Appendix I and excluded studies list in Appendix K.

Four included studies investigate the diagnostic accuracy of FAST imaging in an adult, predominantly blunt trauma population[20,20,48,49,67,67]. Two included studies investigate the diagnostic accuracy of FAST imaging in a paediatric blunt trauma population[45,46,111,111]. No evidence was found on X-ray imaging or a combination of X-ray and FAST for detecting haemorrhage in children or adults.

Table 89: Summary of studies included in the review

Study	Population	No. of patients	Target condition	Index test(s)	Reference standard	Comments
Brooks 2002 [20,20]	Adult patients with multiple or suspected blunt abdominal injury	47	Haemoperitoneum	FAST	Multidetector CT (MDCT), diagnostic peritoneal lavage (DPL), surgery or clinical observation	47% patients did not receive a confirmatory test/exploration.
Fox 2011 [45,46]	Paediatric trauma with a blunt mechanism	357	Clinically important intraperitoneal free fluid (haemoperitoneum)	FAST	MDCT or surgery.	99.7% of patients received MDCT as reference standard (only 1 child had surgery instead).
Gaarder 2009 [48,49]	Potentially unstable patients initiating trauma team activation	104	Haemoperitoneum	FAST	MDCT, DPL, surgery or observation	18% patients did not receive a confirmatory test/exploration. Mixed population with 10% penetrating injury (not stratified) and potentially including some children (not stratified).
Hsu 2007	Potential blunt truncal	410	Intra-abdominal free fluid	FAST	MDCT or surgery.	Mixed population (1% children).

Study	Population	No. of patients	Target condition	Index test(s)	Reference standard	Comments
[67,67]	injuries					
Patel 1999 [111,111]	Paediatric blunt torso trauma	94	Intraperitoneal free fluid	FAST	MDCT, surgery or non-operative management	77% of patients did not receive a confirmatory test/exploration.
[139,140]	People with high-energy pelvic fractures	120	Hemiperitoneum	FAST	Multi-slice CT, and results of laparotomy	Interval between tests not reported

Table 90: Clinical evidence profile: Diagnostic accuracy of FAST for detecting life-threatening haemorrhage

Test	Number of studies	Number of patients	Risk of bias and applicability	Imprecision	Sensitivity	Specificity	GRADE rating
Adult trauma							
FAST	4	Brooks 2002 (n=47) Gaarder 2009 (n=104) Hsu 2007 (n=410) Verbeek 2014 (n=120)	Serious risk of bias (related to reference standard and flow and timing between tests)	Serious imprecision	1.0 (0.48, 1.00) 0.62 (0.41, 0.80) 0.78 (0.69, 0.86) 0.64 (0.48, 0.78) Median 0.64 (0.48 to 0.78)	1.00 (0.92, 1.00) 0.96 (0.89, 0.99) 0.97 (0.95, 0.99) 0.94 (0.86, 0.98) Median 094 (0.86 to 0.98)	VERY LOW
Paediatric trauma							
FAST	2	Fox 2011 (n=357) Patel 1999 (n=94)	Serious risk of bias (related to reference standard and flow and timing between tests)	Serious imprecision	0.52 (0.31, 0.73) 0.38 (0.14, 0.68)	0.96 (0.93, 0.98) 1.00 (0.96, 1.00)	LOW

11.2.6 Economic evidence

Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow chart in Appendix E.

New cost-effectiveness analysis

This area was prioritised for economic modelling; with the model looking at the timing of imaging for a major haemorrhage/suspected major haemorrhage population. However, due to a lack of data on treatment effect, this model was deemed unfeasible. Please see Appendix M for more detail.

Unit costs

Table 91: Diagnostic modality costs

Imaging modality	Description	Cost
X-ray	Direct Access Plain Film	£28
US scan	US scan, less than 20 minutes	£59
	US scan, 20 minutes and over	£40
FAST scan	US cost as a proxy	
CT	CT scan, one area, no contrast, 19 years and over	£60
	CT scan, one area, with post contrast only, 19 years and over	£71
	CT scan, one area, pre and post contrast	£301
	CT scan, two areas without contrast	£58
	CT scan, two areas with contrast	£76

Note: These costs are sourced from NHS reference costs 2012/13 [37]. Further detail on the costs such as the ranges and number of submissions can be found in Appendix O.

Table 92: Other resources

Resource	Description	Cost
ICU cost per day	Adult critical care unit costs (dependent upon number of organs being supported)	£619 –£1,867

Note: These costs are sourced from NHS reference costs 2012/13 [37]. Further detail on the costs such as the ranges and number of submissions can be found in Appendix O.

11.2.7 Evidence statements

Clinical

FAST imaging in adult trauma

Very low quality evidence from four diagnostic studies involving 681 people showed that FAST imaging has a median sensitivity of 0.64 (0.48 to 0.78) and a median specificity of 1.0 (0.96 to 1.0) for detecting haemoperitoneum or intra-abdominal free fluid resulting from predominately blunt trauma.

No evidence was found on X-ray imaging in adult trauma.

FAST imaging in paediatric trauma

Low quality evidence from two diagnostic studies involving 451 children showed that FAST imaging has a median sensitivity of 0.38 (0.14 to 0.68) and a median specificity of 0.96 (0.93 to 0.98) for detecting intraperitoneal free fluid resulting from blunt trauma.

No evidence was found on X-ray imaging in paediatric trauma.

Economic

No relevant economic evaluations were identified.

11.2.8 Recommendations and link to evidence

Recommendations	**Adults and children** **45. Limit diagnostic imaging (such as chest and pelvis X-rays or FAST [focused assessment with sonography for trauma]) to the minimum needed to direct intervention in patients with suspected haemorrhage and haemodynamic instability who are not responding to volume resuscitation.** **46. Be aware that a negative FAST does not exclude intraperitoneal or retroperitoneal haemorrhage.** **47. Consider immediate CT for patients with suspected haemorrhage if they are responding to resuscitation or if their haemodynamic status is normal.** **48. Do not use FAST or other diagnostic imaging before immediate CT in patients with major trauma.** **49. Do not use FAST as a screening modality to determine the need for CT in patients with major trauma.**
Relative values of different outcomes	The outcomes for this diagnostic review question are sensitivity and specificity of the index tests relative to a reference test (which is assumed to give the 'true' diagnosis). Sensitivity is an important outcome, because poor sensitivity may result in people with potentially serious haemorrhage being undiagnosed and therefore, untreated. In contrast, low specificity, leading to incorrect positive diagnoses, will lead to unnecessary treatments. Though carrying a risk of unnecessary adverse events and higher costs, such additional treatments secondary to misdiagnoses are unlikely to be as much of a risk to the patient as missed diagnoses.
Trade-off between clinical benefits and harms	While diagnostic cohort studies can tell us about the relative accuracy of a diagnostic test compared with a reference standard, they do not tell us whether adopting a particular diagnostic strategy improves patient outcomes. Evidence on patient outcomes is only available from diagnostic RCTs which compare two diagnostic interventions with identical subsequent treatment as indicated by the diagnostic test. No such evidence was identified. Four included studies investigate the diagnostic accuracy of FAST imaging in an adult, predominantly blunt trauma population. Two included studies investigate the

	diagnostic accuracy of FAST imaging in a paediatric blunt trauma population. No evidence was found on X-ray imaging or a combination of X-ray and FAST for detecting haemorrhage in children or adults. The median sensitivity and specificity of FAST in the adult studies was 0.71 (0.48 to 0.86) and 0.96 (0.86 to 0.99). The two studies in children reported a sensitivity of 0.52 (0.31, 0.73) and 0.38 (0.14, 0.68) and a specificity of 0.96 (0.93, 0.98) and 1.00 (0.96, 1.00). The trade-off involved with diagnostic imaging of this kind relate to adverse events and additional costs of non-essential imaging versus potentially fatal missed injury and deterioration of the injured person. Note that the superior sensitivity and specificity of the gold standard (CT) may lead to additional nonessential imaging or non-therapeutic surgery to address injuries that are not of clinical importance. There is also a general desire to minimise any potential radiation risk, especially in children. However, missed haemorrhage is one of the main contributors to preventable deaths in major trauma. The GDG discussed the benefits of a FAST scan compared with other imaging modalities when diagnosing haemorrhage for adults and children. The GDG agreed that FAST scanning was not sensitive enough to diagnose haemorrhage. A positive FAST may result in an unstable patient being treated in theatre. A negative FAST may still miss lacerations of organs and therefore result in missed diagnosis.
Trade-off between net health benefits and resource use	There was no published economic evidence to inform this question. The GDG took into account the intervention cost of each diagnostic modality, and assessed each modality as outlined in the methods section in their deliberations (that is, taking into account the prevalence, predictive powers, the consequences of each diagnostic outcome in terms of potential net clinical benefit and cost of onward management and potential incidental findings). More detail on this can be found in Appendix O. The GDG were presented with the costs of the different diagnostic modalities; X-ray had the lowest unit cost (£28), followed by US and FAST (the US cost being used as a proxy for FAST), and CT had the highest unit cost (£71 – one area post contrast). [37] It was noted that accuracy of interpretation (and therefore, cost effectiveness) of FAST was operator dependent and may be improved with experience and in settings when presentation of the particular injury is common. FAST is also not always as readily available as X-ray in the ED. The evidence suggested that FAST did not give any benefit over observation and monitoring in people who had a low risk of haemorrhage, indicated by haemodynamic stability. Therefore, a strategy involving FAST in this subpopulation is likely to be dominated by a wait and see approach (which would occur post FAST results in any case). For people with haemodynamic instability, the GDG considered FAST to have sufficient accuracy to enable a decision to go straight to treatment if it was known where the bleeding was coming from, therefore, avoiding the incremental cost and potential delay in undertaking CT (the incremental cost per patient of imaging with CT compared with FAST is approximately £10-£30 per patient). It was discussed how FAST and X-ray could sometimes take as long as CT. The benefit, as well as a potential time saving, is that with X-ray or FAST the patients can stay in the resuscitation area of the hospital where the facilities are available to deal with the patient's instability. However, due to poor sensitivity, if FAST was negative, haemorrhage could not necessarily be ruled out and further imaging may be necessary, incurring additional cost.

	Cost effectiveness of employing FAST as a first-line detection strategy in part will depend on the number of people screened in whom the result was returned negative (a product of prevalence as well as accuracy), and the potential health and financial costs of delaying treatment. Without such information, cost effectiveness remains unclear. It was noted by the GDG that a commonly accepted marker of diagnostic outcomes is length of ICU stay; which can vary in cost from around £600 to nearly £2,000 per day depending on the number of organs being supported. Furthermore, it was felt that CT could be better indicated by clinical observations than on the basis of FAST. Therefore, FAST was not felt to be a cost effective strategy to indicate CT due to the poor sensitivity (which was even poorer for children) and resulting in missed injuries. This recommendation may be cost-saving if imaging prior to CT is reduced, as it is likely that CT will be indicated anyway for the major trauma population in question.
Quality of evidence	The evidence identified was of low quality in adults and very low quality in children. The main limitations leading to a high risk of bias rating include lack of blinding, unclear flow and timing between index tests and reference standards, and use of different reference standards. Additionally, while no meta-analysis was possible, visual inspection of the wide confidence intervals around the point estimates mean that there is uncertainty in the results. **Economics** **NHS reference costs** Costs for the diagnostic modalities were sourced from NHS reference costs [37]. Whether these costs are reflective of the true cost of the test is dependent on the number of submissions from hospitals. The cost of US was of particular concern to the GDG as the cost of US for less than 20 minutes was higher than the cost of US for more than 20 minutes. There were only submissions from 3 hospitals with a total of 13 units of activity for US more than 20 minutes, compared with 5 submissions with a total of 1,977 units of activity for US less than 20 minutes. This could be implying that the cost for US more than 20 minutes are slightly skewed as there are not enough units of activity to generate a nationally representative average cost. It would be assumed that a longer scan would cost more due to more staff time for example. However, there may be other reasons for the costs being higher for a shorter duration of US, such as more highly qualified or senior staff taking less time to do the US. CT also did not have many submissions (for no contrast: 4, with 70 units of activity. For post contrast: 1 submission, with 10 units of activity). X-ray had the most with 153 submissions and over 5 million units of activity). Additionally, it has been agreed with the GDG that the US cost can be used as a proxy for FAST, however, the actual cost was felt to be lower because FAST is most commonly carried out by a member of the trauma team rather than a radiologist (usually CT4 or above) and takes about 5 minutes. The US machine is in the resuscitation room and is actually usually a much more basic and cheaper machine than used in radiology.
Other considerations	The GDG felt it was important to discuss the skill level of the person performing and interpreting the image (radiographer versus emergency clinician trained in specific imaging modality). Considerations around the availability of specific imaging tools, especially in non-major trauma centres on night-time shifts and weekends. In the trauma unit setting, most will have single CT scanner that will be heavily booked with procedural CTs.

	FAST is a focused assessment sonography (a modality for looking specifically for free fluid or blood) for trauma and should not be used as a definitive diagnosis. FAST will delay the process if the patient is stable and already having a CT. The GDG acknowledged that due to the low sensitivity of FAST, further imaging or surgery may be required following a negative FAST scan. The absence of fluid on fast does not exclude significant haemorrhage in children, particularly the smaller child In children, it was felt that major haemorrhage was relatively rare, with approximately 740 cases of children presenting with an injury severity score of greater than 15 in England and Wales in 2012[134] In children, if the clinical concerns are not strong enough to warrant a CT then observation is justifiable. FAST should not be used as a way of deciding who should go on to have CT. Using FAST in children who are haemodynamically stable does not change management.

11.3 Whole-body CT

11.3.1 Introduction

Early diagnosis and treatment are associated with better prognosis in patients following major trauma. Currently, whole-body CT commonly refers to extending CT as far as to the pelvis. Whole-body CT provides early and accurate diagnostic assessment and has been suggested to improve mortality in a number of studies. While the feasibility of the technique has been proven, its exact role and clinical value compared with other imaging modes (including targeted CT and focussed assessment with sonography for trauma [FAST]), remains a matter of debate. Specifically, in regards to the greater radiation exposure associated with a whole-body CT and potential downstream adverse effects, such as malignancy.

11.3.2 Review question: What is the clinical and cost effectiveness of whole-body CT imaging in major trauma?

For full details see review protocol in Appendix C.

Table 93: PICO characteristics of review question

Population	Children, young people and adults who have experienced a traumatic incident.
Intervention(s)	Whole-body CT scan
Comparison(s)	Selective imaging (including CT, X-ray and US)

Outcomes	Critical:
	• Mortality at 24 hours, 30 days/1month and 12 months
	• Health-related quality of life
	• Blood product use:
	  ○ RBCs
	  ○ platelets
	  ○ plasma
	  ○ cryoprecipitate)
	• Length of intensive care stay
	
	Important:
	• Time to definitive control of haemorrhage

	• Time to surgery • Patient reported outcomes (psychosocial wellbeing) • Long-term radiation risk • Delayed/missed injury
Study design	RCTs or systematic reviews of RCTs; cohort studies that use multivariate analysis to adjust for key confounders (injury severity score [ISS], age, depth of shock, degree of head injury) or were matched at baseline for these if no RCTs retrieved

11.3.3 Clinical evidence

A single study was included in the review[142] and is summarised in Table 94 below. Evidence from this study is summarised in the clinical evidence summary below (Table 95). See also the study selection flow chart in Appendix D study evidence tables in Appendix G, forest plots in Appendix J, GRADE tables in Appendix I and excluded studies list in Appendix K.

Table 94: Summary of studies included in the review

Study	Intervention and comparison	Population	Outcomes	Comments
Yeguiayan 2010[142,142]	Whole-body CT – head to pelvis versus selective imaging	1950 adult patients with a severe blunt trauma.	Mortality at 30 days	Data presented following a post-hoc analysis.

Table 95: Clinical evidence summary: Full body CT versus selective Imaging

Outcome	Number of studies (participants)	Imprecision	GRADE rating	Absolute Difference	Control event rate (per 1000)	Relative OR (95%CI) (adjusted)	Control group value for continuous outcomes
Mortality	1 (n = 1607)	Serious	VERY LOW	-	-	OR 0.68 (0.45 to 1.03)	-

11.3.4 Economic evidence

Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow chart in Appendix E.

New cost-effectiveness analysis

This area was prioritised for economic modelling; with the model looking at the timing of imaging for a major haemorrhage/suspected major haemorrhage population. However, due to a lack of data on treatment effect, this model was deemed unfeasible. Please see Appendix M for more detail.

Unit costs

Table 96: Diagnostic modality costs

Imaging modality	Description	Cost
CT	CT scan, one area, no contrast, 19 years and over	£60
	CT scan, one area, with post contrast only, 19 years and over	£71
	CT scan, one area, pre and post contrast	£301
	CT scan, two areas without contrast	£58
	CT scan, two areas with contrast	£76
	CT scan, more than three areas	£146
X-ray	Direct access plain film	£28
Ultrasound scan	US scan, less than 20 minutes	£59
	US scan, 20 minutes and over	£40
FAST	US cost used as a proxy	

(a) All CT costs included for comparison.
(b) The costs are sourced from NHS reference costs 2012/13 [37]. Further detail on the costs, such as the ranges and number of submissions, can be found in Appendix O.

11.3.5 Evidence statements

Clinical

Clinical evidence summary: Whole-body CT (head to pelvis) versus selected imaging

Low quality evidence from a single observational comprising of 1607 participants demonstrated a clinical benefit with whole body when compared with selective imaging with regards to mortality at 30 days, with serious imprecision.

Economic

No relevant economic evaluations were identified.

11.3.6 Recommendations and link to evidence

Recommendations	**50. Use whole-body CT (consisting of a vertex-to-toes scanogram followed by a CT from vertex to mid-thigh) in adults (16 or over) with blunt major trauma and suspected multiple injuries. Patients should not be repositioned during whole-body CT.** **51. Use clinical findings and the scanogram to direct CT of the limbs in adults (16 or over) with limb trauma.** **52. Do not routinely use whole-body CT to image children (under 16s). Use clinical judgement to limit CT to the body areas where assessment is needed.**
	Although the major trauma GDG reviewed the question of whole- body CT these recommendations were developed and supported by the evidence reviews addressing the scope area on imaging in each of the four clinical guidelines: • Complex fractures: assessment and management of complex fractures (including pelvic fractures and open fractures of limbs) • Fractures: diagnosis, management and follow up of fractures (excluding head and hip, pelvis, open and spinal) • Major trauma: assessment and management of airway, breathing and ventilation, circulation, haemorrhage and temperature control. • Spinal injury assessment: assessment and imaging, and early management for spinal injury (spinal column or spinal cord injury) In particular the Spinal injuries clinical guideline chapter 10 on radiation and risk should be read in conjunction with this chapter. **Developing the recommendations** Imaging recommendations were developed across the trauma guidelines suite by all the individual GDGs. Evidence reviews were completed for all the guidelines and the separate GDGs reviewed the evidence and drafted recommendations. The overall guideline population of patients with major trauma meant that similarities and duplication between the draft recommendations were inevitable. This needed careful consideration when evaluating all the imaging recommendations with particular thought to the person with multiple injuries. The recommendations were taken to project executive team (PET) for coherence and consistency checking, the PET also had the advantage of identifying gaps in the separate guidelines that had been addressed in another guideline. The PET agreed on a core set of draft recommendations. The core set of recommendations were taken back to each of the separate GDGs for review and agreement. The GDGs had access to the reviews underpinning the recommendations.
Relative values of different outcomes	The GDG considered the following outcomes to be critical in decision making for this review: mortality, health-related quality of life, blood product use and length of intensive care stay. Time to definitive control of haemorrhage, time to surgery, patient-reported

	outcomes (psychosocial wellbeing), long-term radiation risk and delayed/missed injury were considered important. This is because, although time to control of haemorrhage and time to surgery are correlated with patient outcomes, there were too many confounding factors to both these surrogate outcomes for them to be critical to decision making. Psychosocial wellbeing and individual patient-reported outcomes were agreed to be important, but not critical as measures of quality of life encompass all of these and, in some cases, also take into account preferences. Long-term radiation risk and delayed or missed injury, although considered to be very important factors by the GDG, were also felt to be difficult to measure in any meaningful way and so were not critical to decision making. Data was reported for mortality at 30 days only.
Trade-off between clinical benefits and harms	**Adults** The GDG commented on a single observational study comparing trauma patients who underwent a whole-body CT and selective CT imaging, The evidence suggested a clinical benefit with whole-body CT for mortality at 30 days. The GDG discussed the study in consideration with their clinical experience and indicated that whole-body CT was useful in the rapid diagnosis of trauma patients (particularly in those with an ISS above 15).The GDG noted the high sensitivity and accuracy of CT scanners and indicated that a whole-body CT would help physicians prioritise the treatment strategy in order to treat the most life-threatening disorder. Moreover, they noted that the advent of multi-slice CT scanners into many major trauma units has made whole-body CT scanning both technically feasible and common practice. The GDG discussed the limitations with the whole-body CT approach which included delay to definitive treatment. In particular, haemodynamically unstable patients were thought to be at particular risk as CT scanner rooms are not equipped as well to manage deteriorating patients as the resuscitation room. The GDG noted that modern CT machines acquired data quicker, reducing time on the CT scanner and provided directed and beneficial information for definitive treatment. Moreover, trauma CT rooms are geographically closer to the resuscitation room and the patients can be moved relatively quickly. The GDG also identified lifetime radiation risk to be a clinical harm of whole-body CT. The GDG also noted that whole-body CT may lead to unnecessary follow-up appointments for injuries that are not clinically important. In particular, the GDG noted that a whole-body CT scan will give them a radiation dose of more than 20 millisievert. This is twice the level required to give an adult aged 40 years a 1 in 1000 chance of future cancer, as defined by the National Academy of Science's Seventh Assembly of the Committee on Biologic Effects of Ionizing Radiation (ref). The radiation dose alone is, therefore, a valid reason to limit the amount of trauma call patients with low ISS scores routinely undergoing CT scans. The GDG considered the benefits and harms of whole-body CT, along with the evidence, and used consensus to indicate that patients may receive benefits with earlier treatment. This may be particularly relevant for the identification of some injuries, such as spinal injury. Whole-body CT may also reduce missed injuries, and reduce the need for further imaging and is likely to be beneficial in patients with major trauma.

	In the person with suspected multiple injuries it is efficient to scan the person for all potential injuries at one point than to return to the scanner. **Children** The GDG noted that paediatric trauma patients who present with suspected multiple injuries often only have single injury (children with multiple injuries are approximately one in seven cases; TARN children's trauma report 2012). This is in contrary to adult trauma patients, where many adults presenting with a suspected single injury are subsequently identified as having multiple injuries. As a consequence, the potential clinical benefit of whole-body CT may be higher in adult trauma patients. The trade-off in children, particularly for stable patients, is between the high radiation risk from a CT and doing multiple images of other modalities which could be less accurate and also not as good at picking up incidental findings. The GDG felt that it was important to emphasise they would not recommend offering whole-body CT to children, unless it was specifically clinically indicated. At such times they would suggest sticking to the 'as low as reasonably achievable' (ALARA) principle in order to minimise radiation exposure ALARA.
Trade-off between net health benefits and resource use	There was no published economic evidence to inform this question. The GDG took into account the intervention cost of each diagnostic modality, and assessed each modality as outlined in the methods section in their deliberations (that is, taking into account the prevalence, predictive powers, the consequences of each diagnostic outcome in terms of potential net clinical benefit and cost of onward management, and potential incidental findings). The additional exposure to radiation was discussed in relation to the findings of the evidence review undertaken for spinal injuries. The GDG were presented with the costs of the different diagnostic modalities; X-ray had the lowest unit cost (£28), followed by US and FAST (US cost being used as a proxy for FAST), selective CT and whole-body CT had the highest unit cost (£71 for one area and £146 for more than three areas). Strategies involving selective CT would involve the cost of primary assessment (which may incur cost of US or X-ray), and potentially followed by further CT. However, further imaging may be necessary if further areas of the body need investigating but these were not picked up in the initial primary assessment. Whole-body CT on the other hand may also incur some costs involved with primary assessment (that is, to indicate the need for CT) but less likely to incur costs of additional imaging from injuries initially missed in the primary assessment or complications caused by delay to treatment. Whole-body CT may have additional benefits by picking up incidental findings that are not the main injury of interest, however, finding these early could have a positive impact because they could be treated earlier before they lead to a large and potentially fatal impact on the patient. However, whether these findings are clinically meaningful is important. There is also a potential time difference between the two interventions as patients could be taken to the CT scanner for whole-body CT immediately with primary assessment taking place whilst the patient is in the scanner. An assumption might be made that the quicker a patient is imaged the quicker they will be managed definitively. The benefit and cost effectiveness of whole-body CT will depend on the proportion of patients with multiple injuries and/or where their injury has systemic

	consequences and it is difficult to identify the cause. There is a risk that if all patients with traumatic injury undertook a strategy of whole-body CT, that non-clinically significant findings would be worked up at expense. The GDG were particularly mindful that overall specificity and negative predictive power for any injury decreases as more indications are investigated by a diagnostic test, potentially leading to unnecessary use of healthcare resources with increasing false positive results. The GDG came to a consensus that where there is clear evidence of an isolated injury, whole-body CT is unlikely to be cost effective. The GDG considered patients suspected of blunt trauma with multiple injuries to be highly likely to benefit from the strategy, and whole-body CT would be a cost effective strategy in this subgroup. The additional radiation risk of whole-body CT was also discussed; however, it was felt that the benefit of whole-body CT to suspected multiply injured patients would outweigh this risk. Whole-body CT in adults is advocated in current practice; therefore, it was not suspected that the recommendation would result in a large cost impact.
Quality of evidence	A single observational study was identified from the evidence. The populations in both imaging arms were not matched for injury severity, but analysis was conducted using propensity score matching. However, baseline data in the analysed group was not presented and absolute differences could not be reported. Moreover, the evidence demonstrated imprecision and was determined to be very low quality evidence. The GDG also discussed the fact there were no comparisons between full-body CT and other imaging techniques, but were confident that CT would provide the best accuracy and is generally considered the gold standard in diagnosis following major trauma.
Other considerations	If the room is too small to allow full excursion of the patient through the scanner the patient should not be taken out and turned around to allow scanning to feet. This has a delaying effect, and therefore clinical and cost implications.

11.4 Damage control surgery

11.4.1 Introduction

People involved in a traumatic injury that has led to serious active bleeding may experience a potentially lethal triad of effects. Firstly, metabolic acidosis may occur due to poor tissue perfusion and a switch to anaerobic metabolism. Secondly, coagulopathy due to hypoperfusion and tissue injury may ensue. Thirdly, hypothermia due to impaired metabolism and exposure may develop. Together, these effects can quickly lead to the death of the patient. For prevention of the lethal triad, two factors are essential; early control of bleeding and prevention of further heat loss. Damage control surgery may achieve these by avoiding extensive procedures on unstable patients, and instead focussing on stabilising potentially fatal problems at initial operation. This may require an ‘open abdomen’ for several hours or days in intensive care, followed by staged surgery once the patient is stable. In contrast, the more traditional definitive surgery approach, where an attempt is made to fix most surgical problems in one continuous procedure, may avoid the disadvantages inherent with an ‘open abdomen’, such as greater risk of infection and renal failure. However, it is believed that this comprehensive strategy may lead to insufficient emphasis on the priority procedures to prevent the lethal triad. There is little consensus on the best approach, with a wide variation in practice across England and Wales.

11.4.2 Review question: What are the most clinically and cost-effective surgical intervention strategies in the major trauma patient with active haemorrhage (damage control versus definitive surgery)?

For full details see review protocol in Appendix C.

Table 97: PICO characteristics of review question

Population	Children, young people and adults experiencing a traumatic incident.
Intervention	Damage control surgery followed by definitive surgery
Comparison	Definitive surgery
Outcomes	Critical: • Mortality at 24 hours (post damage control surgery and pre-definitive surgery), 30 days/1 month and 12 months • Health-related quality of life • Adverse effects (complications of surgery) Important: • Patient-reported outcomes (psychological wellbeing). • Blood components • Length of stay on ICU
Study design	RCTs or systematic reviews of RCTs; cohorts if no RCTs retrieved (matched at baseline or adjusted for age, Glasgow coma scale, injury severity score and shock)

11.4.3 Clinical evidence

No clinical evidence.

See also the clinical article selection flow diagram in Appendix D and excluded studies list in Appendix K.

11.4.4 Economic evidence

Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow diagram in Appendix E.

Unit costs

Damage control surgery and definitive surgery are management approaches, as opposed to the names of procedures. There are many procedures that can be included within these approaches depending on where/which organ the patient is haemorrhaging from. However, generally damage control surgery will involve temporarily packing the area that is haemorrhaging to try and control the bleed until the patient has become more stable, at which point the patient will be taken back into theatre where the source of the haemorrhage will be definitively controlled. This strategy is compared with straight to definitive surgery.

Effectively, damage control surgery followed by definitive surgery would be two operations whereas straight to definitive surgery would only involve one operation (assuming there is no need for re-operations which might happen in a small numbers of cases).

Both of these management approaches would generally involve a laparotomy of some description.

Costing by procedure

An exploratory laparotomy has an OPCS code (a procedure code) of T30.9 (sourced through OPCS version 4.6. reviewer software)[62]. This OPCS codes to the Health Resource Groups (HRG) detailed in Table 98.

Table 98: HRG code data [37]

Intervention/ diagnosis	Reference cost HRG	National average unit cost	Lower Quartile Unit Cost	Upper Quartile Unit Cost	Average cost of excess bed day	Lower quartile unit cost	Upper quartile unit cost	Weighted national average	Average length of stay	Notes
Exploratory laparotomy (OPCS code T30.9)	Complex General Abdominal Procedures with CC Score 3-5 (FZ79D)	**£3,342**	£3,342	£3,342	NA	NA	NA	NA	6	Only 1 data submission Setting is: non-elective inpatient long stay
Exploratory laparotomy (OPCS code T30.9)	Complex General Abdominal Procedures with CC Score 0-2 (FZ79E)	**£9,020**	£8,050	£9,990	NA	NA	NA	NA	22.5	Only 2 data submissions Setting is: non-elective inpatient long stay

Notes: HRG chapter FZ represents the 'Digestive system procedure and disorders' subchapter of the HRG groupings, and the HRG code FZ79 describes 'Complex general abdominal procedures'.

CC stands for 'complications and co-morbidities', a higher score reflects more major complications and co-morbidities.

There are no submissions under the category trauma and orthopaedics for CC score 6+, therefore, these costs have not been weighted for complications and comorbidities.

Different costs are associated for the same HRG code depending on the service description, the costs presented in the table above are those associated with the 'Trauma and Orthopaedics' service description.

This data should be taken with caution as there are various limitations:

- Exploratory laparotomy is one example of the type of surgery that could take place, and is dependent on where the haemorrhage is (the above costs relate to abdominal surgery). Given the wide array of surgery that these management techniques could include, it is likely that the coding of surgery will also be variable between patients and between hospitals. This means costs presented should be interpreted with caution.
- Both management approaches may have been coded within this one HRG code, so incremental differences in cost cannot be assumed.
- These costs are based on very few data submissions with FZ79E being based only on two patient episodes, and FZ79D being based only on one patient episode. This means that these costs are not likely to be representative due to the poor quality data, in other words, there are not enough submissions to represent meaningful national averages of what the procedures cost to undertake.
- There is also a third category of complications and co-morbidities (CC score of 6+), however, there was no submission for this under the service description code of 'Trauma and orthopaedics', therefore, it was not possible to take a weighted average of all the CC categories.
- Additionally, we tend to weight the NHS reference costs by excess bed days (to ensure a like for like comparison of activity and costs, NHS reference costs show separately the costs of bed days that fall inside and outside nationally set lengths of stay, known as trim points. Costs that fall outside the trim point are known as excess bed day costs), however, no excess bed day costs were reported for these HRG codes with our desired service description (trauma and orthopaedics).

If we continue with the simple fact that our intervention strategy of damage control surgery first followed by definitive surgery will essentially involve two operations, whereas the comparator of straight to definitive surgery will involve one, then one can make the assumption that on a basic level, the intervention will cost roughly twice that of the comparator. However, caution must be taken when using this cost data as there is uncertainty as to how these procedures would be coded and therefore, it may not necessarily be the case that the damage control strategy would be twice the cost of the estimates above, especially if some aspects of the first procedure negates time being spent on the same aspects of the second procedure.

Costing by theatre time

Another method to identify the costs of the surgical strategies is to cost up the theatre time that would be involved. GDG member opinion was that damage control surgery would involve 1 hour of theatre time, whereas definitive surgery could take between 2 and 3 hours.

Table 99: Duration of operations

Surgery type	Approximate duration	Source
Damage control	Maximum 1 hour	Expert clinical opinion
Definitive surgery	2-3 hours	Expert clinical opinion
Strategy as defined by protocol	**Total approximate theatre time**	**Source**
Damage control and definitive surgery	3-4 hours	Expert clinical opinion
Definitive surgery	2-3 hours	Expert clinical opinion

Cost of theatre time per minute was identified through GDG contact. This cost is based on 2013/14 data from one hospital[b] and includes general theatre pay and non-pay costs (including nursing costs,

[b] Sourced from University Hospital Southampton cost data. Based on E and F level theatre costs combined (with F level theatres doing mainly orthopaedic work).

surgical equipment and consumables), consultant costs (one anaesthetist and one consultant) and overheads at a rate of 15% of the direct costs. This leads to a total theatre cost of £16.48 per minute.

Table 100: Cost of strategies using cost per theatre minute approach

Surgery type	Total approximate theatre time	Total number of minutes	Total cost
Damage control and definitive surgery	3-4 hours	240	£3,956
Definitive surgery	2-3 hours	180	£2,967

Note: The total cost is based on the maximum time, so for the damage control strategy this is 4 hours multiplied by the cost per minute of £16.48.

These costs are estimates and should be taken with caution. Furthermore, we have not accounted for the care given to the patient before or after each surgical procedure (that is, time on ICU, need for transfer) or the costs due to differential clinical outcomes (complications, blood product use). The staff costs are based on the service delivery scenario of one hospital. Cost of staffing may increase or decrease according to the specific service arrangement in place (such as on call, on site, size of rota staffing arrangements).

Costs of adverse events and outcomes

In order to give an indication of the potential resource use involved, we looked at applicable studies of the clinical review which were excluded due to methodological limitations.

Table 101: Unit costs and example resource use

Resource	Cost per unit	Example resource use (assumption)	Example costing for a patient	Source
ICU stay[a]	£852 per day	10 days	£8,519	NHS reference costs 2012/13.[37] Adult critical care unit costs
Blood products				
pRBCs	£122 per pack	10 units	£1,221	Blood and Transplant Price List 2014/15 [105]
FFP [b]	£28 per pack	10 units	£280	Blood and Transplant Price List 2014/15
Platelets	£197 per pack (one adult therapeutic dose)	7.5 units	£1,477	Blood and Transplant Price List 2014/15
Pooled cryoprecipitate (5 packs)[b]	£181	2 pooled packs	£362	Blood and Transplant Price List 2014/15
Crystalloids				
0.9% Sodium Chloride	£0.70 per 1000 ml bag	2000 ml	£1.40	CG174 Intravenous fluid therapy in adults in hospital: Appendix M (Types of intravenous fluids for resuscitation) ref
Hartmann's Solution	£0.85 per 1000 ml bag	2000 ml	£1.70	
Plasmalyte M	£0.91 per 1000 ml bag	2000 ml	£1.84	
Ringer's Lactate	£1.25 per 500 ml bag	2000 ml	£5.00	

Abbreviations: pRBC, packed red blood cells; FFP, fresh frozen plasma; ICU, intensive care unit

(a) This cost is for 1 organ being supported (conservative assumption that the haemorrhage is coming from a vital organ).
(b) These products are more expensive for those born after 1996 as they must use methylene blue-treated products.
(c) Please note that the literature was not informative of the potential resource use of factor 7 or crystalloids, despite having citing the use of these products as important to measure in their outcomes. We asked the GDG to advise if they have any information which would assist the costing of these products.

11.4.5 Evidence statements

Clinical

No relevant clinical evaluations were identified.

Economic

No relevant economic evaluations were identified.

11.4.6 Recommendations and link to evidence

Recommendations	**53. Use damage control surgery in patients with haemodynamic instability who are not responding to volume resuscitation.** **54. Consider definitive surgery in patients with haemodynamic instability who are responding to volume resuscitation.** **55. Use definitive surgery in patients whose haemodynamic status is normal.**
Relative values of different outcomes	The critical outcomes for decision making were mortality, health related quality of life and complications from surgery. Important outcomes were blood product use for haemodynamic status, ICU length of stay and patient reported outcomes.
Trade-off between clinical benefits and harms	In the absence of any eligible evidence, the GDG discussed the benefits and harms of damage control surgery compared with definitive surgery for adults and children who have experienced a major trauma. It was felt that adults and children assessed in the emergency department as being haemodynamically stable should be offered definitive surgery as damage control surgery may carry the risk of more abdominal complications. However, it was also felt that those adults who are assessed as being unstable and deteriorating would require urgent damage control surgery, as only this approach meets their primary need to achieve haemostability through control of their haemorrhage. This was considered by the group to be standard practice, but they identified that variation in practice occurs due to triage destination in the pre-hospital phase of a patient's care pathway.
Trade-off between net health benefits and resource use	No economic evidence was identified comparing damage control surgery followed by definitive surgery versus straight to definitive surgery. The GDG were presented with cost estimates for the two strategies. Using NHS reference costs was one method used to try and derive the cost of the strategies, by linking an OPCS code related to 'exploratory laparotomy' to a HRG. However, limitations of this method include lack of clarity as to how the strategies would be coded, therefore, implying there might not be an incremental cost difference using this method, additionally there were very few data submissions. A second method used to derive the costs of the strategies involved costing up the

	total theatre time involved. A cost per minute of theatre time was derived through GDG contact (£16.48 – including one consultant, one anaesthetist, nursing staff, consumables and overheads); multiplying this by the estimated time taken for the two strategies (4 hours for the intervention and 3 hours for the control) gave total procedure costs of £3,956, and £2,967, respectively. No clinical evidence was identified due to methodological flaws within the potentially includable studies. Thus, it was not possible to identify the difference in benefit, complication rates or resource use between the strategies. However, using the potentially includable studies, estimates of potential resource use, such as ICU stay, and blood components were presented to the GDG. The intervention of damage control surgery followed by definitive surgery will involve more staff time as this is essentially two operations. Furthermore, resources may be invested in the intermediate time between damage control surgery and the definitive control of surgery (that is, time on ICU). However, differences in the complication rate from the two strategies may have a higher impact on total costs from a strategy than the intervention costs themselves. The GDG took a practical approach of recommending damage control surgery in the unstable patients not responding to volume resuscitation, and definitive surgery in the responding and stable patients. This was seen to be standard practice.
Quality of evidence	No clinical evidence was found. **Economics** Costs were gathered for surgery from NHS reference costs by identifying which HRG code included and OPCS code related to exploratory laparotomy. The costs identified had only one or two data submissions; therefore, this is very low quality data that cannot be used to draw any firm conclusions.
Other considerations	Damage control surgery should be deliverable in major trauma centres and all trauma units. Expertise, skills and resources should be available to deliver this. The GDG did not identifying any considerations specific to children.

11.5 Interventional radiology

11.5.1 Introduction

Endovascular techniques to achieve haemostasis are well established in the non-trauma setting; however, their role in trauma is less defined. The use of interventional radiology may increase the number of patients who are successfully managed non-operatively or act as a bridge to definitive surgery in initially unstable patients.

The aim of this review was to determine whether the use of interventional radiology for definitive haemorrhage control in major trauma patients is clinically and cost effective.

11.5.2 Review question: Is the use of interventional radiology for definitive haemorrhage control in major trauma patients clinically and cost effective?

For full details see review protocol in Appendix C.

Table 102: PICO characteristics of review question

Population	Children, young people and adults experiencing haemorrhage due to a traumatic incident.

Intervention(s)	Therapeutic interventional radiology • Stent grafts • Embolization (coil, plug, embolotherapy)
Comparison(s)	Definitive Surgery Damage control surgery No intervention
Outcomes	Critical: • Mortality at 24 hours, 30 days/1 month and 12 months • Health-related quality of life • Failure rate or re-intervention rate • Adverse effects ○ ischaemic damage ○ necrosis ○ renal failure • Blood product use • Length of intensive care stay • Time to definitive control of haemorrhage Important: • Patient-reported outcomes: ○ pain/discomfort ○ return to normal activities ○ psychological wellbeing
Study design	RCTs or systematic reviews of RCTs; cohorts if no RCTs retrieved (matched at baseline or adjusted for age, Glasgow coma scale, injury severity score [ISS] and shock)

11.5.3 Clinical evidence

Three cohort studies were identified [9,10]; [35,36]; [74,74]. Two cohort studies, one retrospective and one prospective, were on blunt aortic injuries [9,10]; [35,36]. One retrospective cohort study was on pelvic fracture. These are summarised in Table 103 below. In only one study were all patients actively bleeding[74,74]. Evidence from these studies is summarised in the clinical evidence summary below.

Table 103: Summary of studies included in the review

Study	Intervention/ comparison	Population	Outcomes	Comments
Azizzadeh 2013[9,10]	Endovascular repair (TAG and Talent); n=50 Operative repair; n=56	Blunt traumatic aortic injuries 2002-2010. Included patients with intramural haemorrhage and aortic pseudoaneurysm who underwent elective repair after treatment for associated injuries and patients with free rupture who underwent immediate repair. Mean (SD) age: operative repair n=32 (14) Endovascular repair 41	Complications including in-hospital mortality ICU length of stay	Prospective cohort with adjust analysis. Before 2005 all patients underwent operative repair. The suitability for endovascular repair was determined by the aortic diameter according to the manufacturers sizing recommendations.

Study	Intervention/ comparison	Population	Outcomes	Comments
		(20)		
Demetriades 2008[35,36]	Endovascular repair (stent graft); n=125 Operative repair; n=68	Blunt thoracic aortic injuries. Initial tear n=20.5% Aneurysm 58.4% Dissection 25.4% Mean (SD) ISS 39.5 (11.7) Mean (SD) age 40.2 (18.7) years	In-hospital mortality Any systemic complication ICU length of stay	Retrospective cohort with adjusted analysis. Intervention decided by surgeon preference. Multicentre Hours from injury to procedure (all patients) mean (SD) 54.6 (101.6)
Katsura 2013[74,74]	Endovascular repair (trancatheter arterial embolization); n=194 Operative repair; n=123	Blunt pelvic fracture and haemoperitoneum. Excluded severe head injury (abbreviated injury score ≥5) and those who underwent different first initial intervention. Mean age (SD) 48.8 (22.5) years. mean ISS (SD) 37.4 (13.9)	Mortality (in-hospital)	Retrospective cohort with adjusted analysis. Multicentre. No details of time to intervention.

Table 104: Clinical evidence summary: blunt aortic injuries – open versus endovascular

Outcome	Number of studies (no. of patients)	Imprecision	GRADE rating	Absolute difference	Control event rate (per 1000)	Relative OR (95%CI) (adjusted) Open versus endovascular	Control event rate for continuous outcomes
Mortality (in hospital)	1 (n=193)	None	VERY LOW	-	-	8.42 (2.76 to 25.69)	-
Any systemic complication	1 (n=193)	Very serious	VERY LOW	-	-	1.41 (0.75 to 2.34)	-
ICU length of stay days	1 (n=193)	None	VERY LOW	MD 1.28 higher (2.41 lower to 4.98 higher)	-	-	-
Hospital length of stay days	1 (n=193)	None	VERY LOW	MD 4.77 higher (5.33 lower to 14.86 higher)	-	-	-
Blood transfusion units	1 (n=193)	None	VERY LOW	MD 4.98 higher (0.14 to 9.82 higher)	-	-	-

Table 105: Clinical evidence summary: blunt aortic injuries – endovascular versus open

Outcome	Number of studies (no. of patients)	Imprecision	GRADE rating	Absolute difference	Control event rate (per 1000)	Relative OR (95%CI) (adjusted) Endovascular versus open	Control event rate for continuous outcomes
Any systemic complication	1 (n=106)	Serious	VERY LOW	-	-	0.33 (0.11 to 0.99)	-
ICU length of stay days	1 (n=106)	Serious	VERY LOW	MD 1.85 lower (7.79 lower to 4.09 higher)	-	-	17.43

Table106: Clinical evidence summary: pelvic fracture

Outcome	Number of studies	Imprecision	GRADE rating	Absolute Difference	Control event rate (per 1000)	Relative OR (95%CI) (adjusted) Open versus endovascular	Control event rate for continuous outcomes
Mortality (in hospital) (regression analysis)	1 (n=317)	Very serious	VERY LOW	-	-	1.20 (0.61 to 2.39)	-
Mortality (in hospital) (propensity score)	1 (n=317)	Very serious	VERY LOW	-	-	1.13 (0.69 to 2.01)	-

Narrative review

Complications

One prospective cohort study on patients with blunt thoracic aortic injuries[35,36] reported the following complications in the endovascular group:

- Endoleak 13.6%
- Any stent graft complication 18.4%
- Any stent graft related complication excluding endoleak 4.9%
- Procedure-related paraplegia was reported in 2.9% open repair and 0.8% endovascular repair (p=0.28)

11.5.4 Economic evidence

Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow chart in Appendix E.

Unit costs

Some examples of the costs of the types of interventional radiology can be found below. The specific names of the procedures and Health Resource Groups (HRG) codes have been provided by GDG members.

Table 107: Interventional radiology costs from NHS reference costs 2013/14[38]

Intervention	Reference cost HRG	Weighted national average cost[a]
Embolisation	Percutaneous Transluminal Embolisation of Blood Vessel; Weighted for complications and co morbidities for HRG codes: YR21A and YR21B; as recorded for Non-Elective Inpatients long stay	£5,620
Stent graft[b]	Percutaneous transluminal angioplasty with insertion of stent graft into peripheral blood vessel; YR12Z, as recorded for non-elective inpatients	£9,067

(a) Weighted for excess bed days.
(b) The specific HRG for thoracic stent grafts could not be identified, however GDG opinion was that this would cost around £10,000. This is likely to include the costs of the stents.

For surgery costs please see section 11.4.4. Note these are likely to be underestimated for aortic injury patients.

11.5.5 Evidence statements

Clinical

Blunt aortic injuries

Very low quality evidence from 1 cohort study comprising 193 participants showed that open repair was associated with a clinically important higher mortality rate in-hospital compared with endovascular repair, with no imprecision.

Very low quality evidence from 1 cohort study comprising 193 participants showed that open repair was associated with a clinically important higher rate of any systemic complication compared with endovascular repair, with very serious imprecision.

Very low quality evidence from 1 cohort study comprising 193 participants showed that open repair was associated with a clinically important longer length of ICU and hospital stay compared with endovascular repair, with no imprecision.

Very low quality evidence from 1 cohort study comprising 193 participants showed that open repair was associated with a clinically important higher rate of blood components transfused compared with endovascular repair, with no imprecision.

Very low quality evidence from 1 cohort study comprising 106 participants showed that endovascular repair was associated with a clinically important rate of any systemic complication compared with open repair, with serious imprecision.

Very low quality evidence from 1 cohort study comprising 106 participants showed that endovascular repair was associated with a clinically important lower length of ICU stay rate compared with open repair, with serious imprecision.

Pelvic injury

Very low quality evidence from 1 cohort study comprising 317 participants showed that there was no clinical difference between open repair and endovascular repair in terms of mortality, with very serious imprecision

Economic

No relevant economic evaluations were identified.

11.5.6 Recommendations and link to evidence

Recommendations	**56. Use interventional radiology techniques in patients with active arterial pelvic haemorrhage unless immediate open surgery is needed to control bleeding from other injuries.** **57. Consider interventional radiology techniques in patients with solid-organ (spleen, liver or kidney) arterial haemorrhage.** **58. Consider a joint interventional radiology and surgery strategy for arterial haemorrhage that extends to surgically inaccessible regions.** **59. Use an endovascular stent graft in patients with blunt thoracic aortic injury.**

	In addition to the major trauma GDG reviewing the clinical and cost effectiveness of the use of interventional radiology for definitive control, the complex fractures GDG reviewed what was the most clinically and cost effectiveness invasive technique for control of bleeding in pelvic ring fractures. Developing the recommendations Evidence reviews were completed for all the guidelines and the separate GDGs reviewed the evidence and drafted recommendations. The same evidence was identified for both reviews. The overall guideline population of patients with pelvic bleeding meant that similarities and duplication between the draft recommendations were inevitable. The recommendations were taken to the project executive team (PET) for coherence and consistency checking. The PET agreed with the recommendations in both of the guidelines.
Relative values of different outcomes	The critical outcomes were mortality, health related quality of life, failure rate or re-intervention rate, adverse events, blood product use, length of intensive stay and time to definitive control of haemorrhage. Important outcomes were patient-reported outcomes, pain/discomfort, return to normal activities and psychological wellbeing.
Trade-off between clinical benefits and harms	**Blunt traumatic aortic injury** One study (Dematrides) on thoracic aortic injury reported that open repair was associated with a clinically important higher rate of mortality compared with endovascular repair, with no imprecision. Open repair was also associated with a clinically important higher rate of systemic complications compared with endovascular repair, but with very serious imprecision. Length of ICU and hospital stay was longer with open than endovascular repair. The number of blood components used was higher with open repair than endovascular repair. The incidence of procedure related paraplegia was lower with interventional radiology than open repair. The second study (Azizzadeh) reported that endovascular repair compared with open repair was associated with a clinically important reduction in any complication, including in-hospital mortality (serious imprecision), and length of intensive care stay (no imprecision). It was noted that not all patients in either study underwent immediate interventional radiology and those that did were not reported separately. Some minor aortic injuries do not need surgery and can be managed with observation. The GDG noted that endovascular repair avoids thoracotomy, single-lung ventilation, aortic cross-clamping or cardiopulmonary bypass, and the more complex anaesthetic techniques required for open repair. This must be balanced against the need for long-term imaging surveillance in those treated with a stent-graft **Active arterial pelvic haemorrhage** One study of pelvic fractures reported no clinical difference in mortality between endovascular and open repair, but with serious imprecision. The GDG considered that the less invasive option of embolisation (interventional radiology) should be used where the available evidence reports equivalent mortality rates as they might differ in more subtle ways, such as the re-operation rate, adverse effects or length of stay. **Solid organ arterial haemorrhage** No evidence was identified. Unplanned splenectomy is associated with high rates of infection and mortality. Embolisation on the spleen preserves the splenic bulk and immune

	function. Interventional radiology of the kidney preserves tissue whereas surgery often involves nephrectomy. Generally for embolisation, the size of the arterial supply that is occluded (greater surety of haemorrhage control) needs to be balanced against the risk of ischaemic damage. If bleeding recurs embolisation can be repeated.
Trade-off between net health benefits and resource use	No economic evidence was identified for this question. Interventional radiology uses angiography to guide treatment and is performed by inserting tubes of a wide range of sizes (depending on the treatment being performed) into blood vessels, most commonly via the groin. Interventional radiology requires specialist X-ray imaging equipment and an interventional radiology team (radiologist, radiology scrub nurse and radiographer) to be available and thus, may take more time to prepare when teams are on-call. Interventional radiology doesn't usually take place in theatre, however, hybrid theatre and interventional radiology suites are becoming increasingly common. The procedure is not as invasive as surgery (less physiological insult), and the costs of setting up the theatre (for example, theatre staff, including surgeons and anaesthetists) are likely to be similar to those of preparing the interventional radiology in hybrid theatres. Additionally, only interventional radiology is likely to be a definitive procedure if successful. In surgery fixation, clamps and packing are temporary measures of haemorrhage control and likely to involve subsequent operations to definitively control the haemorrhage. There are 2 common populations with a traumatic haemorrhage which are likely to be selected for interventional radiology; those with arterial or solid organ injury that could be treated with embolisation, and those with aortic injury who could be treated using stents. In terms of costs, both surgery and interventional radiology can cost thousands of pounds depending on the time taken due to the complexity of individual cases, and the staff needed. The cost of embolization is variable depending on the agent used and the number of bleeding sites treated. Embolisation of aneurysm of a blood vessel can cost around £5,000 to £6,000 (NHS reference costs). Whereas surgery (damage control followed by definitive surgery if costed by theatre time) costs under £5,000. The success rate of interventional radiology will determine if further operations are needed. Assuming that embolisation is successful in 95% of cases. Then 5% will require an operation after embolisation. If definitive haemorrhage control takes 3 hours (which equates to roughly £3,000), then the cost of embolisation would actually be £5,620 + (0.05*£3,000) = £5,770. When factoring in the costs of the re-operations that are likely to be needed for definitive control from other interventions, then interventional radiology may be cheaper than other interventions. Additionally, if the interventional radiology is done within theatre or in an adjoining suite surgery can continue on from the interventional radiology if necessary. This reduces the re-operation cost further, as the costs of setting up the theatre and the staff involved would already apply for the interventional radiology. The GDG felt that it is quite rare that interventional radiology fails, and therefore, the cost is likely to be lower than demonstrated here.

	The complication rates of the two methods also need to be taken into account, which can vary depending on the location of the bleed as mentioned above and the patient's physiological status. Surgery is assumed to be riskier because of the nature if it being more invasive. For aortic injuries, surgery is likely to be more complex as patients may need to be put on bypass so more equipment is needed. Additionally, there are higher risks with aortic surgery, such as paraplegia (these can be as high as 16-18% of cases, in GDG opinion) as the thoracic aorta supplies the spine with blood. Therefore, the surgery cost mentioned in the preceding paragraph, is likely to be underestimated for aortic patients. Thoracic stent grafts cost varies by length, with the most commonly used length used to treat traumatic aortic injury costing around £10,000 (from NHS reference costs). Resource use, such as length of hospital stay, and blood components use are also important to consider when comparing the interventions and comparators. The less invasive technique may need more follow up appointments (for example, imaging) to check the integrity and stability of a thoracic stent graft, however, may have a shorter hospital stay compared with surgery because it is less invasive. In summary, for pelvic injuries, the cost of interventional radiology is likely to be slightly higher than that of surgery, however, for aortic injuries it is possible that surgery costs will be higher. In addition, other factors, such as adverse events and downstream resource use, may favour interventional radiology in terms of cost effectiveness. The GDG felt that the benefits of interventional radiology were likely to outweigh the additional costs. The GDG discussed how interventional radiology services across the country are variable [107], however, access to interventional radiology is available in major trauma centres (MTCs), but time to access could improve to be in line with that of surgery. Consensus recommendations were therefore agreed to try and set a standard for the use of interventional radiology and which injuries would benefit from this. Service delivery implications around interventional radiology are discussed in the major trauma services guideline.
Quality of evidence	The three included studies were all cohort studies with adjusted analysis. For the two studies on thoracic aortic injury the type of intervention was according to clinician preference. The cohort study on the pelvic haemorrhage was limited by possible selection and attrition bias. The study conducted a propensity score-adjusted regression analysis, adjusting for age, ISS and other potential confounders. All of the outcomes were graded very low. No data was reported for time to definitive control of haemorrhage, failure rate or re-intervention rate, health-related quality of life or any of the important outcomes.
Other considerations	The GDG discussed the following when considering the evidence. The studies may be prone to survivor bias. The patients who get open surgery operated on might die before interventional radiology is available, thus making mortality look higher from surgery. However, it is possible that the selection bias might apply in reverse with the frail elderly getting interventional

	radiology and the physiologically fit young being selected for surgery. This makes it difficult to interpret the mortality data when comparing open surgery and interventional radiology. In current specifications for MTCs there must be access to surgery within 30 minutes and interventional radiology within 60 minutes. The GDG believe that interventional radiology should also be available within 30minutes. The patient shouldn't be disadvantaged by the modality of definitive intervention. The GDG recognised that delivering interventional radiology treatment within 30 minutes of identification of the need for treatment would require pre-alert systems for interventional radiology teams in many MTCs. The GDG noted that patients who are actively bleeding or at risk of bleeding should ideally be treated in a MTC and that appropriate resuscitation facilities should be available in the interventional radiology suite. Trauma units do not have the capacity to perform immediate interventional radiology. The GDG clarified 'inaccessible body regions', an example of body regions that may be inaccessible and need joint interventional radiology/surgical intervention deep in the pelvis and behind the mandible. The GDG did not identify any considerations specific to children.

12 Monitoring

12.1 Coagulation testing

12.1.1 Introduction

People who have traumatic injuries can experience coagulopathy. This is normally diagnosed and treated on the basis of a number of laboratory tests, for example a clotting screen. These tests take place outside of the resuscitation room and have a turnaround time of at least 30 minutes from sample delivery to the laboratory. There are now point-of-care (POC) tests that can be run by the trauma team in the resuscitation room that have much faster turnaround times and possibly superior outputs. These include POC international normalised ratio (INR) devices, for example, CoaguChek. These devices are typically hand-held and mimic a clotting screen by measuring the INR of a patient's blood. They have a turnaround time under 5 minutes. POC thromboelastography (TEG) and rotational thromboelastometry (ROTEM) are more complex diagnostic tools that are currently used to detect coagulopathy in ITU and surgical settings and could be useful in the context of trauma care. They measure a range of parameters, for example the maximum clot firmness (MCF) of blood. These are different parameters to those measured by laboratory tests. Their turnaround times vary depending on parameter but initial results can be available after 15 minutes.

12.1.2 Review questions:

a) **Is the use of point-of-care coagulation testing versus laboratory coagulation testing clinically and cost effective in people with major trauma?**
b) **What is the diagnostic accuracy of point-of-care coagulation testing versus laboratory coagulation testing in people with major trauma?**

This review sought to identify whether POC coagulation testing leads to better outcomes for people who have experienced a traumatic incident than laboratory coagulation testing. Initially, we developed a diagnostic RCT review protocol to examine the clinical and cost-effectiveness of the different testing modalities (question A). However, the literature searches indicated that there were no relevant RCTs, and as per the review protocol, a second question was drafted to find the diagnostic accuracy (question B) of POC coagulation testing. For full details of both protocols, see Appendix C.

Table 108: PICO characteristics of diagnostic RCT review question

Population	Children, young people and adults with haemorrhage who have experienced a traumatic incident.

Interventions	• TEG
	• Modified TEG
	• ROTEM
	• POC INR:
	  ○ CoaguChek
	  ○ INRatio
	  ○ ProTime

Comparisons	• Clotting screen • Laboratory TEG or ROTEM • Fibrinogen • Platelet count
Outcomes	Critical:

	• Mortality at 24 hours, 30 days/1month and 12 months • Health-related quality of life • Length of intensive care stay • Blood product use Important: • Time to definitive control of haemorrhage • Time to availability of result
Study design	RCTs or systematic reviews of RCTs

Table 109: PICO characteristics of diagnostic accuracy review question

Population	Children, young people and adults with haemorrhage who have experienced a traumatic incident.

Index tests	• TEG
	• Modified TEG
	• ROTEM
	• POC INR:
	  ○ CoaguChek
	  ○ INRatio
	  ○ ProTime

Reference standards	• Clotting screen • Laboratory TEG or ROTEM • Fibrinogen • Platelet count
Outcomes	Diagnostic accuracy
Study design	Observational studies

12.1.3 Clinical evidence

Diagnostic RCT review

No relevant clinical studies were identified.

Diagnostic accuracy review

Nine studies were included in the review.[25,25,31-33,33,59,60,69,70,83,83,90,91,124,124,141,141]

Four of these studies[25,25,31-33,33,90,91] evaluated the diagnostic accuracy of hand held INR devices against a reference standard (laboratory tests) and are summarised in Table 110 with clinical evidence profiles in Table 113.

Three of these studies[59,60,83,83,124,124,141,141] evaluated the diagnostic accuracy of POC ROTEM against a reference standard (laboratory tests) and are summarised in Table 111 with clinical evidence profiles in Table 114.

One study[69,70] evaluated the diagnostic accuracy of POC TEG against a reference standard (future need for transfusion) and is summarised in Table 112 with clinical evidence profile in Table 115.

A cut-off is a threshold at which a test is considered positive, for example an INR of greater than 1.4 might be considered a positive test for coagulopathy. These are well established for the reference standards (laboratory tests), but are not well established for the index tests. Some investigators specified a cut-off before their study began (pre-set) and others chose the best possible cut-off after

the study was completed on the basis of the results (optimised). Optimised cut-offs give an idea of how good a test could be in ideal circumstances while pre-set cut-offs are a better model of real world clinical practice. Four studies[25,25,69,70,83,83,124,124] used an optimised cut-off for their accuracy calculations and four[31-33,33,90,91,141,141] used a pre-set cut-off. One study reported both.[59,60]

See also the study selection flow chart in Appendix D study evidence tables in Appendix G, forest plots in Appendix J, GRADE tables in Appendix I and excluded studies list in Appendix K.

Table 110: Summary of diagnostic accuracy of hand held INR devices (CoaguChek XS/INRatio) studies included in the review

Study	Population	Index test(s)	Reference test/ target condition	Comments
Cotte 2013[25,25]	n=40 Trauma patients (adults and children) French military hospital in Afghanistan 70% penetrating injuries, 95% male. Excluded pre-existing non-traumatic coagulopathy	CoaguChek XS Performed by a hospital anaesthesiologist	Laboratory prothrombin time (PT)	Optimised cut-off for accuracy calculations
Davenport 2011[31,32]	n=300 Trauma patients (>15 years) who met local criteria for full trauma team activation UK Excluded patients taking anticoagulant medications and those with a known bleeding diathesis	CoaguChek XS	Laboratory PT	Pre-set cut-off for accuracy calculations
David 2012[33,33]	n=48 Trauma patients France Excluding those on VKA treatment	INRatio Monitoring System	Standard INR laboratory coagulation assay	Non-consecutive people Pre-set cut-off for accuracy calculations and post-hoc analysis
Mitra 2012[90,91]	n=72 Trauma patients (who met trauma call-out criteria and COAST score ≥3) Australia	CoaguChek XS Performed In resuscitation bay	Standard INR laboratory coagulation assay Target condition: acute traumatic coagulopathy	Pre-set cut-off for accuracy calculations

Table 111: Summary of diagnostic accuracy of ROTEM studies included in the review

Study	Population	Index test(s)	Reference test/ target condition	Comments
Hagemo 2015[59,60]	n=808 Adult trauma patients requiring full trauma team	ROTEM Test performed	Massive transfusion (10 or more units of PRBC within 24 hours)	Pre-set and optimised cut-offs used for

Study	Population	Index test(s)	Reference test/ target condition	Comments
	activation UK, Denmark, Norway Excluded patients on oral anticoagulant treatment (except aspirin)	by dedicated study personnel		accuracy calculations
Levrat 2008[83,83]	n=23 Trauma patients France Excluded patients on oral anticoagulant treatment.	ROTEM	Euglobulin lysis time (ELT). Target condition: hyperfibrinolysis.	Optimised cut-off for accuracy calculations
Rugeri 2007[124,124]	n=88 Trauma patients (not on oral anticoagulant treatment) France Excluded patients on oral anticoagulant treatment.	ROTEM	Laboratory PT, INR, activated partial thromboplastin time (aPTT), fibrinogen, platelets, haemoglobin Target condition: need for transfusion	Optimised cut-off for accuracy calculations
Woolley 2013[141,141]	n=48 Trauma patients who met criteria for full trauma team activation UK military hospital in Afghanistan 100% male	ROTEM Performed by designated OR staff	Laboratory PT Target condition: coagulopathy.	18 (38%) patients did not receive index test or gold standard Pre-set cut-off for accuracy calculations

Table 112: Summary of diagnostic accuracy of TEG studies included in the review

Study	Population	Index test(s)	Reference test/ target condition	Comments
Jeger 2012[69,70]	n=76 Trauma patients (>16 years) with suspected multiple injuries Switzerland	Kaolin TEG Rapid TEG Performed by physician in resuscitation bay	Future need for transfusion within 24 hours	Non-consecutive patients. Optimised cut-off for accuracy calculations

Table 113: Clinical evidence profile: diagnostic accuracy of hand held INR (CoaguChek XS/INRatio)

Number of studies	n	Risk of bias	Inconsistency	Indirectness	Imprecision	Sensitivity (95% CI)	Specificity (95% CI)	Quality
CoaguChek XS in comparison to reference standard (laboratory PT/ INR)								
1	40	Not serious	NA	None	Serious[d]	0.77[b]	0.94	MODERATE
1	300	Not serious	NA	None	Serious[d]	0.77[a]	0.77	MODERATE
1	72	Not serious	NA	None	Very serious[d]	0.63[a] (0.46 to 0.78)	0.88 (0.73 to 0.97)	LOW
INRatio in comparison to reference standard (laboratory PT/INR)								
1	48	Serious[c]	NA	None	Very serious[d]	0.50[a] (0.21 to 0.79)	1 (0.91 to 1)	VERY LOW
1	48	Serious[c]	NA	None	Very serious[d]	0.83 (0.52 to 0.98)	0.89 (0.75 to 0.97)	VERY LOW
1	48	Serious[c]	NA	None	Very serious[d]	0.92 (0.62 to 1)	0.79 (0.63 to 0.90)	VERY LOW

(a) Pre-set cut-off for all accuracy calculations.
(b) Optimised cut-off for all accuracy calculations.
(c) Studies were downgraded by one increment for limitations in one risk of bias domain or by two increments for risk of bias in two or more domains. Studies were assessed using the QUADAS –II criteria. Risk of bias domains: patient selection, index test, reference standard, flow and timing.
(d) Imprecision was assessed using the confidence interval of the sensitivity value. For studies with only area under the curve (AUC) data precision was based on the corresponding 95% CI. Downgrading by one increment was applied for confidence intervals 10-20% or by two increments for confidence intervals more than 20%. If no variance data was available (imprecision could not be assessed) the studies were downgraded by one increment.

Table 114: Clinical evidence profile: diagnostic accuracy of ROTEM

Number of studies	n	Risk of bias	Inconsistency	Indirectness	Imprecision	Sensitivity (95% CI)	Specificity (95% CI)	Quality
ROTEM in comparison to reference standard (ELT) to identify hyperfibrinolysis								
1	23	Not serious	NA	None				
	Parameter: CA_{10}				Serious[d]	1[b] (0.81 to 1)	1 (0.48 to 1)	MODERATE
	Parameter: CA_{15}				Serious[d]	1[b] (0.81 to 1)	1 (0.48 to 1)	MODERATE
	Parameter: MCF				Serious[d]	1[b] (0.81 to 1)	1 (0.48 to 1)	MODERATE

Number of studies	n	Risk of bias	Inconsistency	Indirectness	Imprecision	Sensitivity (95% CI)	Specificity (95% CI)	Quality
	Parameter: CLI_{30}				Very serious[d]	1[b] (0.75 to 1)	1 (0.75 to 1)	LOW
	Parameter: CLI_{60}				Very serious[d]	1[b] (0.63 to 1)	1 (0.4 to 1)	LOW
	Parameter: ΔMCF				Serious[d]	1[b] (0.81 to 1)	0.8 (0.29 to 0.97)	MODERATE
	Parameter: ΔCA_{15}				Serious[d]	1[b] (0.81 to 1)	0.6 (0.15 to 0.94)	MODERATE
	Parameter: ΔCLI_{30}				Very serious[d]	1[b] (0.71 to 1)	0.75 (0.2 to 0.96)	LOW
	Parameter: ΔCLI_{60}				Very serious[d]	1[b] (0.63 to 1)	1 (0.4 to 1)	LOW
ROTEM in comparison to reference standards (laboratory PT, INR, aPTT, fibrinogen, platelets, haemoglobin) to identify need for transfusion								
1	88	Not serious	NA	None				
	CA_{15}-EXTEM				Serious[d]	0.87[b] (0.72 to 0.87)	1 (0.99 to 1)	MODERATE
	CFT-INTEM				Serious[d]	1[b] (0.84 to 1)	0.74 (0.73 to 0.74)	MODERATE
	CA_{10}-FIBTEM				Very serious[d]	0.91[b] (0.72 to 0.93)	0.85 (0.84 to 0.86)	LOW
	CA_{15}-INTEM				Very serious[d]	1[b] (0.71 to 1)	0.83 (0.82 to 0.83)	LOW
ROTEM in comparison to reference standard (laboratory PT) to identify coagulopathy								
1	48	Serious[c]	NA	None	Very serious[d]	0.43[a] (0.18 to 0.71)	0.65 (0.44 to 0.83)	VERY LOW
ROTEM in comparison to reference standard (future transfusion) to predict future massive transfusion								
1	808	Serious[c]	NA	None				
	Clotting time (CT)				Serious[d]	0.29[a]	0.91	LOW
	CA_{5}-EXTEM				Serious[d]	0.46[a]	0.84	LOW
	α-angle				Serious[d]	0.37[a]	0.88	LOW
ROTEM in comparison to reference standard (future transfusion) to predict future massive transfusion								
1	808	Serious[c]	NA	None				
	CA_{5}-EXTEM				Very serious[d]	0.73[b] (0.57 to 0.85)	0.69 (0.65 to 0.72)	VERY LOW
	CA_{5}-FIBTEM				Very serious[d]	0.78[b] (0.62 to 0.89)	0.67 (0.64 to 0.71)	VERY LOW
ROTEM in comparison to reference standard (laboratory PT) to predict acute traumatic coagulopathy								
1	808	Serious[c]	NA	None				
	CA_{5}-EXTEM				Very serious[d]	0.66[b] (0.55 to 0.76)	0.81 (0.78 to 0.84)	VERY LOW
	CA_{5}-FIBTEM				Very serious[d]	0.68[b] (0.56 to 0.78)	0.79 (0.76 to 0.82)	VERY LOW

Δ parameter = (parameters_APTEM – parameter_EXTEM)/ parameter_EXTEM) × 100

(a) Pre-set cut-off for all accuracy calculations.

(b) Optimised cut-off for all accuracy calculations.

(c) Studies were downgraded by one increment for limitations in one risk of bias domain or by two increments for risk of bias in two or more domains. Studies were assessed using the QUADAS –II criteria. Risk of bias domains: patient selection, index test, reference standard, flow and timing.

(d) Imprecision was assessed using the confidence interval of the sensitivity value. For studies with only AUC data precision was based on the corresponding 95%CI. Downgrading by one increment was applied for confidence intervals 10-20% or by two increments for confidence intervals more than 20%. If no variance data was available (imprecision could not be assessed) the studies were downgraded by one increment.

Table 115: Clinical evidence profile: diagnostic accuracy of TEG

Number of studies	n	Risk of bias	Inconsistency	Indirectness	Imprecision	Sensitivity (95% CI)	Specificity (95% CI)	Quality
TEG in comparison to reference standard (future transfusion) to predict future transfusion								
1	76	Serious[c]	NA	None				
	Rapid K				Serious[d]	0.68[b]	0.78	LOW
	Rapid α-angle				Serious[d]	0.84[b]	0.57	LOW
	Rapid MA				Serious[d]	0.68[b]	0.80	LOW
	Rapid TMA				Serious[d]	0.76[b]	0.57	LOW
	Rapid G				Serious[d]	0.68[b]	0.78	LOW
	Kaolin K				Serious[d]	0.68[b]	0.59	LOW
	Kaolin α-angle				Serious[d]	0.72[b]	0.61	LOW
	Kaolin MA				Serious[d]	0.56[b]	0.88	LOW
	Kaolin TMA				Serious[d]	0.64[b]	0.63	LOW
	Kaolin G				Serious[d]	0.56[b]	0.88	LOW

(a) Pre-set cut-off for all accuracy calculations.

(b) Optimised cut-off for all accuracy calculations.

(c) Studies were downgraded by one increment for limitations in one risk of bias domain or by two increments for risk of bias in two or more domains. Studies were assessed using the QUADAS –II criteria. Risk of bias domains: patient selection, index test, reference standard, flow and timing.

(d) Imprecision was assessed using the confidence interval of the sensitivity value. For studies with only AUC data precision was based on the corresponding 95%CI. Downgrading by one increment was applied for confidence intervals 10-20% or by two increments for confidence intervals more than 20%. If no variance data was available (imprecision could not be assessed) the studies were downgraded by one increment.

12.1.4 Economic evidence

Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow chart in Appendix E.

Unit costs

The costs of POC TEG and ROTEM have been obtained from an ongoing diagnostic assessment report being undertaken by NICE, looking at 'Viscoelastic POC testing to assist with the diagnosis, management and monitoring of haemostasis'. This includes looking at the clinical and cost effectiveness of TEG and ROTEM compared with standard laboratory tests for a population with coagulopathy induced by trauma.

This report is confidential until published; therefore, the costs below are tentative until they appear in the published version (due for publication August 2014).

Table 116: Costs of POC coagulation tests and laboratory coagulation tests

Intervention	Cost per patient	Source
POC coagulation tests[d]		
TEG[a]	£34.03	NICE Diagnostic Assessment Report
ROTEM[b]	£40.69	NICE Diagnostic Assessment Report
CoaguChek[c]	£2.84	Through GDG member contact
Laboratory coagulation tests		
TEG	£31.89	Through GDG member contact
ROTEM[e]		
Clotting screen (INR, aPTT)	£26 standard lab tests (fibrinogen concentration, PT, protein C, activated clotting time, aPTT)	NICE Diagnostic Assessment Report (inflated to 2013 costs from the costs reported in Scottish HTA)
Clotting screen (INR, aPTT)	£17.05 Clotting screen (aPTT, PT, thrombin time)	Through GDG member contact
Fibrinogen	£7.75	Through GDG member contact
Platelet count	£4.26	Through GDG member contact (note that this cost is for a full blood count)

(a) These costs can be further broken down into material cost of the device per patient (£17.33 for TEG, this includes 4-channel device, connectivity kit, software/database commander, printer, trolley, after care and training costs, and assuming 3 years of use and 500 tests per year), and then the cost of undertaking the test itself (£16.70 for TEG, this includes the cost of the rapidTEG assay, and the cup and pin). Please see Appendix O for more detail on what is included within these costs for TEG.

(b) These costs can be further broken down into material cost of the device per patient (£26.67 for ROTEM, this includes 4-channel device, connectivity kit, software/database commander, printer, trolley, after care and training costs, and assuming 3 years of use and 500 tests per year), and then the cost of undertaking the test itself (£14.02 for ROTEM, this includes the INTEM, EXTEM and FIBTEM assays, and the cost of 3 cups and pins). Please see Appendix O for more detail on what is included within these costs for ROTEM.

(c) Included in this cost is the CoaguChek device with barcode scanner, rechargeable battery pack, base unit, manual and professional lancing system, test strips, sterets, and control kits. Please see Appendix G for more detail on the how this cost per patient was derived.
(d) Costs could not be sourced for INRatio and proTime devices.
(e) Cost of laboratory ROTEM could not be sourced, however this is likely to be similar to the point of care version as the same equipment is used.

12.1.5 Evidence statements

Clinical

CoaguChek XS

One Moderate quality diagnostic study comprising 40 people showed CoaguChek XS has a sensitivity of 0.77 and specificity of 0.94 in detecting coagulopathy (laboratory PT more than 60%).

One Moderate quality diagnostic study comprising 300 people showed CoaguChek XS has a sensitivity of 0.77 and specificity of 0.77 in detecting coagulopathy (laboratory PT more than 1.2).

One Low quality diagnostic study comprising 72 people showed CoaguChek XS has a sensitivity of 0.63 and specificity of 0.88 in detecting coagulopathy (laboratory INR more than 1.5).

INRatio

One Very low quality diagnostic study comprising 48 people showed INRatio has a sensitivity of 0.50 and specificity of 1.00 in detecting coagulopathy (laboratory INR more than 1.5).

One Very low quality diagnostic study comprising 48 people showed INRatio has a sensitivity of 0.83 and specificity of 0.89 in detecting coagulopathy (laboratory INR more than 1.4).

One Very low quality diagnostic study comprising 48 people showed INRatio has a sensitivity of 0.92 and specificity of 0.79 in detecting coagulopathy (laboratory INR more than 1.3).

ROTEM

One Moderate quality diagnostic study comprising 23 people showed ROTEM parameter CA_{10} (10 mm and under) has a sensitivity of 1.0 and specificity of 1.0 in detecting hyperfibrinolysis (laboratory ELT less than 90 minutes).

One Moderate quality diagnostic study comprising 23 people showed ROTEM parameter CA_{15} (12 mm and under) has a sensitivity of 1.0 and specificity of 1.0 in detecting hyperfibrinolysis (laboratory ELT less than90 minutes).

One Moderate quality diagnostic study comprising 23 people showed ROTEM parameter MCF (18 mm and under) has a sensitivity of 1.0 and specificity of 1.0 in detecting hyperfibrinolysis (laboratory ELT less than 90 minutes).

One Low quality diagnostic study comprising 23 people showed ROTEM parameter CLI_{30} (71% and under) has a sensitivity of 1.0 and specificity of 1.0 in detecting hyperfibrinolysis laboratory (ELT less than 90 minutes).

One Low quality diagnostic study comprising 23 people showed ROTEM parameter CLI_{60} (1% and under) has a sensitivity of 1.0 and specificity of 1.0 in detecting hyperfibrinolysis (laboratory ELT less than 90 minutes).

One Moderate quality diagnostic study comprising 23 people showed ROTEM parameter ΔMCF (more than 7%) has a sensitivity of 1.0 and specificity of 0.8 in detecting hyperfibrinolysis (laboratory ELT less than 90 minutes).

One Moderate quality diagnostic study comprising 23 people showed ROTEM parameter ΔCA_{15} (more than 4%) has a sensitivity of 1.0 and specificity of 0.6 in detecting hyperfibrinolysis laboratory (ELT less than 90 minutes).

One Low quality diagnostic study comprising 23 people showed ROTEM parameter ΔCLI_{30} (more than 2%) has a sensitivity of 1.0 and specificity of 0.75 in detecting hyperfibrinolysis (laboratory ELT less than 90 minutes).

One Low quality diagnostic study comprising 23 people showed ROTEM parameter ΔCLI_{60} (more than 43%) has a sensitivity of 1.0 and specificity of 0.75 in detecting hyperfibrinolysis (laboratory ELT less than 90 minutes).

One Moderate quality diagnostic study comprising 88 people showed ROTEM parameter CA_{15}-EXTEM (32 mm and under) has a sensitivity of 0.87 and specificity of 1.0 in detecting need for transfusion (laboratory PT more than 1.5 of control value).

One Moderate quality diagnostic study comprising 88 people showed ROTEM parameter CFT-INTEM (112 seconds and under) has a sensitivity of 1.0 and specificity of 0.74 in detecting need for transfusion (laboratory APTT more than 1.5 of control value).

One Low quality diagnostic study comprising 88 people showed ROTEM parameter CA_{10}- FIBTEM (5 mm and under) has a sensitivity of 0.91 and specificity of 0.85 in detecting need for transfusion (laboratory fibrinogen less than 1 g/litre).

One Low quality diagnostic study comprising 88 people showed ROTEM parameter CA15-INTEM (46 mm and under) has a sensitivity of 1.0 and specificity of 0.83 in detecting need for transfusion (laboratory platelet count $<50 \times 10^9$ litre^{-1}).

One Very low quality diagnostic study comprising 88 people showed ROTEM parameter MCF-EXTEM (less than 40 mm) has a sensitivity of 0.43 and specificity of 0.65 in detecting coagulopathy (laboratory PT more than 1.5 normal values).

One Low quality diagnostic study comprising 808 people showed ROTEM parameter clotting time (CT) (more than 94 seconds) has a sensitivity of 0.29 and specificity of 0.91 in detecting future massive transfusion.

One Low quality diagnostic study comprising 808 people showed ROTEM parameter CA_{5}-EXTEM (35 mm and under) has a sensitivity of 0.46 and specificity of 0.84 in detecting future massive transfusion.

One Low quality diagnostic study comprising 808 people showed ROTEM parameter α-angle (less than 65 degrees) has a sensitivity of 0.37 and specificity of 0.88 in detecting future massive transfusion.

One Very low quality diagnostic study comprising 808 people showed ROTEM parameter CA_{5}-EXTEM (40 mm and under) has a sensitivity of 0.73 and specificity of 0.69 in in detecting future massive transfusion.

One Very low quality diagnostic study comprising 808 people showed ROTEM parameter CA_{5}-FIBTEM (9 mm and under) has a sensitivity of 0.78 and specificity of 0.67 in in detecting future massive transfusion.

One Very low quality diagnostic study comprising 808 people showed ROTEM parameter CA_{5}-EXTEM (37 mm and under) has a sensitivity of 0.66 and specificity of 0.81 in detecting acute traumatic coagulopathy (laboratory PT more than 1.2).

One Very low quality diagnostic study comprising 808 people showed ROTEM parameter CA_{5}-FIBTEM (8 mm and under) has a sensitivity of 0.68 and specificity of 0.79 in detecting acute traumatic coagulopathy (laboratory PT more than 1.2).

TEG

One Low quality diagnostic study comprising 76 people showed Rapid TEG parameter K (more than 1.8 minutes) has a sensitivity of 0.68 and specificity of 0.78 in detecting future transfusion.

One Low quality diagnostic study comprising 76 people showed Rapid TEG parameter α-angle (less than 75 degrees) has a sensitivity of 0.84 and specificity of 0.57 in detecting future transfusion.

One Low quality diagnostic study comprising 76 people showed Rapid TEG parameter MA (less than 60 mm) has a sensitivity of 0.68 and specificity of 0.8 in detecting future transfusion.

One Low quality diagnostic study comprising 76 people showed Rapid TEG parameter TMA (more than 17 minutes) has a sensitivity of 0.76 and specificity of 0.57 in detecting future transfusion.

One Low quality diagnostic study comprising 76 people showed Rapid TEG parameter G (less than7374 d/sc) has a sensitivity of 0.68 and specificity of 0.78 in detecting future transfusion.

One Low quality diagnostic study comprising 76 people showed Rapid TEG parameter K (more than 1.7 minutes) has a sensitivity of 0.68 and specificity of 0.59 in detecting future transfusion.

One Low quality diagnostic study comprising 76 people showed Kaolin TEG parameter α-angle (less than 59 degrees) has a sensitivity of 0.72 and specificity of 0.61 in detecting future transfusion.

One Low quality diagnostic study comprising 76 people showed Kaolin TEG parameter MA (less than 58 mm) has a sensitivity of 0.56 and specificity of 0.88 in detecting future transfusion.

One Low quality diagnostic study comprising 76 people showed Kaolin TEG parameter TMA (more than 25 minutes) has a sensitivity of 0.64 and specificity of 0.63 in detecting future transfusion.

One Low quality diagnostic study comprising 76 people showed Kaolin TEG parameter G (less than 7073 d/sc) has a sensitivity of 0.56 and specificity of 0.88 in detecting future transfusion.

Economic

No relevant economic evaluations were identified.

12.1.6 Recommendations and link to evidence

Recommendations	**Research recommendation: What is the clinical and cost effectiveness of point-of-care coagulation testing using rotational thromboelastrometry (ROTEM) or thromboelastography (TEG) to target treatment, compared with standard laboratory coagulation testing?**
Relative values of different outcomes	The critical outcomes for this diagnostic review question were sensitivity and specificity of the index tests relative to a reference test (which is assumed to give the 'true' diagnosis). Testing for coagulopathy influences decisions regarding transfusion which is costly and carries potential harm. Sensitivity is the most critical outcome, because poor

	sensitivity may result in people with coagulopathy being undiagnosed and therefore, untreated. In contrast, low specificity, leading to false positive diagnoses, will lead to unnecessary treatments. Though carrying a risk of unnecessary adverse events and higher costs, such additional treatments due to misdiagnoses are unlikely to be as much of a risk to the patient as missed diagnoses.
Trade-off between clinical benefits and harms	POC INR devices are typically hand-held and are easy to use (applying whole blood to a testing strip) and have a very fast turnaround time (under 5 minutes for results). This could potentially reduce time to treatment. While diagnostic cohort studies can tell us about the relative accuracy of a diagnostic test compared with a reference standard, they do not tell us whether adopting a particular diagnostic strategy improves patient outcomes. Evidence on patient outcomes is only available from diagnostic RCTs which compare two diagnostic interventions with identical subsequent treatment as indicated by the diagnostic test. No such evidence was identified. CoaguChek and INRatio devices were compared against a reference standard of conventional coagulation tests. They were found to have sensitivities that ranged from 0.5 to 0.92 and specificities that ranged from 0.77 to 1. The GDG agreed that the sensitivity of INR devices were too poor to allow a recommendation supporting their use in the trauma setting. POC ROTEM and TEG are used successfully in surgery and ICU settings. They are not directly comparable to standard laboratory tests as they measure different parameters. They can produce useful results in 15 minutes but some parameters take up to one hour. They are more complex than POC INR devices and resuscitation room staff will require in-depth training in their calibration, use and upkeep. The GDG noted that the included studies investigating POC ROTEM and TEG used varying reference standards that may not all directly relate to coagulopathy. Their sensitivities ranged from 0.29 to 1 and specificities ranged from 0.57 to 1. The GDG considered these results to be of limited reliability because the laboratory reference standards against which POC ROTEM and TEG were evaluated were not directly comparable because they measured different parameters. One study did not use a laboratory test as a reference standard and instead compared rapid TEG with the need for future transfusion. This was not considered to be a useful reference standard for the test because the need for future transfusion could be heavily confounded by other factors, for example, treatment for haemorrhage the patients received after their test but before their transfusion.
Trade-off between net health benefits and resource use	No published economic evidence was identified to inform this question. POC tests, such as TEG or ROTEM tests, monitor coagulation and the results of these may influence whether transfusions are necessary, for example, special equipment is needed to undertake these tests, which can be costly. However, this equipment is a one-off capital investment. The cost per patient use depends on the lifetime of the equipment and how many patients are tested within that timeframe. POC testing will, however, lead to less blood product use and thus, less wastage than using a major haemorrhage protocol which is not guided by point of care testing. There is likely to be some difference in costs between the traditional laboratory tests and the newer methods, such as TEG/ROTEM, as there are also ongoing costs with the TEG or ROTEM systems, such as after care costs, and consumables needed per test. For TEG and ROTEM, POC testing was in the same cost range as the laboratory versions of these tests. POC INR testing, such as CoaguChek, had a lower cost per

patient than POC TEG or ROTEM, this is likely to be because the upfront costs of TEG and ROTEM are much higher and are used on less patients than point of care INR testing.

Laboratory tests may also vary depending on the number of tests involved and individual hospital laboratory arrangements.

POC testing may be utilised by the bedside by the attending clinician who may require training and current quality assurance systems for point of care testing are acknowledged to be non-standardised across the country. The difference in costs between the tests are not thought to be substantial, however, training costs of POC testing need to be taken into consideration alongside the cost of the testing equipment. On the other hand, laboratories have their own overheads and are generally staffed by at least three scientists (out of hours costs may need to be considered), although, it is generally accepted that in settings accepting major trauma, laboratory services are already available on a 24/7 basis.

It is unlikely that the intervention costs of the POC tests are less than those associated with laboratory costing. For POC testing to be cost effective over laboratory testing, a clinical benefit should be suspected (with associated reduction in healthcare resource use).

Different tests give different aspects of information regarding a person's coagulopathy status: The GDG felt that use of PT was not accurate enough to inform clinical management and therefore, probably not a cost effective test for this indication. Other tests which inform on the extent of 'lysis' often will give results only after tranexamic acid has been given and may have already begun to correct for this indication.

The GDG expected the proportion of patients presenting with major trauma who will have traumatic coagulopathy to be in the region of 10% to 25%, meaning that positive predictive power will be reasonably high. Testing for coagulopathy assists decisions regarding transfusion and blood product use, both of which are costly and carry potential harm. Therefore both sensitivity and specificity are important considerations.

Costs may be offset by the changes in management they lead to which could be lifesaving and also offset by avoidance of unnecessary transfusions. However, no evidence was identified to inform whether point of care testing in comparison to laboratory testing provided a clinical benefit in the way in which a patient is managed. A key benefit which is thought to offset a potentially lower accuracy of point of care testing or more expensive laboratory testing is a shorter turnaround time which in turn may facilitate timely clinical action (TEG, for example, takes approximately 10-12 minutes compared with a longer than average turnaround time of 2 hours from laboratory testing , although this is anecdotally reported). However, again no evidence was retrieved to inform this aspect. It was also noted that information from tests, such as ROTEM and TEG, can be read out in real time on the monitor although the complete picture can take up to 1 hour.

Accuracy estimates in isolation were not sufficient to make informed conclusions regarding the clinical benefit which may result from point of care testing and justify the cost in a change of practice. Cost effectiveness of point of care testing in relation to standard care or laboratory testing is unclear, and this topic may benefit from further research given the potentially large capital outweigh in investing in the specialist equipment of the point of care testing machines.

	To note, most laboratories currently do not undertake TEG based testing, and a recommendation in favour would have a cost impact.
Quality of evidence	**Clinical evidence** All studies were graded between moderate and very low quality. Risk of bias was either not serious or serious for all outcomes, when it was serious this was usually due to non-consecutive patient selection. There was serious or very serious imprecision for all outcomes due to the width of the 95% CIs or lack of variance data (if no variance data was available the studies were downgraded by one increment). **Economic evidence** The costs obtained for the point of care tests as well as laboratory tests are based on a variety of sources. As the laboratory costs obtained are based on a micro-costing approach (from individual hospitals or published sources), these may be overestimates compared with a national average.
Other considerations	Overall, the GDG concluded that there was not sufficient evidence of improved accuracy to currently recommend point of care testing in major trauma patients. However, the GDG did consider POC ROTEM and TEG to be potentially useful in the trauma setting. This was in light of their successful adoption in surgery and ICU settings and the limited comparability of the reference standards against which they were evaluated in the trauma studies. The GDG stated that the evidence base does not currently answer the following question: Is the use of POC coagulation testing (ROTEM and TEG) to target treatment better than using standard laboratory coagulation testing? The GDG identified no considerations specific to children.

12.2 Frequency of blood testing

12.2.1 Introduction

Blood tests allow trauma teams to monitor and treat conditions such as coagulopathy effectively. However, there is no consensus on the frequency at which such tests should be undertaken. While overuse of blood through monitoring has largely been eliminated by tests that require smaller quantities, there are still trade-offs in terms of health professional time and costs. This question aims to find the optimum frequency of monitoring five types of blood test.

12.2.2 Review question: What is the most clinically and cost effective frequency of blood test monitoring for people with suspected haemorrhage following major trauma?

For full details see review protocol in Appendix C.

Table 117: PICO characteristics of review question

Population	Children, young people and adults in the emergency department who have a suspected haemorrhage following a traumatic incident.
Intervention	Set frequencies of blood testing within 48 hours of injury Blood tests of interest: • Coagulation tests • Haemoglobin test • Haematocrit • Lactate • Base excess/deficit

Comparison	Alternative frequencies of blood testing

Outcomes	Critical:
	• Mortality at 24 hours, 30 days/1 month, and 12 months
	• Health-related quality of life
	• Length of intensive care stay
	• Blood product use:
	  ○ red blood cells
	  ○ platelets
	  ○ plasma
	  ○ cryoprecipitate
	
	Important:
	• Patient-reported outcomes:
	  ○ pain/discomfort
	  ○ return to normal activities
	  ○ psychological wellbeing
	• Time to definitive control of shock/haemorrhage

Study design	RCTs or systematic reviews of RCTs; cohort/case control studies if RCT evidence is insufficient. Only cohort/case control studies accounting for important confounding factors will be considered (severity of shock, severity of injury, degree of head injury, age)

12.2.3 Clinical evidence

No relevant clinical studies were identified.

12.2.4 Economic evidence

Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow chart in Appendix E.

Unit costs

Some examples of the costs of blood tests can be found below.

Table 118: Blood test costs

Intervention	Cost per patient	Source
Clotting screen	£26 standard lab tests (fibrinogen concentration, PT, protein C, activated clotting time, activated partial thromboplastin time [aPTT])	NICE Diagnostic Assessment Report (inflated to 2013 costs from the costs reported in Scottish HTA)
	£17.05 Clotting screen (aPTT, PT, thrombin time)	Through GDG member contact

12.2.5 Evidence statements

Clinical

No relevant clinical studies were identified.

Economic

No relevant economic evaluations were identified.

12.2.6 Recommendations and link to evidence

Recommendations	No recommendation made
Relative values of different outcomes	Mortality, health-related quality of life, length of intensive care stay and blood product use were critical outcomes for the review. The patient-reported outcomes: pain/discomfort, return to normal activities and psychological wellbeing were considered important, along with time to definitive control of haemorrhage.
Trade-off between clinical benefits and harms	No clinical evidence was found to evaluate the trade-off between clinical benefits and harms of different frequencies of blood test monitoring. The GDG discussed the risks of not doing enough blood tests and missing important clinical signs with stating a minimum number of tests, they concluded that considering the diverse nature of patients with major trauma, in particular, patients with multiple trauma, this was an impossible and potentially harmful task.
Trade-off between net health benefits and resource use	No economic evidence was identified for this question. Costs for clotting screening tests can vary at around £20. The other tests that were included in the protocol are likely to be less costly as they would not involve testing for as many things. The main trade off here involves the additional cost of the increased frequency that blood testing occurs versus the increased likelihood of picking up clinically significant/relevant changes in a patient's condition. There were many factors which were felt to influence the frequency with which testing may take place, most of which were patient and injury specific, such as the rate of deterioration of the patient. The cost of missing a clinically significant change in the patient's condition, which could impact management and their outcome, could outweigh the cost of testing more frequently. However, cost effectiveness of different frequencies remains uncertain. The GDG felt that it would be inappropriate to recommend a specific frequency because in practice, this is most likely clinically driven and clinicians are best placed to judge the frequency of testing that patients will need. No recommendation was made. As there will be no change in practice, this question is not anticipated to have a cost impact.
Quality of evidence	**Economic evidence** The costs obtained for tests are based on a variety of sources. These may be overestimates compared with a national average.
Other considerations	The GDG decided not to make a recommendation. This decision was based on the lack of evidence and because a recommendation based on expert consensus was inappropriate for this question.

	The frequency of blood testing of a major trauma patient varies dramatically over the course of the disease. The GDG agreed that the frequency of blood tests in current practice is largely determined by the presentation of individual patients and is based on clinical judgement. It was for this reason the GDG felt that an expert consensus recommendation was inappropriate. Any consensus recommendation based on set frequencies of blood testing would be too simplistic and not effectively represent the complexity of clinical judgement that is required in major trauma scenarios. The recommendation made for the haemorrhage protocols calls for a move from an empiric protocol to a laboratory led protocol at the earliest opportunity. The GDG considered this to be an adequate steer for trauma physicians in that it requires regular blood tests to guide treatment. The GDG identified no considerations specific to children.

12.3 Lactate levels

12.3.1 Introduction

Haemorrhage is a major cause of preventable death in patients with major trauma. A significant loss of blood can result in hypovolemic shock, where the heart is unable to circulate enough blood around the body. This can lead to organ failure and death. In current practice, treatment for hypovolemic shock is guided by patient haemodynamic levels; such as heart rate and blood pressure. However, some research indicates that these measures can be slow to respond to changes in blood volume. This review investigated whether guiding treatment by lactate levels may be a more clinically and cost effective strategy in treating hypovolemic shock in major trauma patients.

12.3.2 Review question: Does monitoring of lactate levels to guide management of hypovolemic shock improve outcomes?

For full details see review protocol in Appendix C.

Table 119: PICO characteristics of review question

Population	Children, young people and adults experiencing a traumatic incident.
Intervention(s)	Treatment guided by the monitoring of lactate levels
Comparison(s)	Treatment for shock not guided by monitoring lactate levels Treatment for shock guided by monitoring heart rate, blood pressure and other haemodynamic levels
Outcomes	Critical: • Mortality at 24 hours, 30 days and 12-months • Health-related quality of life • Length of intensive care stay • Adverse effects: over-transfusion-related morbidity, thromboembolism, transfusion-reactions • Blood product use (red blood cells [RBCs], platelets, plasma, cryoprecipitate) Important: • Patient-reported outcomes (psychological wellbeing) • Time to definitive control of haemorrhage

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)

This review sought to identify studies that investigated whether treatment for shock that was guided by the monitoring of lactate levels improved patient outcomes, as compared with treatment guided by haemodynamic indicators or treatment as usual. Treatment for shock was defined as either surgery or fluid resuscitation. Studies that investigated the accuracy of lactate levels in identifying the presence of shock, in addition to correlational studies examining the relationship between lactate levels /clearance and patient outcomes, were excluded from the review.

12.3.3 Clinical evidence

No relevant clinical studies comparing treatment guided by the monitoring of lactate levels with either treatment as usual or treatment guided by haemodynamic levels were identified.

12.3.4 Economic evidence

Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow chart in Appendix E.

Unit costs

Handheld pre-hospital devices exist which cost in the region of £25 (additional costs for strips may be needed).

Table 120: Blood product costs

Resource	Cost	Source
RBCs	£122 220-300 ml per pack	NHS Blood and Transplant price list 2014/15 [105]
Fresh frozen plasma	£28 Mean: 271 ml per pack (240-280 is common)	NHS Blood and Transplant price list 2014/15
Platelets	£197 (one adult therapeutic dose)	NHS Blood and Transplant price list 2014/15
Pooled cryoprecipitate (5 pack)	£181 Mean: 199 ml per pooled pack	NHS Blood and Transplant price list 2014/15

Note: All costs are per unit/pack

12.3.5 Evidence statements

Clinical

No evidence was identified

Economic

No relevant economic evaluations were identified.

12.3.6 Recommendations and link to evidence

Recommendations	Research recommendation: Is lactate monitoring in patients with major trauma clinically and cost effective?
Relative values of different outcomes	The aim of this question was to identify whether guiding treatment for hypovolemic shock by patients' blood lactate levels could improve outcomes compared with treatment guided by haemodynamic levels or treatment as usual. The GDG identified mortality, patient health-related quality of life, length of intensive care stay, adverse effects of treatment and blood product use as critical outcomes in this review. Patient psychological wellbeing, time to definitive control of haemorrhage and blood product waste were also identified as important outcome measures.
Trade-off between clinical benefits and harms	The GDG agreed that due to no evidence retrieved, it would not be appropriate to make a recommendation because of the potential harm for over-resuscitation and over-fluid therapy. Therefore, this area was prioritised for a research recommendation.
Trade-off between net health benefits and resource use	No economic studies that addressed the review question were identified. Assessment and identification of haemorrhagic shock may occur either pre-hospital or in hospital. Current practice is to use changes in blood pressure, pulse and other haemodynamic levels (such as central venous pressure, cardiac output and urine output) to indicate shock in the first instance, and/or monitor the patient in case of suspected decline. Other methods, such as the use of lactate levels to monitor patients and guide treatment is less common, especially in the pre-hospital setting. Pre-hospital devices used to measure lactate levels are available but not across all ambulance services. It is more common in the hospital setting, but is used on an ad hoc basis, and would also be used as a complement to current practice as opposed to an alternative; therefore, the added benefit over routine care would be smaller than the absolute benefit if this were to be used instead of current practice. Lactate levels are suspected to be a good measure of shock because traditional haemodynamic levels tend to change late and correct early. There is, therefore, a danger that the patient is believed to no longer be in shock, when actually, there is still inadequate organ perfusion occurring (for example, blood pressure may go back to normal but the patient is still in shock). The cost of resources used to measure lactate levels are most likely small (hand-held pre-hospital devices are around £25, and in hospital it is a quick test not taking much more time than current practice), however, the health benefit remains unknown. Missing life-threatening haemorrhage will most likely lead to death and mistakenly treating haemorrhage can lead to potentially inappropriate invasive treatments (with associated clinical harm) and increased resource use (such as blood components). The cost effectiveness of methods to guide the management of haemorrhagic shock will stem from their accuracy in determining the severity of shock and the appropriate use of blood components, and how this information translates into improved management (that is, tailored and cost effective use of blood components, and management decisions downstream). Without clinical evidence to inform what the added value of lactate monitoring is and whether it does improve the management of haemorrhagic shock/clinical damage early on, cost effectiveness of the investment in lactate monitoring devices remains unclear. The GDG felt they were unable to make a recommendation given the lack of evidence and thought a research recommendation would be helpful as there is

	generally a lack of evidence on lactate goal-directed therapy. There is some evidence from other conditions, such as sepsis, but it was mentioned that there is also uncertainty around this evidence, and a stronger research base is needed before a recommendation can be made.
Quality of evidence	No evidence was retrieved for this clinical question.
Other considerations	Research has found a strong correlation between lactate levels and the presence of shock. However, the GDG noted that the association between the two factors did not necessarily indicate that treatment guided by lactate levels would be clinically and cost effective. A research recommendation was made to address this question.

13 Warming

13.1 Introduction

Following major trauma, patients are often exposed to adverse weather conditions and are at risk of developing hypothermia, which is associated with worse outcome and higher mortality. Moreover, the cold conditions can be uncomfortable for patients and actions to reduce cold exposure and prevent further heat loss have been integrated as part of standard pre-hospital primary care. Measures to prevent heat loss can include simple practical interventions, such as moving the patient into shelter, removing wet clothing and providing insulation from ambient weather conditions with adequate wind and waterproof insulation (passive warming). In addition, and depending on the victim's physiological status, body temperature and clinical assessment interventions which apply heat externally (active warming) can also be considered. These are more aggressive and include administration of warmed intravenous (IV) fluid chemical heat pads and electric blankets. Despite the wide-spread usage of various warming in the pre-hospital setting, limited evidence exists detailing its benefit and national guidance is required.

13.2 Review question: Is warming clinically and cost effective in people who have experienced major trauma?

For full details see review protocol in Appendix C.

Table 121: PICO characteristics of review question

Population	Children and adults experiencing a traumatic incident

Intervention(s)	Pre-hospital:
	External:
	• Bubble wrap
	• Foil blankets
	• Active heating chemical blankets
	
	Internal:
	• IV fluid warmed devices (including IV solutions/blood components)
	
	Emergency department
	Active external rewarming :
	• Convection warming units
	  ○ air convection (Bair hugger/WarmAir)
	  ○ fluid convection
	• Warming mattress (Inditherm warming mattress)
	• Radiant warmers/heater
	
	Active internal rewarming:
	• Warmed IV solutions
	• Ventilation with warmed, humidified air or oxygen
	
	A combination of the above.

Comparison(s)	A comparison of the above. Standard care (standard blankets)

Outcomes	Critical: • Mortality at 24 hours, 30days/1month, and 12 months • Health-related quality of life • Length of intensive care stay • Adverse effects: ○ skin burns ○ hyperthermia ○ infection) • Neurological outcome Important: • Patient-reported outcomes: ○ pain/discomfort ○ return to normal activities, psychological wellbeing).
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)

13.3 Clinical evidence

One study was included in the review[54,54]; details of which are summarised in Table 122 below. Evidence from this study is summarised in the clinical evidence summary (Table 123). See also the study selection flow chart in Appendix D, forest plots in Appendix J, GRADE tables in Appendix I and excluded studies list in Appendix K.

The included study was a randomised prospective clinical trial comparing intra-arterial warming using continuous arteriovenous rewarming (CAVR) plus conventional care with conventional care alone. The search was expanded to cohort studies for other comparisons but no evidence was found.

Table 122: Summary of studies included in the review

Study	Intervention and comparison	Population	Outcomes	Comments
Gentilello 1997 [54,54]	29 CAVR plus conventional care versus 28 conventional care (warm IV fluids, airway re-warming, convective blanket, aluminized Therma Drape).	Patients of 18 years or older admitted after injury and the initial core temperature reading was <34.5 Celsius	Mortality	

Table 123: Clinical evidence summary: CAVR plus standard care versus standard care

Outcome	Number of studies (participants)	Imprecision	GRADE rating	Absolute difference	Control event rate (per 1000)
Mortality	1 (n=57)	Serious	LOW	292 fewer per 1000 (from 51 fewer to 378 fewer)	429

13.4 Economic evidence

Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow chart in Appendix E.

Unit costs

Table 124: Intervention costs

Intervention	Cost	Cost per patient	Source
Standard care			
Blanket thermal	£270.65 (Box of 50)	£5.41	NHS Supply Chain [3]
Pre-hospital interventions – external warming			
Full body blanket ~ reusable	-	£1,347.06	NHS Supply Chain
Bubble wrap			
LESS thermal bag LS3010	-	£25	GDG contact
Foil blankets			
Emergency thermal/foil blanket Adult 204 cm x 140 cm	-	£0.46	NHS Supply Chain
Chemical blankets			
Easywarm active warming blanket 92x152 cm	£125.52 (Box of 10)	£12.55	NHS Supply Chain
Ready Heat 2. Disposable blanket	-	£19.95	GDG contact
Pre-hospital and in-hospital interventions – internal warming			
Mediheat 900 portable IV warmer	£399.00	£0.08[a]	NHS supplier
Hotline blood and fluid warmer 230 v	£2,493.51	£0.50[a]	
In hospital interventions – active external warming			
Patient Warming and Cooling Unit	£27,428.57	Likely to be small	
Reusable warming mattress Full-length narrow plus Reusable warming mattress control unit - For use with reusable adult and paediatric blankets and mattresses	£1,699.29 £732.00	£0.34[b] £0.15[b]	NHS Supply Chain
Total		£0.49	

(a) Assuming can be used on 5000 patients. This does not include maintenance costs of the product, the fluids that will be used, and equipment to attach an IV line to patients.
(b) Assuming can be used on 5000 patients.

13.5 Evidence statements

Clinical

CAVR versus conventional Care

Low quality evidence from 1 RCT comprising of 57 participants demonstrated a clinical benefit of CAVR over conventional warming for mortality, with serious imprecision.

Economic

No relevant economic evaluations were identified.

13.6 Recommendations and link to evidence

Recommendations	**60.Minimise ongoing heat loss in patients with major trauma.** **Research recommendation: Is warming clinically and cost effective in patients with major trauma? If so, which groups of patients will benefit from warming and what is the best method of warming?**
Relative values of different outcomes	Critical outcomes for decision making were mortality, health-related quality of life, length of intensive care stay, and adverse effects of treatment Patient-reported outcomes were agreed to be important.
Trade-off between clinical benefits and harms	A single RCT demonstrated a clinical benefit of intra-arterial warming using continuous arteriovenous rewarming (CAVR) plus conventional care with conventional care alone for the risk of mortality following major trauma. However, the GDG noted that the study used a specialised invasive technique and conventional care that are not routine practice in the UK. Therefore, the GDG did not feel the evidence was applicable to the UK population and was not useful in making a recommendation. The GDG noted that there is uncertainty about the clinical benefit of warming patients who have experienced major trauma. They also discussed the range of interventions used but accepted that these are rarely effective, particularly in the pre-hospital setting. Current UK practice is for patients to be warmed using active (generating heat) and passive (reducing heat loss) interventions. Interventions can also be described as internal (such as warmed fluids) or external (heated blanket ambulance). The GDG indicated that internal methods are generally more expensive and are likely to have more complications. The GDG discussed the fact that no studies were found to demonstrate a clinical benefit of warming a patient following major trauma. Conversely, no studies were found indicating a clinical harm of heating and loss of heat was generally thought to be detrimental to patients. To highlight this, the GDG mentioned studies which demonstrated defects in clotting when the body temperature drops below 32^{o}C. The GDG also noted there are uncertainties about this and anecdotal evidence suggests that cooling in some trauma may be beneficial. The GDG then discussed the rationale of warming patients and noted that one reason for warming arises from a humanitarian perspective; for example, wrapping a patient in a blanket is generally felt to be an appropriate course of action. Furthermore, reference was made to the perioperative warming guidelines (CG65) – (which states that temperature should be 36^{o}C or above

Trade-off between net health benefits and resource use	No economic evidence was identified for this question. The current practice is to use passive warming, such as blankets. However, more active methods of warming exist which can be either internal (warmed fluids) or external (such as forced air warming or chemical blankets). The GDG were presented with examples of costs for some of the interventions on the protocol. It was highlighted how variable the cost of the different interventions can be despite their being a lack of evidence as to the benefit of warming patients. Equipment to warm patients internally or externally has substantial one off costs which when spread on a per patient basis may be minimal (however, this does not include the cost of maintenance for example). Active external warming can also be expensive as products such as warming blankets which are in theory re-usable may not in fact get re-used if the patient was bleeding. Given the lack of clinical evidence, a recommendation was made emphasising that on-going heat loss should be prevented, and a research recommendation was also made.
	before transfer to theatre, unless there is urgency). It was noted that patients following major trauma would fall into the urgent category but once a patient is stable and in-hospital, the GDG felt that CG65 should be followed. The GDG agreed that effort should be made to maintain body temperature and prevent on-going heat loss using simple methods, such as minimising exposure or creating a warm environment.
Quality of evidence	The evidence was of low quality and demonstrated a serious risk of bias due to lack of blinding and also serious imprecision in the clinical outcome. However, the GDG did not consider it for the recommendation as it compared a specialised in-hospital technique not commonly used in UK practice.
Other considerations	Although the evidence suggested that warming benefits patients following major trauma, it was felt the intervention used in the study did not apply to the wider UK population and the data was of insufficient quality to make a recommendation. Considering the uncertainty within the field the GDG recommended maintaining current practice and to make a research recommendation. The GDG indicated that cold fluids should not be used and temperature should be measured regularly to monitor decline or hypothermia. Patient transfer time (particularly in rural areas) may also affect warming strategy and more aggressive methods may be considered. The GDG specifically commented on children and the fact that smaller children, in particular, are at increased risk for ongoing heat loss. However, the evidence does not exist to say children should be treated differently and the GDG felt that they should managed using the same principles (that is, to maintain body temperature). The GDG identified noted that particular care must be taken in children due to rapid heat loss secondary to their large surface area to weight ratio. It was suggested that there may be some benefit to cooling in some patient groups, for example, head injuries. However, the GDG noted the lack of evidence for this practice. It was agreed that clinicians do not know which groups of patients may benefit with warming or cooling and also which methods to use. Therefore, a research recommendation was also made.

14 Pain

14.1 Pain assessment

14.1.1 Introduction

Pain is a subjective, personal experience, and its assessment is particularly challenging in the presence of severe cognitive impairment, communication difficulties or language and cultural barriers. Following trauma, almost all patients experience pain and assessment of pain is critical for providing optimal pain management interventions. Pain is generally assessed on a severity scale and a range of tools have now been validated for specific populations (such as children and adults), and are widely used in clinical practice. Despite this, pain assessment and management remains one of the most areas of complaints for patients within the NHS and healthcare professions require a standardised and practical tool to assess pain across the trauma system.

14.1.2 Review question: What is the most appropriate pain assessment tool (pre-hospital and hospital) in patients with major trauma?

For full details see review protocol in Appendix C.

Table 125: PICO characteristics of review question

Population	Children, young people and adults who have experienced a traumatic incident.
Intervention(s)	• Pictorial scales • Numerical scales • Verbal scales • Visual scales
Comparison(s)	A comparison of the above Standard/usual care (clinical examination and judgement) No intervention
Outcomes	Critical: • Patient satisfaction • Health-related quality of life Important: • Patient-reported outcomes (psychological wellbeing).
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)

14.1.3 Clinical evidence

No relevant studies were identified.

14.1.4 Economic evidence

Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow chart in Appendix E.

14.1.5 Evidence statements

Clinical

No relevant clinical studies were identified.

Economic

No relevant economic evaluations were identified.

14.1.6 Recommendations and link to evidence

Recommendations	**61. See the NICE guideline on patient experience in adult NHS services for advice on assessing pain in adults.** **62. Assess pain regularly in patients with major trauma using a pain assessment scale suitable for the patient's age, developmental stage and cognitive function.** **63. Continue to assess pain in hospital using the same pain assessment scale that was used in the pre-hospital setting.**
Relative values of different outcomes	Patient satisfaction and health-related quality of life were selected as critical outcomes. The GDG felt that these would capture patient-centred effects most comprehensively and reflect a good assessment of pain. Psychosocial wellbeing and individual patient-reported outcomes were agreed to be important but not as critical as measures of quality of life, as the GDG felt these would be captured within health related quality of life.
Trade-off between clinical benefits and harms	No clinical evidence was found to evaluate the trade-off between clinical benefits and harms of assessment of pain using different scales in the pre-hospital or hospital setting. Assessment of patient's pain was considered essential to allow a patient to enter the pain management pathway, but the GDG acknowledged that it is not possible to assess pain in an unconscious patient. Different scales have been adapted to specific populations but the GDG felt the application of any particular scale over another was unlikely to affect clinical management. The GDG made specific reference to scales for young children and those with learning difficulties and suggested a number of appropriate scales (such as the Wong-Baker Face scale). As no evidence was found to support the use of any particular scale in children or in adults the GDG did not make a recommendation for a specific pain scale. The GDG felt that it was important that any scale used to measure pain could be applied equally in the pre-hospital and hospital settings, as this would allow consistent communication between healthcare professionals. Clinicians were more likely to use their clinical experience when assessing pain, but this could be problematic as pain was felt to be subjective and varied between individual patients. The GDG noted that clinicians should consider patients opinions in accordance with the patient experience guideline. A reliable scale may have the additional utility of allowing clinicians to assess the possibility to reduce pain relief.

	The GDG used informal expert consensus and cross-referred current guidance – CG138.
Trade-off between net health benefits and resource use	No economic evidence was identified for comparing different methods of assessing pain. In terms of the assessment of pain relief, this may be done through a tool, either numerical or pictorial or other methods. Resource implications may include the time taken to undertake the assessment using the tools; however, the GDG felt this would be minimal. Resources consumed also depend in part on downstream implications (that is, whether the assessment directs treatment and the modality of that treatment). The GDG also felt that re-assessment is an important issue which can add to the time taken. Different methods may also have a different impact on downstream resource use, as the level on alternative scales at which the highest dose of pain relief will be given might differ. The tools could, therefore, be quite arbitrary and ultimately involve clinical judgment which cannot be directly measured or evaluated. A clinician's experience of analgesic requirements associated with a specific injury pattern is an important factor as well as the management of the patient's perception of their pain, and can contribute to the clinical decision on the dose of pain relief to provide. The GDG discussed that satisfaction of the patient is linked to the intervention (pain relief) as opposed to the tool being used. However, appropriate pain relief implies that the pain was correctly identified. In other words, if a tool was successful in identifying pain which led to successful administration of pain relief then the patient would be satisfied with the tool. However, if the tool did not lead to successful pain relief, then this could imply the tool may have inadequately identified the pain relief. Current practice mostly involves using a numerical scale. Using other scales may take similar amount of time, depending if equipment needs to be sourced/used, for example, pictorial charts. The cost effectiveness of different methods depends upon the accuracy of the methods of predicting pain and the thresholds at which pain relief is given using the results of the scales. Downstream consequences also need to be considered as if pain is not accurately identified and managed, then this can potentially lead to downstream resource use from increased length of stay and clinical complications, as well as delays in treating other injuries whilst attempting to manage the pain. Pain relief drugs have potential to harm. Where the patient is not in pain, their use involves both health and financial cost. Therefore, the GDG felt it was cost effective practice that pain relief should always be guided through assessment of the patient's pain. No clinical evidence, however, was retrieved to inform which pain scale may be most cost effective.
Quality of evidence	No clinical evidence was identified for this question.
Other considerations	None.

14.2 Pain management

14.2.1 Introduction

Virtually all victims of major trauma experience moderate to severe pain requiring immediate and effective analgesia. Inadequate pain relief can lead to delayed healing, reduced functional recovery and has also been shown to reduce morbidity and improve long-term outcomes (that is, reduce

chronic pain and disability). Moreover, improved pain management is associated with increased comfort in trauma patients and the importance of pain relief is emphasised across multiple guidelines. Despite this, no evidence-based guidelines have been developed to address the effectiveness and safety of commonly used interventions for pain management following trauma.

14.2.2 Review question: What are the most clinically and cost effective first-line pharmacological pain management strategies (pre-hospital and hospital) in patients with major trauma?

For full details see review protocol in Appendix C.

Table 126: PICO characteristics of review question

Population	Children, young people and adults who have experienced a traumatic incident.
Intervention(s)	Intra-nasal: • Opiates • Ketamine Intra-muscular: • Opiates • Ketamine Inhaled: • Entonox/nitrous oxide Intravenous (IV): • Opiates • Ketamine • Paracetamol
Comparison(s)	A comparison of the above
Outcomes	Critical: • Pain levels (Pictorial scales, Numerical scales, Verbal scales, Visual scales) • Health-related quality of life • Adverse effects: nausea and respiratory depression, hallucinations • Level of consciousness Important: • Patient-reported outcomes (psychological wellbeing).
Study design	RCTs or systematic reviews of RCTs

14.2.3 Clinical evidence

We searched for RCTs comparing the effectiveness of pain management interventions in major trauma. A variety of pain management interventions were used (see Table 127). For full details see review protocol in Appendix C.

All studies extracted were from adults following a traumatic incident, although definition of trauma varied between studies (see Table 127). Major trauma, defined as life-threatening or altering injury, represented our target population. None of the studies included in the review fulfilled this directly and may present as indirect evidence. Examples of included populations include those with a numeric rating of 6/10 on pain scale.

Eight studies were included in the review;[17,28,43,52,58,72,129,135] these are summarised in Table 127 below.

Evidence from these studies is summarised in the GRADE clinical evidence profile and clinical evidence summaries below (Table 128 and Table 129, respectively). See also the study selection flow chart in Appendix D, study evidence tables in Appendix E, forest plots in Appendix J, GRADE tables in Appendix I and excluded studies list in Appendix K.

Table 127: Summary of studies included in the review

Study	Intervention/comparison	Population	Outcomes	Comments
Bounes 2010 [17,17]	Randomised 1:1 IV morphine versus IV fentanyl (sufentanil). n=108.	Patients were eligible for inclusion if aged 18 years or older, with acute severe pain (defined as a numeric rating scale score of 6/10 or higher) caused by trauma.	• Pain levels • Adverse effects (incidence of nausea) • Adverse effects (respiratory depression) • Loss of consciousness (Ramsey Score)	• Pain measurement was reported as dichotomous. • Scale used to define loss of consciousness is not well defined.
Craig 2012 [28,28]	Randomised 1:1 IV morphine versus IV acetaminophen (paracetamol). n =55.	Isolated limb trauma, Moderate to severe pain, with initial verbal pain score of 7 or more, Age >15 and <66 years, Estimated weight >50 kg.	• Pain levels • Incidence of adverse effects • Patient reporting outcomes (patient satisfaction)	• Major trauma patients listed to be excluded but meet other criteria. • Adverse effects grouped together and not reported separately.
Farsi 2013[43,43]	Randomised 1:1 IV intermediate-dose morphine versus IV high-dose morphine. n=200.	Patients over 20 years of age presenting to the emergency department (ED) with pain following acute limb trauma of less than three days' duration, and considered by the ED attending professors to require opioid analgesia, were suitable for inclusion.	• Pain levels • Adverse effects (Incidence of nausea) • Adverse effects (incidence of respiratory depression) • Loss of consciousness – (Glasgow coma score [GCS])	Does not specify the GCS at which causes loss of consciousness
Galinkski 2007 ([52,52]	Randomised 1:1 IV morphine versus IV ketamine. n=73.	Patients were eligible for inclusion if they presented a trauma with a severe acute pain defined as a visual analogue	• Pain levels • Adverse effects (incidence of nausea) • Loss of consciousness – (Ramsay score)	

Study	Intervention/comparison	Population	Outcomes	Comments
		scale score of at least 60/100; were aged between 18 and 70 years; and were without acute respiratory, hemodynamic, or neurologic compromise (respiratory distress signs, systolic blood pressure V90 mmHg, GCS greater or equal to 15).	• Patient reporting outcomes (patient satisfaction)	
Gurnani 1996 [58,58]	Randomised 1:1 IV morphine versus IV ketamine. n=40.	Patients suffering from acute musculoskeletal trauma not requiring immediate corrective surgical intervention.	• Pain levels • Adverse effects (incidence of nausea) • Adverse effects : (incidence of hallucinations	Data for pain levels reported indirectly (high risk of reporting bias). No standard deviation of confidence intervals available.
Jennings 2012[71,72]	Randomised 1:1 IV morphine versus IV morphine/ketamine. n=135.	Patients were eligible for enrolment if they were assessed by the attending paramedics as having all of the following: were aged 18 years or older, conscious (GCS score=15), reporting traumatic pain with a verbal numeric rating scale pain score greater than or equal to 5 (out of 10) after a total dose of IV morphine of 5 mg/litre.	• Pain levels • Adverse effects (incidence of nausea). • Adverse effects (hallucinations). • Loss of consciousness – GCS) • Health-related quality of life	Health-related quality of life data extracted from Jennings 2013
Smith 2012 [129,130]	Randomised 1:1 IV morphine versus IV fentanyl. n=214.	Patients were enrolled if they reported pain and could communicate to the medical crew their pain severity on a numeric pain scale.	• Pain levels at 40 minutes (average of both groups). • Adverse effects (Incidence of nausea) • Loss of consciousness (Ramsay scale)	

Study	Intervention/comparison	Population	Outcomes	Comments
Tran 2014[135,135]	Cluster randomised 1:1 IV morphine versus IV ketamine	Trauma patients in need of analgesia referred to a provincial general hospital.	• Pain levels • Nausea	Study at very high risk or bias due to poor outcome reporting and no blinding.

Table 128: Clinical evidence summary: Morphine versus ketamine

Outcome	Number of studies	Imprecision	GRADE rating	Absolute difference	Control event rate (per 1000)	Control event rate for continuous outcomes
Pain Levels (Final score) – (Scale 0-100)	1 (n=65)	No serious imprecision	MODERATE	MD 5.4 higher (3.2 to 7.6 higher)	-	34.1
Pain levels (Change score) – (Scale 0-10)	1 (n=135)	Serious imprecision	LOW	MD 2.40 higher (1.40 to 3.40 higher)	-	-5.6
Quality of life (SF-36) – Physical component (Scale 0-100)	1 (n=97)	No serious imprecision	MODERATE	MD 1.1 lower (5.48 lower to 3.28 higher)	-	49
Quality of life (SF-36) – Mental component (Scale 0-100)	1 (n=97)	No serious imprecision	MODERATE	MD 0.0 (5.02 lower to 5.02 higher)	-	50
Adverse events (Nausea)	3 (n=240)	Very serious imprecision	VERY LOW	Random effects RR: 71 more per 1000 (from 57 fewer to 762 more)	89	-
Adverse events (Hallucinations)	2 (n=175)	No serious imprecision	MODERATE	Peto Odds Ratio: 70 fewer per 1000 (from 130 to 10 fewer)	67	-
Loss of consciousness – Ramsey Score	1 (n=65)	Very serious imprecision	VERY LOW	151 fewer per 1000 (from 197 fewer to 66 more)	212	-
Loss of consciousness – GCS	1 (n=135)	Very serious imprecision	LOW	Peto Odds Ratio: 30 fewer per 1000 (from 80 fewer to 30 more)	43	-
Patient Satisfaction	1 (n =65)	Serious imprecision	VERY LOW	142 more per 1000 (from 82 fewer to 469 more)	545	-

Table 129: Clinical evidence summary: Morphine versus acetaminophen

Outcome	Number of studies	Imprecision	GRADE rating	Absolute difference	Control event rate (per 1000)	Control event rate for continuous outcomes
Pain Levels (follow-up 15-minutes; measured with: Final pain score scale 0-100)	1 (n=55)	Serious imprecision	LOW	MD 8.3 lower (18.26 lower to 1.66 higher)	-	69.9
Pain Levels (follow-up 30-minutes; measured with: Final pain score scale 0-100)	1 (n=55)	Serious imprecision	LOW	MD 8.5 lower (22.42lower to 5.42 higher)	-	63.5
Pain Levels (follow-up 60-minutes; measured with: Final pain score scale 0-100)	1 (n=55)	Serious imprecision	LOW	MD 8.9 lower (22.3 lower to 4.5 higher)	-	52.9
Adverse events (nausea)	1 (n=55)	Serious imprecision	VERY LOW	212 more per 1000 (from 7 fewer to 1000 more)	74	-
Patient Satisfaction	1 (n=55)	Serious imprecision	LOW	180 more per 1000 (from 76 fewer to 652 more)	360	-

Table 130: Clinical evidence summary: Intermediate dose morphine versus high-dose morphine

Outcome	Number of studies	Imprecision	GRADE rating	Absolute difference	Control event rate (per 1000)	Control event rate for continuous outcomes
Pain Levels (follow-up 60-minutes; measured with: Final pain score scale 0-10)	1 (n=200)	No serious imprecision	MODERATE	MD 0.49 lower (1.2 lower to 0.22 higher)	-	5.69
Adverse events (nausea)	1 (n=200)	Very serious imprecision	VERY LOW	20 fewer per 1000 (from 67 fewer to 94 more)	100	-
Loss of consciousness – GCS	1 (n=200)	Very serious imprecision	VERY LOW	10 fewer per 1000 (from 39 fewer to 95 more)	50	-

Table 131: Clinical evidence summary: Morphine versus fentanyl

Outcome	Number of studies	Imprecision	GRADE rating	Absolute difference	Control event rate (per 1000)	Control event rate for continuous outcomes
Pain Levels (follow-up 60 minutes; measured with: Final pain score scale 0-10)	1 (n=200)	No imprecision	HIGH	MD 0.3 higher (0.41 lower to 1.01 higher)	-	5.5
Pain Levels (follow-up 30 minutes; measured with: Change in Pain Score (dichotomised)	1 (n=108)	Serious imprecision	MODERATE	37 fewer per 1000 (from 185 fewer to 148 more)	704	-
Adverse events (nausea)	2 (n=308)	Very serious imprecision	VERY LOW	Peto odds ratio: 20 fewer per 1000 (from 50 fewer to 10 more)	20	-
Adverse events (respiratory depression)	1 (n=108)	Very serious imprecision	LOW	Peto odds ratio: 20 more per 1000 (from 40 fewer to 80 more)	19	-
Loss of consciousness (Ramsay Scale)	1 (n=108)	Very serious	VERY LOW	56 fewer per 1000 (from 85 fewer to 90 more)	93	-

Table 132: Clinical evidence summary: Morphine (intramuscular [IM]) versus ketamine (IV)

Outcome	Number of studies	Imprecision	GRADE rating	Absolute difference	Control event rate (per 1000)	Control event rate for continuous outcomes
Adverse events (nausea)	1 (n=312)	No imprecision	LOW	143 more per 1000 (from 42 more to 358 more)	100	-

14.2.4 Economic evidence

Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow chart in Appendix E.

Unit costs

Relevant unit costs are provided below to aid consideration of cost effectiveness. The clinical review protocol included 4 different methods of pain relief administration, which should be considered additional to the drug acquisition costs.

Table 133: Equipment needed for the different methods of access

Intervention	Resources needed	Cost	Cost per patient	Source
Intra nasal	Syringe hypodermic concentric luer slip – 10 ml	£84.32 Case of 1600	£0.05	NHS supply chain [3]
	Blunt filter drawing up needle 18 g x 38 mm	£44.70 Box of 100	£0.45	NHS supply chain
	Nasal atomisation device	£269.52 Box of 100	£2.70	NHS supply chain
Total			**£3.19**	
Intra muscular	Syringe hypodermic concentric luer slip – 10 ml	£84.32 Case of 1600	£0.05	NHS supply chain
	Blunt filter drawing up needle 18 g x 38 mm	£44.70 Box of 100	£0.45	NHS supply chain
	Needle hypodermic sterile - Green 21 gauge x 1.5 inch	£1.70 Pack of 100	£0.02	NHS supply chain
	Pre injection 70% isopropyl alcohol wipe 60 mm x 30 mm (10,000 sachets)	£105.88 10000 sachets	£0.01	NHS supply chain
Total			**£0.53**	
Inhaled	Entonox cylinder rental cost	Approximately £5 a month [a]		Entonox supplier
	Entonox delivery circuit mask	£59.81 Box of 10	£5.98	NHS supply chain
	Entonox delivery circuit mouthpiece	£79.09 Box of 20	£3.95	NHS supply chain
	Entonox mouthpiece filter	£74.23 Box of 50	£1.48	NHS supply chain
	Demand valve	£280 [b]	£0.06	Entonox supplier
Total			**£11.48 (+ cylinder rental)**	
IV [c]	Pre injection 70% isopropyl alcohol wipe 60 mm x 30 mm	£105.88 10,000 sachets	£0.01	NHS supply chain

Intervention	Resources needed	Cost	Cost per patient	Source
	(10,000 sachets)			
	cannulas (22-14G)	£42 box of 50	£0.84	The Air Ambulance Service (through GDG contact)
	Tegaderm Film	£28.82 box of 100	£0.29	The Air Ambulance Service (through GDG contact)
	10-ml syringe green 21 gauge x 0.5-inch needle (x2)	£26.30 Box of 100	£0.53	NHS Supply chain
	10ml sodium chloride	£3.36 pack of 10	£0.34	Drug tariff [106]
Total			**£2**	

(a) Other negligible costs per patient here include the Entonox gas itself and the demand valve that would need to be purchased for use with the cylinder.
(b) Assumed can be used on 5000 patients.
(c) Additional costs could include a controlled flow giving set which is used for giving paracetamol intravenously

Table 134: Drug costs

Drug	Dose	Cost	Method of access suitable for	Source
Pain relief				
Morphine	10-mg ampoule	£0.94	Intranasal, IM, IV	Drug Tariff [106]
Diamorphine	10-mg ampoule	£2.57	Intranasal, IM, IV	BNF [73]
Fentanyl	50 micrograms/ml, 2-ml ampoule (=100 micrograms)	£0.30	Intranasal, IM, IV	BNF
	50-micrograms/metered spray	£5.95	Intranasal	BNF
Alfentanyl	500 micrograms/ml, 2-ml amp (=1,000 micrograms = 1 mg)	£0.70	Intranasal, IM, IV	BNF
Ketamine	10 mg/ml, 20-ml vial (=200 mg)	£5.06	Intranasal, IM, IV	BNF
Paracetamol	10 mg/ml, 100-ml vial (=1000 mg)	£1.20	Intranasal, IM, IV	BNF
Antiemetic (administered with morphine or diamorphine to prevent nausea)				
Cyclizine lactate	50 mg/ml, 1-ml amp	£0.65		BNF
Metoclopramide	5 mg/ml, 2-ml amp (=10 mg)	£0.30		BNF

As an example of the dose taken from one of the clinical review papers (0.1 mg/kg of morphine, followed by 3 mg every 5 minutes until pain score was below 30/100. Duration of 30 minutes):

Assuming an average weight of 75 kg:

- Initial dose cost of 0.1mg/kg is £0.71
- Additional dose of 3 mg 6 times (every 5 minutes for 30 minutes) is £1.69
- Equals a total cost of £2.40

14.2.5 Evidence statements

Clinical

Morphine versus ketamine

Moderate quality evidence from 1 RCT comprising of 65 participants demonstrated a clinical benefit of the combination of ketamine and morphine for pain level (30 minutes), with no imprecision.

Low quality evidence from 1 RCT with 135 participants demonstrated a clinical benefit with combination of ketamine and morphine over morphine alone for pain level (47 minutes), with serious imprecision.

Moderate quality evidence 1 single RCT comprising of 97 participants demonstrated no clinical difference between morphine and the combination of morphine and ketamine for health-related quality of life (SF-36 Physical Component), with serious risk of bias.

Moderate quality evidence 1 single RCT comprising of 97 participants demonstrated no clinical difference between morphine and the combination of morphine and ketamine for health-related quality of life (SF36 Mental Component), with serious risk of bias.

Very low quality evidence from 3 RCTs comprising 240 participants demonstrated a clinical benefit of morphine and ketamine compared with morphine alone for nausea, with serious imprecision.

Moderate quality evidence from 2 RCTs comprising of 175 participants demonstrated a clinical benefit with morphine alone compared with the combination of morphine and ketamine for hallucinations, with no imprecision

Very low quality evidence from 1 RCT comprising 65 participants demonstrated a clinical benefit of morphine compared with morphine and ketamine in combination for loss of consciousness measured by the Ramsey Score, with very serious imprecision.

Low quality evidence from 1 RCT comprising 135 participants demonstrated no clinical difference between morphine and morphine and ketamine in combination for loss of consciousness measured by the GCS, with very serious imprecision.

Very low quality evidence from 1 RCT comprising 65 participants demonstrated a clinical benefit with combination of ketamine and morphine over morphine alone for patient satisfaction, with serious imprecision.

Morphine versus acetaminophen

Low quality evidence from 1 RCT comprising of 55 participants demonstrated a clinical benefit of morphine over acetaminophen for pain levels (15 minutes), with serious imprecision.

Low quality evidence from 1 RCT comprising of 55 participants demonstrated a clinical benefit of morphine over acetaminophen for pain levels (30 minutes), with serious imprecision.

Low quality evidence from 1 RCT comprising of 55 participants demonstrated a clinical benefit of morphine over acetaminophen for pain levels (60 minutes), with serious imprecision.

Very low quality evidence from 1 RCT comprising 55 participants demonstrated a clinical benefit of acetaminophen over morphine for adverse effect, with serious imprecision.

Low quality evidence from 1 RCT comprising 55 participants demonstrated a clinical benefit of morphine over acetaminophen for patient satisfaction, with serious imprecision

Intermediate dose morphine versus high dose morphine

Moderate quality evidence from 1 RCT comprising of 200 participants demonstrated no clinical difference between intermediate and high dose morphine for pain level (60 minutes), with no imprecision.

Very low quality evidence from 1 RCT comprising 200 patients demonstrated no clinical difference between intermediate dose morphine and high dose morphine for incidence of nausea, with serious imprecision.

Very low quality evidence from 1 RCT comprising 200 participants demonstrated no clinical difference between intermediate dose morphine and high dose morphine for loss of consciousness measured by the GCS, with very serious imprecision.

Morphine versus fentanyl

High quality evidence from 1 RCT comprising of 200 participants demonstrated no clinical difference between morphine and fentanyl for pain levels (60 minutes), with no imprecision.

Moderate quality evidence from 1RCT comprising of 108 participants demonstrated no clinical difference between the interventions for pain level (30 minutes), with very serious imprecision.

Very low quality evidence from 2 RCT's comprising 308 patients demonstrated no clinical difference between morphine and fentanyl alone for nausea demonstrated no difference, with serious imprecision.

Low quality evidence from 1 RCT comprising 108 patients demonstrated no clinical difference between morphine and fentanyl for respiratory depression, with very serious imprecision.

Very low quality evidence from 1 RCT comprising 108 demonstrated no clinical difference between intermediate dose morphine and high dose morphine for loss of consciousness measured by the Ramsey Scale, with very serious imprecision.

Morphine (IM) versus ketamine (IV)

Low quality evidence from 1 RCT comprising 312 patients demonstrated a clinical benefit of IV ketamine over IM morphine for incidence of nausea, with no imprecision.

Economic

No relevant economic evaluations were identified.

14.2.6 Recommendations and link to evidence

Recommendations	**Pre-hospital for adults and children** **64. For patients with major trauma, use intravenous morphine as the first-line analgesic and adjust the dose as needed to achieve adequate pain relief.** **65. If intravenous access has not been established, consider the intranasal route for atomised delivery of diamorphine or ketamine[c].**

c At the time of publication (February 2016), neither intranasal diamorphine nor intranasal ketamine had a UK marketing authorisation for this indication. The prescriber should follow relevant professional guidance, taking full responsibility

	66.Consider ketamine in analgesic doses as a second-line agent. **Research recommendation: Is morphine clinically and cost effective compared with ketamine for first-line pharmacological pain management (in both pre-hospital and hospital settings) in patients with major trauma?**
Relative values of different outcomes	Patient-reported pain scores were considered critical as they reflect patient satisfaction with the intervention and offer the best outcome to distinguish clinical efficacy. Health-related quality of life was also considered critical as it could reflect short- and long-term effects of the interventions. All interventions used had a well-established risk profile and the GDG felt that it was critical to assess these as they could lead to severe adverse effects (including nausea, respiratory depression, hallucinations, and level of consciousness). Patient-reported outcomes, including psychological wellbeing were only considered important as it was felt it would be captured by other outcomes, including health-related quality of life.
Trade-off between clinical benefits and harms	**Morphine versus morphine plus ketamine** Two studies considered the effect of adding IV ketamine to IV morphine and found a greater analgesic effect with combination therapy. There was a clinical risk of nausea with morphine while ketamine increased risk of loss of consciousness in both studies. Morphine was shown to clinically improve patient satisfaction score, but no difference was found for health-related quality of life. The GDG discussed the evidence and felt that due to its reduced side-effect profile and more general clinical use, morphine should be used preferentially over ketamine as a first-line analgesic pain management in major trauma. Despite this, the added benefit of ketamine with regards to mild sedation (allowing for manipulation of limbs and calming of the patient), opiate sparing and for the reduction in post-traumatic stress disorder was noted. The GDG also noted that there is recent evidence that ketamine may be protective but the evidence remains inconclusive. **Morphine versus paracetamol** A single study compared IV morphine with IV paracetamol and found morphine to be a superior analgesic. Morphine was also found to be a better for patient satisfaction but associated with an increased adverse effect profile. The GDG discussed the evidence and felt that paracetamol would not be appropriate as a single intervention within a major trauma population. It was noted that it may have morphine sparing effects when used in combination with morphine, but morphine should always be considered preferentially as the first-line intervention. **Intermediate-dose morphine versus high-dose morphine** A single study demonstrated no difference between intermediate and high IV dosing for pain levels, nausea and loss of consciousness. The GDG discussed the different doses and felt that both would be used in major trauma. The lower dose (0.10 mg/kg) is more commonly used in current practice and is likely to provide sufficient analgesia. **Morphine versus fentanyl**

for the decision. Informed consent should be obtained and documented. See the General Medical Council's Prescribing guidance: prescribing unlicensed medicines for further information.

	Two studies compared IV morphine with IV fentanyl and found no difference between the interventions for pain relief and adverse side effects. The GDG discussed the evidence and noted that both drugs were from the same class and lack of difference in clinical efficacy would be largely expected. **Children** No evidence was found in children but the GDG were happy to extrapolate the data and recommendation from adult studies. The GDG indicated that IV administration of opioids is a common and effective form of analgesia in children and is likely to offer the best option. The GDG noted that the efficacy of ketamine for analgesia was not well studied in children but were not aware of any major side effects associated with its administration. **The GDG noted the importance of titrating morphine in response to the effect especially in the patient with active bleeding** The GDG also made reference to hypotensive patients following trauma, as administration of morphine could exacerbate problems in the hypotensive patient. The patient should be monitored closely and dose tittered to effect.
Trade-off between net health benefits and resource use	There was no published economic evidence to inform this question. **Application method** The GDG considered the cost of different application methods of pain relief; from oral medication having no cost, to inhaled medication having a cost of around £11 per application in consumables plus rental of the cylinder which would equate to approximately £5 per month ongoing, plus negligible costs for the Entonox gas itself. The GDG considered inhaled forms of medication unlikely to be useful in the pre-hospital setting. Use of Entonox is problematic as the patient needs to be able to actively inhale the medication and manage the equipment. Furthermore, it prevents a full concentration of oxygen to be given and potentially therefore could indirectly deny the patient health benefit of oxygen administration. Considering the use of Entonox is the most expensive form of delivery yet and possibly the form which would deliver least net benefit, the GDG thought its use in a major trauma population was unlikely to be cost effective, even if it allows for temporary pain relief whilst other pain relief medications are being prepared. It is also contra-indicated under certain circumstances that are not uncommon in major trauma, for example, pneumothorax, in the presence of intra-cranial air or intra-abdominal perforation. The IM route had low costs, although, in a poorly perfused patient, the onset of drug action may be relatively slow and unpredictable. The GDG therefore considered IV, intraosseous (IO), oral and intranasal as potentially cost-effective options to administer pain relief, dependent on ease and speed of access of administration (please refer to the access question for IO costs in section 10.6) and time to take effect. Although oral medication incurred no unit cost in its application, its use may be limited by its relatively slow onset of action. IV access was seen as the preferred method of providing pain relief, however, the GDG felt that intranasal could also be used if gaining IV access was difficult. The intranasal route may need certain specialised equipment, such as an atomiser, to convert the liquid form of a drug to a mist, however, including this in the cost of the intranasal route still makes this route of delivery relatively cheap (around £3 – only

	slightly more than IV access). **Choice of drug** The GDG considered the unit costs of each drug, noting that the cost would be incurred for a whole ampoule or vial, even if not all of the ampoule or vile was used. It was thought that costs would not increase substantially according to dose, however, as the clinical review did not suggest a differential effect according to a larger does, a lower dose is likely to be most cost effective with titration upwards according to effect. In terms of downstream costs associated with side effects, the GDG noted that loss of consciousness or a reduction in GCS may complicate downstream clinical assessment and treatment options, which would incur cost. Admission to ICU, for example, was more likely to be necessary for an unconscious patient. Paracetamol and fentanyl did not appear to have any substantial clinical advantage over morphine. The GDG also considered IV paracetamol, which is becoming more common in practice. However, IV paracetamol is more expensive than morphine and there is no evidence to support its use as a cost effective option. Without an evidence base, the GDG felt unable to make a 'do not' use recommendation regarding IV paracetamol. Overall, it was thought that Ketamine was a better analgesic, but was more costly and had a higher adverse risk profile than other drugs. For example, ketamine is approximately five times more expensive than morphine (although has the benefit that an antiemetic may not also need to be given as an adjunct). Emetic affects are generally not an issue in children however. There was no clinical evidence to inform whether ketamine in isolation was more effective or cost effective than morphine as a first-line agent and further research would be required before it could be recommended in this capacity. The GDG therefore recommended morphine as a first-line agent for pain, whereby ketamine could only be used as second-line.
Quality of evidence	The quality of evidence ranged from moderate to very low for most comparisons. Most studies demonstrated a serious risk of bias due to lack of evidence for allocation concealment and blinding. Generally, there was no imprecision for changes in pain score but serious or very serious imprecision for dichotomous outcomes, including adverse effects. Some studies were from populations not considered to specifically be major trauma (such as, fracture, limb trauma).The GDG discussed the management of pain and noted that his would be based on clinical interpretation of the patient's pain (that is, if patient is in severe pain they should be managed accordingly) and that studies which defined severe pain as an inclusion criteria (that is, above 7/10 on a pain scoring scale) should be considered. Therefore, the GDG felt that all included studies could be appropriately extrapolated to major trauma populations as many of the interventions would be commonly used.
Other considerations	The GDG considered specific populations in which intranasal administration may be preferable (such as, those in which IV access is difficult to obtain). This route may not provide the same level of analgesia but may be indicated for immediate pain relief. Intranasal is likely to be preferential to IM due to its more rapid action. Moreover, the GDG noted that in current practice drugs can be squirted into the nose, rather than using specific nasal equipment. In patients in whom the IO route is already established, then this route can be used to administer analgesia.

	However, some drugs used for intranasal administration, for example, fentanyl and diamorphine, which come in suitable concentrated forms, are not available in ambulances in all areas and the use is contraindicated in cases of facial trauma or severe head injury. Caution should also be taken when giving pain relief intranasally and then giving IV due to additive dosing effects. Converting the drug to an atomized spray (rather than drops) maximises the surface area coverage with a thin layer of the drug resulting in less drug loss. Fentanyl can only be delivered by trained physicians which limits it use as a first line pain management agent. Entonox was not considered in the clinical evidence as no studies using the intervention were considered to be from a major trauma population. The GDG felt that it should not be used in a major trauma population as it did not provide sufficient pain relief. It was also noted that patients with major trauma regularly have breathing problems and the intervention has limited clinical and logistical use in this population. Nonetheless, it was noted that Entonox could temporarily be used while IV access is being gained and may have additive analgesic effects. Only one very small RCT was identified comparing morphine and ketamine (first and second medications). The GDG made a research recommendation comparing these interventions. The GDG noted that patients may need to be referred for on-going pain management but this was outside of the scope of this guideline.

15 Documentation

15.1 Introduction

Currently, different pre-hospital and hospital service providers use different methods of documentation but standardisation may improve patient outcomes and reduce resource use. Standardisation includes both what is information is documented and in what format it used.

15.2 Review question: Is documentation using a standard form across all clinical settings (pre-hospital and hospital) in which a major trauma patient might be treated clinically and cost effective?

For full details see review protocol in Appendix C.

Table 135: PICO characteristics of review question

Population	Children, young people and adults who have experienced a traumatic incident.
Intervention(s)	Standard documentation across all clinical settings, including proforma, electronic medical records
Comparison(s)	Varying documentation
Outcomes	Critical: • Mortality at 24 hours • Mortality at 30 days/1 month • Mortality at 12 months • Health-related quality of life • Complications Important: • Length of stay • Patient-reported outcome: return to normal activities • Patient-reported outcome: psychological wellbeing. • Missing data • Timing of transfers
Study design	RCT, cohort, observational

15.3 Clinical evidence

Five retrospective cohort studies[78,79]; [111,112]; [34,34]; [126,126]; [94,94] were identified that looked at standardisation documentation across settings. One study implemented a checklist and four electronic medical records.

Table 136: Summary of studies included in the review

Study	Intervention and comparison	Population	Outcomes	Comments
Lee 2014[78,79]	Pre- versus post-intervention. n=1622. Pre intervention: Morning sign-out was an informal process	All patients admitted to the trauma service. Pre-intervention September 2008 to	Complications Mortality ICU length of stay Hospital length of stay	Groups comparable on median age, ISS, mechanisms of injury and rate of ICU admission pre versus

Study	Intervention and comparison	Population	Outcomes	Comments
	consisting of the following: post call surgeon, the on-call surgeon, the distinct trauma intensivist who is solely covering the ICU, physician assistants and trauma case managers. There was no organised structure to the sign out. Implementation of an organ-based checklist during daily sign-out for all admitted trauma patients	January 2009. Post-intervention September 2009 to January 2010. USA.	Hospital length of stay (injury severity score [ISS] >16) Guideline noncompliance	post implementation
Patel 2009[111,112]	Pre- versus post-intervention; n=707 Pre-intervention paper-based handover. Ad hoc Word document which had columns for patient details, location, diagnosis and either hand wrote or typed information to handover in the management plan column. Implementation of web-based software to record a minimum data set (basic demographic data, responsible surgeon, location of patient and diagnosis. Injury details included anatomical site, open or closed fracture, concomitant injuries and treatment plan). The software was designed to facilitate the coordination of an X-ray meeting at the fracture clinic where all members of the orthopaedic team are present to	Patients discussed at an X-ray meeting for trauma patients. Pre-intervention December 2006 to March 2007. Post-intervention April 2007 until July 2007. UK.	Completeness of data recording	No data to compare re versus post intervention patients. The format of the data recording was changed along with what information was recorded.

Study	Intervention and comparison	Population	Outcomes	Comments
	discuss management of trauma patients			
Deckelbaum 2009[34,34]	Pre- versus post-intervention. n=11,234 Pre- versus post-intervention of an electronic medical record.	Trauma and burn patients. Data collected between 2003 and 2006. USA	Mortality Completeness of data recording	Data comparable pre versus post implementation for age, gender, ISS and mechanisms of injury. Unable to determine if what was recorded also changed as well as the format.
Schenarts 2012[126,126]	Pre- versus post-intervention. n=5996. Implementation of an electronic medical record. All forms of documentation including all notes, physicians orders, order sets, critical care bundles, discharge summaries and discharge instructions were electronic.	Trauma patients. Pre-intervention October 2005 to July 2007. Post-intervention July 2009 to February 2011. USA	Mortality Length of stay Complications	Data comparable pre versus post implementation for age, gender, mechanism of injury and ISS. The time span pre versus post is quite long. Treatment may have changed over this time period? There were no specific changes to the chart during the change from paper to computer
Mpletsa 2012[94,94]	Patients chosen at random to compare those with an electronic record with those without an electronic record. n=200. Electronic patients trauma monitoring system in accordance with Advanced Trauma Life Support guidelines.	Trauma patients admitted March 2007 to March 2009. Greece.	Length of stay in emergency department (ED) Time between admission and completion of care Time from completion of care and exit from emergency dept.	Data comparable for electronic versus no electronic record for age, Glasgow scale and severity of injury. Unable to determine if what was recorded also changed as well as the format.

Table 137: Clinical evidence summary: checklist versus no checklist

Outcome	Number of studies (no. of participants)	Imprecision	GRADE rating	Absolute difference	Control event rate (per 1000)	Control group value for continuous outcomes
Mortality	1 (n=1622)	Serious	VERY LOW	9 more per 1000 (from 7 fewer to 36 more)	33	-
Complications	1 (n=1622)	Very serious	VERY LOW	3 more per 1000 (from 11 fewer to 26 more)	29	
ICU length of stay	1 (n=1622)	Not variance data reported	LOW	Median pre 2 versus post 1, p=0.01	-	-
Hospital length of stay	1 (n=1622)	Not variance data reported	LOW	Median pre 2 versus post 2, p <0.001	-	-
Hospital length of stay (ISS > 16)	1 (n=1622)	Not variance data reported	LOW	Median pre 5 versus post 3, p=0.02	-	-

Table 138: Clinical evidence summary table: electronic medical record versus no electronic medical record

Outcomes	Number of studies (no. of participants)	Imprecision	GRADE rating	Absolute difference	Control event rate (per 1000)	Control event rate For continuous outcomes
Mortality	3 (n=7519) (n=200) (n=5999)	No serious imprecision	VERY LOW	9 fewer per 1000 (from 1 fewer to 16 fewer) 2 fewer (from 13 fewer to 11 more) 30 fewer (46 fewer to 51 more)	58 1 50	
Requiring severe surgery	1 (n=200)	Serious	VERY LOW	58 fewer per 1000 (from 175 fewer to 90 more)	530	
Delay in diagnosis	1 (n=200)	Serious	VERY LOW	9 more per 1000	22	

Outcomes	Number of studies (no. of participants)	Imprecision	GRADE rating	Absolute difference	Control event rate (per 1000)	Control event rate For continuous outcomes
				(from 0 more to 20 more)		
Complications - Airway complication	1 (n=5996)	Very serious	VERY LOW	0 more per 1000 (from 3 fewer to 6 more)	7	
Complications - Cardiac arrest	1(n=5996)	Very serious	VERY LOW	3 fewer per 1000 (from 8 fewer to 4 more)	17	
Complications - Wound infection	1(n=5996)	Serious	VERY LOW	2 fewer per 1000 (from 7 fewer to 5 more)	16	
Complications - Drug complication	1(n=5996)	No serious imprecision	LOW	5 fewer per 1000 (from 2 fewer to 6 fewer)	6	
Completeness of data - Floor notes	1(n=5996)	No serious imprecision	VERY LOW	870 more per 1000 (from 623 more to 1000 more)	10	
Completeness of data - Procedure notes	1(n=5996)	No serious imprecision	VERY LOW	172 more per 1000 (from 148 more to 187 more)	780	
Completeness of data - Resuscitation notes	1(n=5996)	No serious imprecision	VERY LOW	162 more per 1000 (from 146 more to 178 more)	810	
Completeness of data - ICU notes	1(n=5996)	Serious	VERY LOW	192 more per 1000 (from 176 more to 208 more)	800	
Missing cases - Demographics	1 (n=807)	No serious imprecision	LOW	344 fewer per 1000 (from 327 fewer to 208 more)	8	
Missing cases - Diagnosis	1(n=807)	No serious	LOW	109 fewer per 1000	8	

Outcomes	Number of studies (no. of participants)	Imprecision	GRADE rating	Absolute difference	Control event rate (per 1000)	Control event rate For continuous outcomes
		imprecision		(from 90 fewer to 115 fewer)		
Missing cases - Mechanism of injury	1(n=807)	No serious imprecision	LOW	258 fewer per 1000 (from 235 fewer to 269 fewer)	22	
Missing cases - Treatment plan	1(n=807)	No serious imprecision	LOW	425 fewer per 1000 (from 90 fewer to 115 fewer)	53	
Length of stay ED (minutes)	1 (n=200)	No serious imprecision	LOW	MD 79 lower (98.92 to 59.08 lower)	206	
Time between admission and completion of care (minutes)	1 (n=200)	No serious imprecision	LOW	MD 49 lower (67.91 to 30.09 lower)	149	
Time between completion of care and exit from ED (minutes)	1 (n=200)	No serious imprecision	LOW	MD 31 lower (35.92 to 26.08 lower)	57	

Narrative review

Table 139: Checklist versus no checklist

Outcome	Median (IQR if reported), p
ICU days	2 versus 1, p=0.007
Hospital length of stay	2 (1 to 5) versus 2 (1 to 4), p=0.000
Hospital length of stay (ISS >16)	5 versus 3, p=0.021

Electronic medical records versus no electronic medical record

One study [111,112] reported the following user feedback:

Table 140: User feedback

Use of service	Feedback
Organisation and time efficiency of post-take ward	30/32 (94%) helpful
Organisation and time efficiency of morning trauma meetings	31/21 (97%) helpful
Quality of information passed on at handover	27/28 (96%) improved quality
Communication of information amongst trauma team (including allied staff)	28/36 (78%) improved communication
Impact of working day time management	22/32 (69%) saved time
Impact on patient management	26/34 (76%) positive
Overall satisfaction	32/43 (94%)

One study [126,126] reported the following outcomes:

Table 141: Outcomes

Outcomes	No electronic medical record	Electronic medical record	p value
Hospital length of stay (days)	7.9	7.1	0.02
ICU length of stay (days)	7.4	6.0	0.001

15.4 Economic evidence

Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow chart in Appendix E.

15.5 Evidence statements

Clinical

Checklist versus no checklist

Very low quality evidence from a single observational study comprising 1622 participants demonstrated no clinical difference between a checklist and no checklist for mortality or complications, with very serious and serious imprecision.

Electronic medical record versus no electronic medical record

Very low quality evidence from three cohort studies comprising 200, 5999 and 7519 participants, respectively, demonstrated no clinical difference between an electronic medical record and no electronic medical record for mortality, with no serious imprecision.

Very low quality evidence from one cohort study comprising 200 participants demonstrated a clinical benefit of an electronic medical record compared with no electronic medical record for requiring severe surgery, with serious imprecision.

Very low quality evidence from one cohort study comprising 200 participants demonstrated no clinical difference between an electronic medical record and no electronic medical record for a delay in diagnosis, with serious imprecision.

Low to very low quality evidence from one cohort study comprising 5996 participants demonstrated no clinical difference between an electronic medical record and no electronic medical record for airway complications, cardiac arrest, wound infection and drug complications, with no to very serious imprecision.

Very low quality evidence from one cohort study comprising 5996 participants demonstrated a clinical benefit of an electronic medical record compared with no electronic medical record for completeness of data (floor notes, procedure notes, resuscitation notes and ICU notes), with no serious to serious imprecision.

Low quality evidence from one cohort study comprising 807 participants demonstrated a clinical benefit of an electronic medical record compared with no electronic medical record for missing cases (diagnosis, mechanism of injury and a treatment plan), with no serious imprecision.

Economic

No relevant economic evaluations were identified.

15.6 Recommendations and link to evidence

Recommendations	**Recording information in pre-hospital settings** **67. Record the following in patients with major trauma in pre-hospital settings:** • **catastrophic haemorrhage** • **airway with in line spinal immobilisation** • **breathing** • **circulation**

	• **disability (neurological)** • **exposure and environment (<C>ABCDE)** **68. If possible, record information on whether the assessments show that the patient's condition is improving or deteriorating.** **69. Record pre-alert information using a structured system and include all of the following:** • **the patient's age and sex** • **time of incident** • **mechanism of injury** • **injuries suspected** • **signs, including vital signs and Glasgow Coma Score** • **treatment so far** • **estimated time of arrival at emergency department** • **special requirements** • **the ambulance call sign, name of the person taking the call and time of call.** **Receiving information in hospital settings** **At the emergency department** **70. A senior nurse or trauma team leader in the emergency department should receive the pre-alert information and determine the level of trauma team response according to agreed and written local guidelines.** **71. The trauma team leader should be easily identifiable to receive the handover and the trauma team ready to receive the information.** **72. The pre-hospital documentation, including the recorded pre-alert information, should be quickly available to the trauma team and placed in the patient's hospital notes.** **Recording information in hospital settings** **73. Record the items listed in recommendation 67, as a minimum, for the primary survey.** **74. One member of the trauma team should be designated to record all trauma team findings and interventions as they occur (take 'contemporaneous notes').** **75. The trauma team leader should be responsible for checking the information recorded to ensure that it is complete.**

	Sharing information in hospital settings **76. Follow a structured process when handing over care within the emergency department (including shift changes) and to other departments. Ensure that the handover is documented.** **77. Ensure that all patient documentation, including images and reports, goes with patients when they are transferred to other departments or centres.** **78. Produce a written summary, which gives the diagnosis, management plan and expected outcome, and:** • **is aimed at and sent to the patient's GP within 24 hours of admission** • **includes a summary written in plain English that is understandable by patients, family members and carers** • **is readily available in the patient's records.**
	These recommendations were developed and supported by the evidence reviews addressing the scope area 'documentation of clinical assessments and management (including pre-hospital and hospital)' in each of the four clinical guidelines: • Complex fractures: assessment and management of complex fractures (including pelvic fractures and open fractures of limbs) • Fractures: diagnosis, management and follow up of fractures (excluding head and hip, pelvis, open and spinal) • Major trauma: assessment and management of airway, breathing and ventilation, circulation, haemorrhage and temperature control. • Spinal injury assessment: assessment and imaging, and early management for spinal injury (spinal column or spinal cord injury) and 'patient documentation and transfer of information' in the major trauma services guidance scope area. The chapters on documentation in these guidelines should be read in conjunction with this chapter. **Developing the recommendations** Documentation recommendations were developed across the trauma guidelines suite by all the individual GDGs. Each GDG was asked to define a clinical question to address the scope area that was specific and important to the population in their scope. Evidence reviews were completed for all the guidelines and the separate GDGs reviewed the evidence and drafted recommendations. It should be noted that the spinal injury and complex fractures populations are subsets of the overall major trauma population. The overall guideline population of patients with major trauma meant that similarities and duplication between the draft recommendations were inevitable. The recommendations were taken to project executive team (PET) for coherence and consistency checking. The PET also had the advantage of identifying gaps in the separate guidelines that had been addressed in another guideline. The PET agreed on a core set of draft recommendations that encompassed the

	separate recommendations. These recommendations are a key set of principles that underline best practice in documenting and communicating the management of a patient with major trauma. Where recommendations were specific to the guideline these were kept separate for publication in that guideline. For example, the spinal injury guideline has a documentation recommendation on the ASIA chart. The core set of recommendations were taken back to each of the separate GDGs for review and agreement. The GDGs had access to the reviews underpinning the recommendations. The recommendations listed in this guideline are clinical aimed at clinical staff The recommendations for organisations are in the Major Trauma services guidance. The LETR in this chapter summarises the decision making of the major trauma GDG.
Relative values of different outcomes	The GDG identified mortality, health-related quality of life and complications as critical outcomes in evaluating the clinical effectiveness of standard documentation for major trauma patients. The GDG also identified hospital length of stay, patient-reported outcomes (return to normal activities and psychological wellbeing), missing patient data, and the timing of patient transfer as important outcomes. No evidence was reported for quality of life.
Trade-off between clinical benefits and harms	Five retrospective cohort studies were included in the review. One study Implemented a checklist and four studies implemented electronic records. Checklists were associated with reduced length of stay but there were no clinically important differences in mortality or complications. Overall, the use of electronic medical records was associated with less missing data, a reduced need for serious surgery and a shorter length of in-hospital stay when compared with non-electronic recording of data. The evidence did not suggest any clinical harm of using standard documentation. The GDG felt that the evidence included in the review did not evaluate the clinical effectiveness of standard documentation, as the studies compared different methods of recording patient data. However, it was likely that the use of electronic records indirectly led to more standardised reporting. The GDG discussed how standard documentation (pre-hospital and hospital) across the trauma networks for trauma patients may improve clinical outcomes for patients by ensuring that all key aspects of patients' needs and treatment plan are recorded, and that these are communicated between clinicians. Using standard reporting forms also facilitates the monitoring of any change in physiological status. However, it was noted that there would be a trade-off between standardisation of procedure to promote consistency and being too prescriptive in that main message may become lost. Too little information recorded may be insufficient to realise the key benefits (such as improved patient outcomes) whereas too much information could hinder timely transfer of information. There would also be trade-offs in between catering for local needs within geographical boundaries versus uniformity across the country. The GDG emphasised the importance of ensuring that the documentation is completed. Whilst the trauma team leader should be responsible for checking that the information is complete, another member of

	the trauma team may be designated with the responsibility of recording findings and interventions and this may vary according to who is in attendance.
Trade-off between net health benefits and resource use	No economic evidence was identified for this question. Staff time is likely to be the major difference in resources of having set procedures or longer forms to fill in. There are potential costs associated with staff training and the development, purchasing and maintenance of electronic systems and software. Some costs may be offset by decreased workloads due to computerisation of manual records and reduced clinical costs of adverse events due to improved safety. It was also noted that uniformity of the documentation process and protocol, through an economy of scale, could be less expensive for the NHS than implementation of disparate systems. There are several benefits that are likely to stem from having a standardised system across settings, for example, less likely to miss key information about the patient, less time spent re-assessing the patient to perhaps fill in missing fields, less time spent transferring the information from one system to another/or one format to another, and therefore less likely for there to be errors which can lead to poorer outcomes or mistakes. Five clinical studies were identified, although, the GDG felt that these did not adequately capture the question, as they compared the recording of data in one form compared with another form, rather than the standardisation of documentation across different settings. However, they did seem to show that electronic systems had a positive impact on outcomes, such as reduced time between admissions and completion of care, and reduced length of stay, which can have an impact on resource use and delay the patient in receiving treatment. The recommendations made list the data that should be included in a standard documentation.
Quality of evidence	All the evidence was from non-randomised, retrospective cohort studies at high or very high risk of bias. Furthermore, the GDG felt that the evidence evaluated the clinical effectiveness of different methods of recording data, but does not fully capture the impact of standardised documentation.
Other considerations	The GDG agreed on a consensus recommendation that would facilitate the integration of systems across clinical settings and allow for seamless transition of documentation when the patient is transferred from one setting to another. The GDG also agreed that the main aim of standardised documentation is to ensure that the information is uniform. This ensures that different services and departments understand each other, this can be with something as simple as using the same words. The GDG developed consensus recommendations that supported the use of minimum data sets in both the pre-hospital and hospital settings. The GDG highlighted the importance of a clear line of responsibility for completing documentation at all stages of the patient journey. These recommendations also facilitate the accurate and complete collection of research and audit data.

16 Information and support

16.1 Introduction

The NICE guideline on 'Patient Experience' (CG138) has established that people receiving medical care, along with their carers and families; require information about their diagnosis, prognosis and treatment. This is in order to optimise a sense of control and minimise psychological stress, as well as to provide useful practical advice and important warnings. Such information is required from the very early stages of assessment and treatment. With respect to the specific context of people with major trauma and their families and carers there is variation in what information is communicated about their injuries and how this is communicated.

In the hours following major trauma people may be disorientated, distressed and coming to terms with multiple injuries. In these frightening circumstances, it is important that an injured person is given the information they need from the very early stages of assessment and treatment to feel safe and reassured. The major trauma GDG explored this question.

Patients and carers may find themselves having to seek out the information themselves, and information that is available may not be in a format suitable for easy consumption in what can be a confusing and angst-ridden setting. Hospital trusts which provide trauma services may have to consider new ways of working and incorporating access to electronic patient information and telemedicine systems to provide adequate support for major trauma patients and their families and carers. The service delivery GDG sought to investigate some of the ways in which information and support could best be provided to the population who receive care from major trauma services.

This chapter describes, through a combination of synthesis of findings from qualitative studies from this guidance and consensus opinion from the service delivery GDG:

- specific thoughts and feelings of people who have experienced major trauma injuries
- ways in which information and support could best be provided to the population who receive care from major trauma services.

The linking evidence to recommendation section in this chapter sets out the decision making that supported how information and support is communicated.

16.2 Review question: What information and support do people with major trauma and their families/carers want in-hospital/on discharge from ED?

For full details see review protocol in Appendix C.

Table 142: Characteristics of review question

Population and setting	Children, young people and adults who have experienced a traumatic incident and where appropriate, their families and carers.
Objective	To determine what information and support should be provided to people who have experienced a traumatic event and their families while in, or on discharge from, the emergency department (ED).
Context	For example: • Content of information/support required and how this information/support is delivered • Information and support to include pain relief

	• Information for carers and family members as well as information for patients • Timing of information/support
Review strategy	Meta-synthesis of qualitative research: Thematic analysis - information synthesised into themes and subthemes. Results presented diagrammatically and as narrative.

16.3 Clinical evidence

Methods

We searched for qualitative studies exploring the perceptions of people who had experienced major trauma, or their families and carers, on the information and support they wanted to receive during the initial experience with first responders and in the ED.

Four qualitative studies were included in the review[51,82,85,128]. These are summarised in Table 143 below. Key findings from these studies are summarised in the evidence summary table (Table 145). See also the study selection flow chart in Appendix D, study evidence tables in Appendix G, and excluded studies list in Appendix K.

Two of the included studies explore peoples' experiences of trauma care following traumatic injury[51,128]. The other two studies included feature a slightly less direct population of family members who were present during resuscitation in the ED[82,85]. Only one of the studies explicitly set out to explore the specific desires of injured patients and their families in relation to information and support[50,51], however, the qualitative nature of the study designs means that further evidence falls out from the experiential findings of the other included studies. A narrative summary of the evidence synthesis is provided in section 16.5.

Table 143: Summary of studies included in the review

Study	Design	Population (n)	Research aim	Comments
Gabbe 2013[50,51]	In-depth semi-structured telephone interview with thematic qualitative analysis.	Adult blunt trauma patients who had received definitive care at an adult major trauma centre (MTC) (n=120)	To investigate injured patients' experiences of trauma care to inform improvements in service delivery.	Highly applicable, including specific questions about the information they had received in relation to their injury during trauma service care.
Leske 2013[82,82]	Open-ended interview with qualitative content analysis	Family members of critically ill patients who were resuscitated in the ED following trauma (n=28)	To describe family experiences of the 'family presence during resuscitation' option after trauma from motor vehicle collisions and gunshot wounds.	Context less applicable to our review protocol.
McGahey-Oakland 2007[85]	Interview including the Parkland Family Presence During Resuscitation/ Invasive Procedures	Family members of children who had resuscitation in the ED (n=10; three children had chronic illnesses, seven had acute	To describe experiences of family members whose children underwent resuscitation in a children's hospital	Population possibly indirect as the life-threatening event experienced was not necessarily trauma. Context less

Study	Design	Population (n)	Research aim	Comments
	Unabridged Family Survey and investigator-developed open-ended questions with thematic analysis.	life-threatening events).	ED, and identify critical information about family experiences to improve circumstances for future families.	applicable to our review protocol.
Sleney 2014[128,128]	Semi-structured telephone interview with thematic qualitative analysis.	People who have experienced an unintentional injury and attended hospital (n=89)	To explore experiences of patients after injury and identify implications for clinical care and support within the hospital setting and primary care.	Highly applicable and recent UK context.

Evidence synthesis

Themes and subthemes derived from the evidence

Table 144: Themes and subthemes

Main theme	Subthemes
Content of information	• Current situation • The future/expectations • Physiotherapy/rehabilitation
Form of information	• Non-technical and timely information • Combination of verbal and written information • Communication of choice/opportunity
Support	• Specific 'go-to' person • On-going support and accessing care

Table 145: Summary of evidence: Theme 1 – content of information

Study design and sample		Descriptors of themes	Quality assessment		
No of studies	Design Sample		Criteria	Rating	Overall
Sub-theme 1.1: Information on the current situation					
4	Interviews	Particular staff taking the time to explain the treatment or procedures that people are receiving. This involves giving sufficient explanations of risks of treatments to ensure informed decision-making. Keeping an open channel of communication about reasons for any delays (often bed shortages or short-staffing), or minimising unexplained or unexpected last minute changes in management (ward moves, changes in pain medication or surgery times). [Links to Form of information theme 2.3: Communication of choice/opportunity, and Support theme 3.1: Specific 'go-to' person].	Limitations of evidence	No limitations	HIGH
			Coherence of findings	Coherent	
			Applicability of evidence	Very applicable	
Sub-theme 1.2: Information about the future/rehabilitation expectations					
2	Interviews	Information about when improvements would be noticeable and when they can use the injured limb/how to manage their injury in the context of day-to-day life. Information about when they can expect improvements in mobility/strength. What to expect in terms of pain and how best to manage this. It is important that people get information about possible effects of their injury on their emotional state: low mood, realisation of changing ability due to their traumatic experience and/or a possible loss of confidence (this is especially important for older adults). Information needs to 'sign-post' people to support groups and services in the community.	Limitations of evidence	No limitations	HIGH
			Coherence of findings	Coherent	
			Applicability of evidence	Very applicable	
Sub-theme 1.3: Information about physiotherapy					

2	Interviews	For those not offered physiotherapy there is a desire to know why they were not offered it (as many felt they would benefit from it). For those offered physiotherapy there is a desire to know why it ended when it did – need for clear expectations and goals. Information on how to improve strength and mobility and how to access help.	Limitations of evidence	No limitations	HIGH
			Coherence of finding	Coherent	
			Applicability of evidence	Very applicable	

Table 146: Summary of evidence: Theme 2 – form of information

Study design and sample			Quality assessment		
No of studies	**Design Sample**	**Descriptors of themes**	**Criteria**	**Rating**	**Overall**
Sub-theme 2.1: Non-technical and timely information					
4	Interviews	Information about future rehabilitation expectations is of particular importance after surgery – imperative that a member of clinical staff offers their time to discuss these uncertainties with the injured person [link to Support theme 3.1: Specific 'go-to' person]. Sometimes the language used is too technical and it would be appreciated if this was accompanied with a lay-person description. Consideration of the current situation and timing was important in terms of some of the more sensitive topics that needed to be discussed, in particular family members felt it was important not to discuss organ donation in such a way that the family may feel ambushed/rushed into making a decision or ill-prepared.	Limitations of evidence	No limitations	MODERATE
			Coherence of finding	Coherent	
			Applicability of evidence	Applicable	
Sub-theme 2.2: Combination of verbal and written information					
2	Interviews	Both verbal and written information were considered helpful but for different reasons and at different time points. Verbal information was appreciated while in hospital (ongoing updates) but was	Limitations of evidence	No limitations	HIGH
			Coherence of finding	Coherent	

		sometimes hard to take in all at once in the post-injury or post-surgery context. Written information to take home with them was appreciated for later contemplation. Particularly any information about caring for or managing their injury moving forward, and what to look out for in terms of any danger signs.	Applicability of evidence	Very applicable	
Sub-theme 2.3: Choice/opportunity					
3	Interviews	The hospital staff need to engage patients' in decision-making where they can (when appropriate). Family members felt it was very important to be given the opportunity to be present in the resuscitation room (this was especially important when the injured person was a child). Many family members felt that while they greatly benefited from being present, that it might not be the best idea for all people so therefore it should be offered as a choice (not a given that all will want to attend).	Limitations of evidence	Serious limitations	LOW
			Coherence of findings	Coherent	
			Applicability of evidence	Not completely applicable	

Table 147: Summary of evidence: Theme 3 – SUPPORT

Study design and sample			Quality assessment		
No of studies	**Design Sample**	**Descriptors of themes**	**Criteria**	**Rating**	**Overall**
Sub-theme 3.1: Specific 'go-to' person					
4	Interviews	Theme 1.1: information on the current situation and theme 2.1: non-technical and timely information, both suggest that having one specific 'go-to' person who is able to communicate with the injured person and family members would be helpful. This person should be approachable and be able to act as a link between the hospital staff and the injured person/family members while care is underway, and social/community services once the person is discharged. There needs to be a consistent point of contact for patients about their on-going management and who can ensure co-ordination of their care.	Limitations of evidence	No limitations	MODERATE
			Coherence of finding	Coherent	
			Applicability of evidence	Applicable	

		There needs to be a policy where a specific person is responsible for asking the families if they'd like to be present in the resuscitation room. This is to ensure consistent treatment (not left to individual clinician discretion). Families want the opportunity to provide clinicians with the appropriate information and be sure that it is getting to the right person (including allergy information, current medication, medical history and what happened at the injury site).			
Sub-theme 3.2: On-going support and accessing care					
2	Interviews	The hospital needs to make sure that the person being discharged has at least one support person and to consider their social circumstances (for example, people with no social support or carer responsibilities). The full care pathway needs to be considered, the hospital should notify the appropriate community serviced to ensure support if mobility is compromised. They need to know who their primary point of post-discharge contact should be. At discharge there needs to be advice on the how their traumatic experience might impact on their emotional state and give them information on where to access on-going support such as psychological/counselling services.	Limitations of evidence	No limitations	HIGH
			Coherence of finding	Coherent	
			Applicability of evidence	Very applicable	

16.4 Economic evidence

Published literature

No relevant economic evaluations were identified.

See also the economic article selection flow chart in Appendix E.

Unit costs

An intervention which has been mentioned as a method of providing information and support to patients and their families is a family support officer of some description. Having a designated person specifically for this role has cost implications.

An example of some of the costs per hour for staff (depending on the NHS agenda for change salary band) are outlined in Appendix O.

16.5 Evidence statements

Four qualitative studies suggested the following about the information and support people experiencing traumatic injury and their families or carers may want during their time in, and upon discharge from, the emergency department:

Content of information

High quality evidence from all four studies suggested it was important to have someone available to give information about current treatments and/or procedures.

High quality evidence from the two studies highlighted the importance the injured people placed on receiving information about their expected recovery and ability to return to normal functioning (or not).

Form of information

Moderate quality evidence from all four studies suggested that information needed to be offered in a timely and non-technical manner.

High quality evidence from the two studies suggested that people want a combination of both verbal and written information.

Support

Moderate quality evidence from all four studies suggested that it would be helpful if there was one specific person whose job it was to be the link between the medical staff and the injured person and their carers or family.

High quality evidence from the two suggested that it is important that hospital staff take into account people's social context when they discharge them, as this impacts their ability to function in the community and to access community services.

Economic

No relevant economic evaluations were identified.

16.6 Recommendations and link to evidence

Recommendations	**Providing support** **79. When communicating with patients, family members and carers:** • **manage expectations and avoid misinformation** • **answer questions and provide information honestly, within the limits of your knowledge** • **do not speculate and avoid being overly optimistic or pessimistic when discussing information on further investigations, diagnosis or prognosis** • **ask if there are any other questions.** **80. The trauma team structure should include a clear point of contact for providing information to patients, family members and carers.** **81. If possible, ask the patient if they want someone (a family member, carer or friend) with them.** **82. If the patient agrees, invite their family member, carer or friend into the resuscitation room. Ensure that they are accompanied by a member of staff and their presence does not affect assessment, diagnosis or treatment.** **Support for children and vulnerable adults** **83. Allocate a dedicated member of staff to contact the next of kin and provide support for unaccompanied children and vulnerable adults.** **84. Contact the mental health team as soon as possible for patients who have a pre-existing psychological or psychiatric condition that might have contributed to their injury, or a mental health problem that might affect their wellbeing or care in hospital.** **85. For a child or vulnerable adult with major trauma, enable their family members or carers to remain within eyesight if appropriate.** **86. Work with family members and carers of children and vulnerable adults to provide information and support. Take into account the age, developmental stage and cognitive function of the child or vulnerable adult.** **87. Include siblings of an injured child when offering support to family members and carers.** **Providing information** **88. Explain to patients, family members and carers what is happening and why it is happening. Provide:**

	• **information on known injuries** • **details of immediate investigations and treatment, and if possible include time schedules** • **information about expected outcomes of treatment, including time to returning to usual activities and the likelihood of permanent effects on quality of life, such as pain, loss of function or psychological effects.** **89. Provide information at each stage of management (including the results of imaging) in face-to-face consultations.** **90. Document all key communications with patients, family members and carers about the management plan.** **Providing information about transfer from an emergency department** **91. For patients who are being transferred from an emergency department to another centre, provide verbal and written information that includes:** • **the reason for the transfer** • **the location of the receiving centre and the patient's destination within the receiving centre** • **the name and contact details of the person responsible for the patient's care at the receiving centre** • **the name and contact details of the person who was responsible for the patient's care at the initial hospital.**
	These recommendations were developed and supported by the evidence reviews addressing the scope area, 'Information and support needs of patients and their families and carers when appropriate' in each of the four clinical guidelines: • Complex fractures: assessment and management of complex fractures (including pelvic fractures and open fractures of limbs) • Fractures: diagnosis, management and follow up of fractures (excluding head and hip, pelvis, open and spinal) • Major trauma: assessment and management of airway, breathing and ventilation, circulation, haemorrhage and temperature control. • Spinal injury assessment: assessment and imaging, and early management for spinal injury (spinal column or spinal cord injury) and 'provision of information and support for families and carers ' in the major trauma services guidance scope area. The chapters on information and support in these guidelines should be read in conjunction with this chapter. **Developing the recommendations** Information and support recommendations were developed across the trauma guidelines suite by all the individual GDGs. Each GDG was asked to define a clinical question to address the scope area that was specific and important to the population in their scope. Evidence reviews were completed for all the guidelines and the separate GDGs reviewed the evidence and drafted recommendations. The overall guideline population of patients with major trauma meant that

	similarities and duplication between the draft recommendations were inevitable. The recommendations were taken to Project Executive Team (PET) for coherence and consistency checking. The PET also had the advantage of identifying gaps in the separate guidelines that had been addressed in another guideline. The PET agreed on a core set of draft recommendations that encompassed the meaning from the separate recommendations. These recommendations are a key set of principles that underline best practice in providing information and support to a patient with major trauma and their families and/or carers Where there were recommendations that were specific to the guideline these were kept separate for publication in that guideline. For example, the spinal injury guideline has a recommendation highlighting the importance of eye contact with a person with suspected spinal injury to avoid movement of their neck. The core set of recommendations were taken back to each of the separate GDGs for review and agreement. The GDGs had access to the reviews underpinning the recommendations. The recommendations listed here are directed at clinical staff. The recommendations aimed at organisations are in the Major trauma services guidance. The LETR in this chapter summarises the decision making of the major trauma GDG.
Relative values of different outcomes	The evidence identified in this review suggested that the information offered to people who have experienced a major trauma and their families should: • Contain details of their current situation (injuries known or suspected, treatment or procedures that they will receive including possible risks to aid informed decision making). • Be provided on an ongoing basis and be updated regularly as part of an open line of communication between the patient and the staff providing them care. • Contain information about the future clinical course or rehabilitation expectations (expected pain levels and how to manage these, expected improvements in mobility/strength/function). • Contain information on physiotherapy or how to access help. • Be offered in a non-technical and timely manner. • Be offered in both verbal and written formats at specific time-points (verbal in hospital, and later this should be accompanied with written information to take away with them). • The evidence suggested that people who have experienced a major trauma and their families would appreciate having a specific 'go-to' person to provide support and act as a consistent point of contact.
Trade-off between clinical benefits and harms	Trusts should have protocols in place to ensure consistency with respect to the information and support they offer the injured person and their family members (including consideration of family presence during resuscitation). Protocols should consider staff availability, address issues that may arise from language and cultural barriers, set out the appropriate process if a relative should panic and acknowledge that the way information and support, if offered, may have to be considered individually within the scope of the patient (if possible) and family member(s) wishes. **Pre-hospital setting and in hospital** The GDG thought it is important to acknowledge that the pre-hospital and ED is an extremely difficult environment within which to process information. Therefore, it is important for health practitioners and medical staff to be aware of the way in which they convey information about the patients' injuries and associated medical care

including: the content of information (treatment/management plan), the timing of information (ongoing updates), and in appropriate formats (considering developmental, language and cultural barriers).

Giving information in the emergency department on what happened before the injured person was admitted (for example, the pre-hospital setting) or any information about prognosis when the full extent of their injuries was not yet known could cause possible harm. Therefore, when giving information about pre-admission events or likely prognoses it is imperative that only the known and correct information is conveyed. Giving information direct to the patient may be impossible or difficult due to impaired consciousness or anxiety, stress or shock.

It was also acknowledged that many major trauma patients will have multiple injuries that will require care from a wide range of specialists. While the patient should be informed of the different aspects of their care, it is important that there is consistency in the information they are receiving. If they have multiple people giving them different information about the management of their injuries this may cause confusion during an already anxious time. This means that one specific person takes responsibility for giving the injured person the information they require to feel safe and reassured that the medical treatment they are receiving will deliver the best possible outcomes.

When proposing family presence during resuscitation it is important to consider that this can be a very distressing event to witness. Medical staff may be distracted from the resuscitation task if the observing family member(s) experience an intense emotional response. It is possible that during resuscitation patient confidentiality could be threatened. The presence of family member(s) in the resuscitation room may inhibit open and frank discussion about the patient's condition, which in turn may delay decision-making. Facilitating the presence of a friend or relative in the resuscitation room should not interfere with the speed and efficiency of primary survey and acquisition of initial diagnostics. However, the evidence from this review suggested that it is common for family members to want to be present during resuscitation, and healthcare professionals should respect the wishes of close relatives. It is possible that seeing what is happening to their loved one is preferable to the anxiety-inducing 'unknown'.

Updating information

The clinical status of a major patient and their management may change rapidly. It is, therefore, important that patients and carers are regularly updated.

Transfer

It is also important to give family members and/or carers information about where the injured person went (in terms of location of hospital) and why (may be a further away location but a better equipped one). The details of the specific person who was responsible for their care or who will be should be provided in conjunction with the name of the trauma coordinator (see service delivery recommendation). Details of the structure and function of the different services that comprise the trauma network should be provided as appropriate.

Children and vulnerable adults

The information and support needs of children and the vulnerable was emphasised by the GDG and information should be tailored to meet their needs. The presence of parents and carers can provide valuable support to children and vulnerable adults.

The GDG stated that the mental health team should be contacted as soon as

	possible so that the relevant health professionals can start to formulate a care plan.
Trade-off between net health benefits and resource use	No economic evidence was identified to inform this recommendation. The resource implications of patient information and support strategies will vary depending on the specific strategy. The GDG discussed the impact of the recommendation on providing a clear point of contact for the patient in the ED. In terms of how information will be supplied/communicated, this could be in written form or verbally. If verbally, this information could be communicated by a clinician, such as one of the trauma team, or be a designated individual whose job is to liaise with the patients and families and provide information and support (such as a family support officer). Examples stem from ICU or other countries, such as the USA. There would be economic implications of having a dedicated individual to support patients and families/carers and their cost effectiveness would depend on the number of patients they were overseeing and what benefit they would have to bring to each in order to make their role cost effective. Some staffing costs separated by the NHS 'agenda for change' band were presented to the GDG as examples of the costs of the types of staff that may be undertake this role. These costs can range from £21 per hour for band 2 to £53 per hour for band 7). It was discussed how it would be difficult to identify who would undertake this responsibility, however, what is important is co-ordination as well as what information is provided, so making sure all the parts of the pathway and services that may be involved in the patients care are connected and the patient/families/carers are aware of what is happening. The content of the information also needs to be thought about and provided in a way that patients understand. In terms of quality of life, anxiety can be reduced by having the appropriate information. There is value in having knowledge/knowing ones diagnosis/prognosis.
Quality of evidence	High quality qualitative evidence advised what specific information given to the injured person and their family or carers should contain. Moderate to high quality evidence suggested the way in which this information should be offered. High quality evidence indicated the type of support the injured person and their family or carers should ideally have access to.
Other considerations	Specific go-to person: This would ensure co-ordination of care and reduce confusion and anxiety caused by receiving different and possibly contradictory messages about their care. This in-hospital support should also include a link with, or consideration of, ongoing information and support needs once the patient has left the ED (whole patient pathway). The GDG agreed that there is a role for a specific person who is responsible for talking to the family about 1) what is happening right now, 2) what is likely to happen in the future or communication of uncertainty. This needs to be an identified role within the trauma team (not necessarily a person who is involved in the injured person's clinical care). They will be of particular importance at hand-over times. The GDG acknowledged the possibility that this may not be an entirely new role, as some hospitals may already provide this kind of service or something similar. This person should give regular updates to the family/carers, including before 'stabilisation'. This same person should also be responsible liaising with the

	next unit to which the patient will be transferred to, and for collating all the data that should go with the patient. Consistency of this staff member is important. **Considerations for children and vulnerable adults:** Cross-refer to safeguarding guideline. **On discharge from the ED:** The GDG discussed that when a patient is discharged many of them go from a context of total care to a context of minimal care. These people are then faced with the challenge of co-ordinating themselves within a context of multi-system rehabilitation. This is why having clear information about who to contact and a list of some physical and psychological/emotional expectations may help manage the person's anxieties moving back into the community. See also NICE guidelines on 'Care of the dying adult' (due to be published December 2015), 'End of life care for infants, children and young people' (due to be published 2016) and Improving supportive and palliative care in adults (update) (due to be published January 2018).

17 Access to the skills required for the management of people with major trauma

17.1 Introduction

Injuries sustained from trauma may be life threatening and could be life changing. People with major trauma sustain injuries that are associated with adverse consequences that can result in long-term disability or death. The consequence of poor clinical management from a patient perspective is devastating and from a societal perspective the burden from lost productivity and NHS costs are substantial.

There is no doubt that the optimal management of a person with any major trauma and potentially life-threatening injuries is to have the right staff, with the right skills, in the right place at the right time. Accordingly, the scope included the topic, 'skills to be present in the multidisciplinary team '. It was anticipated that each guideline developed in these trauma related guidelines: non-complex fractures, complex fractures, major trauma and spinal injury assessment, would reflect the specific skills in the multidisciplinary team required to deliver the recommendations within the specialist guideline. However, as the guidelines were developed together it became clear that trauma care should not be defined by having separate areas of care but as a joined up, connected and coherent service. The concept of a multidisciplinary team that 'belongs' to one area of care is misleading. Some members of the spinal injuries multidisciplinary team will manage and care for people that have other injuries, an example is the emergency department consultant. From a patient perspective, and this is particularly true of people with multiple injuries, their care will span across the trauma service and they have their own unique multidisciplinary team.

With this in mind, access to skills in the multidisciplinary team was addressed across the 4 clinical guidelines (non-complex fractures, complex fractures, major trauma and spinal injury assessment) in the major trauma services guidance taking a trauma systems perspective. See chapter 17 Access to services in the major trauma services guidance for a summary of the services and skills recommended in each of the guidelines and the recommendation for the skills required to manage people with trauma.

18 Acronyms and abbreviations

Acronym or abbreviation	Description
ABPI	Ankle brachial pressure index
ADL	Activities of daily living
AIS	Abbreviated Injury Scale
ASIA score	American Spinal Injury Association Impairment score
ATLS	Advanced Trauma Life Support
CI	Confidence interval
CC	Comparative costing
CCA	Cost-consequences analysis
CEA	Cost-effectiveness analysis
CNS	Central nervous system
CT	Computed tomography
CUA	Cost-utility analysis
DASH Score	The Disabilities of the Arm, Shoulder and Hand Score
DVT/PE	Deep vein thrombosis and pulmonary embolism.
eFAST	Extended Focused Assessment with Sonography for Trauma
EMAS	East Midlands Ambulance Service
FAST	Focused assessment with sonography for trauma
GCS	Glasgow coma scale
GOS	Glasgow outcome scale
INR	International normalised ratio
IO	Intraosseous
IR	Interventional radiology
IV	Intravenous
ISS	Injury Severity Score
JRCALC	Joint Royal Colleges Ambulance Liaison Committee
KED	Kendrick Extrication Device
MDCT	Multi-detector computed tomography
MDT	Multidisciplinary team
MRI	Magnetic resonance imaging
MTC	Major Trauma Centre
NEXUS	National Emergency X Radiography Utilization Study
NNT	Number needed to treat
NPV	Negative predictive value
NSAIDS	Non-steroidal anti-inflammatory drugs
ORIF	Open reduction and internal fixation
PACS	Picture Archiving and Communications Systems
PCC	Prothrombin complex concentrate
PPV	Positive predictive value
QALY	Quality-adjusted life year
RCT	Randomised controlled trial
RSI	Rapid Sequence Induction of anaesthesia and intubation

Acronym or abbreviation	Description
TARN	The Trauma Audit & Research Network
TU	Trauma unit
UTI	Urinary tract infection
VKA	Vitamin K antagonist
VTE	Venous thrombosis embolism

19 Glossary

Term	Definition
Abbreviated Injury Scale (AIS)	Injuries are ranked on a scale of 1 to 6, with 1 being minor, 5 severe and 6 an unsurvivable injury. This represents the 'threat to life' associated with an injury and is not meant to represent a comprehensive measure of severity.
Abstract	Summary of a study, which may be published alone or as an introduction to a full scientific paper.
Active Bleeding	Also known as or related to haemorrhage, loss of blood, bleeding, haemorrhage, bleeding
Activities of daily living (ADL)	Routine activities carried out for personal hygiene and health (including bathing, dressing, feeding) and for operating a household.
Acute	A stage of injury or stroke starting at the onset of symptoms. The opposite of chronic.
Advanced Trauma Life Support (ATLS)	A training program for medical professionals in the management of acute trauma cases, developed by the American College of Surgeons.
Algorithm (in guidelines)	A flow chart of the clinical decision pathway described in the guideline, where decision points are represented with boxes, linked with arrows.
Allocation concealment	The process used to prevent advance knowledge of group assignment in a RCT. The allocation process should be impervious to any influence by the individual making the allocation, by being administered by someone who is not responsible for recruiting participants.
Ambulation	Walking with braces and/or crutches.
American Spinal Injury Association Impairment (ASIA) Score	A system to describe spinal cord injury and help determine future rehabilitation and recovery needs. It is based on a patient's ability to feel sensation at multiple points on the body and also tests motor function. Ideally, it's first given within 72 hours after the initial injury. Scored from A-E; A means complete injury; E means complete recovery.
Angiography	Radiography of blood or lymph vessels, carried out after introduction of a radiopaque substance.
Angular deformity	Deformity of limbs by angulation at joints or in the bones themselves.
Ankle brachial pressure index (ABPI)	The ratio of the blood pressure in the lower legs to the blood pressure in the arms. It is used for decision-making in leg ulcer assessment.
Antero-lateral	Directed from the front towards the side.
Antero-posterior	Directed from the front towards the back.
Anticoagulation	The process of hindering the clotting of blood.
Antifibrinolytic agent	Pharmacological agents that inhibit the activation of plasminogen to plasmin, prevent the break-up of fibrin and maintain clot stability. They are used to prevent excessive bleeding.
Applicability	The degree to which the results of an observation, study or review are likely to hold true in a particular clinical practice setting.
Arm (of a clinical study)	Sub-section of individuals within a study who receive one particular intervention, for example placebo arm
Arterial injury	An injury following a traumatic injury which results in a laceration, contusion, puncture, or crush injury to an artery.
Arterial shunts	An artificial passageway introduced through a surgical procedure that allows blood to flow from through the arteries.
Aspiration event	The event of food or drink entering the airway.
Association	Statistical relationship between two or more events, characteristics or other variables. The relationship may or may not be causal.

Term	Definition
Attrition bias	Bias resulting from the loss of data from analysis. Loss of data from analysis causes bias by disrupting baseline equivalence and also because data from people who drop out are often systematically different from data collected from those who don't drop out. Loss of such data therefore distorts the apparent response of a group to a treatment. For example, those who drop out from a treatment may be the worst responders and so if these are not included in the analysis this may make a treatment look better than it really is. Attrition bias may be reduced by following an intention to treat approach (see 'intention to treat').
Avascular necrosis	Avascular necrosis is cellular death of bone components due to interruption of the blood supply.
Baseline	The initial set of measurements at the beginning of a study (after run-in period where applicable), which may be important in demonstrating how much selection bias is present. They may also be compared with subsequent results in certain study designs.
Basic airway manoeuvres	A set of medical procedures performed in order to prevent airway obstruction and thus ensuring an open pathway. Manoeuvres include encouraging the victim to cough, back blows and abdominal thrusts.
Before-and-after study	A study that investigates the effects of an intervention by measuring particular characteristics of a population both before and after taking the intervention, and assessing any change that occurs. Because there is no control group, this approach is subject to considerable bias (see control group). 'Before and after study' is sometimes also used to denote historical cohort studies that compare two groups separated in time, often before and after the initiation of a new treatment strategy. In such cases the control group is the group treated earlier.
Bias	Systematic (as opposed to random) deviation of the results of a study from the 'true' results that is caused by the way the study is designed or conducted.
Blinding	Keeping the study participants, caregivers, and outcome assessors unaware which interventions the participants have been allocated in a study.
Blood component	A therapeutic component of human blood (red cells, white cells, platelets, plasma and cryoprecipitate)
Blood product	Any therapeutic product derived from human whole blood or plasma donations (for example, prothrombin complex concentrate)
Blunt trauma	A traumatic injury caused by the application of mechanical force to the body by a blunt force, object or instrument or an injury in which the body strikes a surface such as a wall or the ground, in which the skin was not penetrated.
Canadian C-Spine Rules	Selective guidelines developed in Canada for the ordering of cervical spine imaging following acute trauma.
Carer (caregiver)	Someone other than a health professional who is involved in caring for a person with a medical condition.
Case-control study	Comparative observational study in which the investigator selects individuals who have experienced a health-related event (cases) and others who have not (controls), and then collects data to determine relative prior exposure to a possible cause.
Case-series	Report of a number of cases of a given disease, usually covering the course of the disease and the response to treatment. There is no comparison (control) group of patients. See 'before and after ' study.
Central nervous system (CNS)	The brain and spinal cord.
Cervical	High-level nervous structure of the spinal cord responsible for controlling the

Term	Definition
	neck muscles, diaphragm, shoulders, wrists, triceps and fingers.
Cervical collar	A cervical collar (also neck brace) is an orthopaedic medical device used to support a patient's neck and head.
Charlson comorbidity index	A comorbidity index which predicts the ten-year mortality for a patient who may have a range of comorbid conditions. The score is helpful in deciding how aggressively to treat a condition.
Chest decompression	A medical procedure to remove air from the pleural cavity and treat tension pneumothorax injuries. A needle decompression deviceis inserted and advanced in the chest until air is aspirated. The manoeuver effectively converts a tension pneumothorax into a simple pneumothorax.
Chronic spinal cord injury	The stage of spinal cord injury where there is no longer continuing damage or recovery.
Clinical efficacy	The extent to which an intervention produces an overall health benefit when studied under controlled research conditions.
Clinical effectiveness	The extent to which an intervention produces an overall health benefit in routine clinical practice.
Clinician	A healthcare professional providing direct patient care, such as a doctor, nurse or physiotherapist.
Coagulopathy	Coagulopathy is a condition in which the blood's ability to clot (coagulate) is impaired. It can be caused as a result of on-going cycles of dilution and consumption of coagulation factors, hypothermia and acidosis following traumatic incidents.
Cochrane Review	The Cochrane Library consists of a regularly updated collection of evidence-based medicine databases including the Cochrane Database of Systematic Reviews (reviews of randomised controlled trials prepared by the Cochrane Collaboration).
Cohort study	A sample (or cohort) of individuals without a chosen outcome event (such as a disease) are defined on the basis of presence or absence of exposure to one or more suspected risk factors or interventions. The effects of these risk factors or interventions on chosen outcomes are then evaluated at later follow up. Prospective cohort studies are managed by the researchers in real time. This allows the measurement of appropriate potential confounding variables at baseline. Retrospective cohort studies are based on databases that were collected prospectively, often for another purpose, but which are used retrospectively (that is, not in real time) by a researcher. This approach often means that appropriate confounding variables may not have been collected
Comorbidity	One or more additional disorders (other than that being studied or treated) in an individual.
Comparability	Similarity of the groups in characteristics likely to affect the study results (such as health status or age).
Comparative costing (CC)	A type of analysis where costs are compared without the consideration of health benefits
Compartment syndrome	A condition that occurs when the amount of swelling and/or bleeding in a muscle compartment causes pressure that is greater than the capillary pressure and results in tissue ischemia and potential tissue necrosis.
Complete injury	Generally, a spinal cord injury that cuts off all sensory and motor function below the lesion site.
Computed tomography (CT) scan	A scan which produces images of a cross sectional plane of the body. The scan is produced by computer synthesis of X-ray images taken in many different directions in a given plane.

Term	Definition
Comminuted fracture	A fracture in which the bone shatters into three or more pieces.
Compound Fracture	A fracture in which broken bone fragments lacerate soft tissue and protrude through an open wound in the skin. This term is synonymous with 'open fracture'. See open fracture
Conceptual mapping	Activity which involves diagrammatically representing the relationships between different areas and the interactions between interventions and outcomes.
Conceptual modelling	Activity in which the participants' understanding of the decision problem is represented in a mathematical model which can be discussed and agreed by the participants.
Concordance	This is a recent term whose meaning has changed. It was initially applied to the consultation process in which doctor and patient agree therapeutic decisions that incorporate their respective views, but now includes patient support in medicine taking as well as prescribing communication. Concordance reflects social values but does not address medicine-taking and may not lead to improved adherence.
Concussion	Reversible paralysis following brain trauma, usually involving loss of consciousness and/or a transient state of confusion.
Confidence interval (CI)	A range of values for an unknown population parameter with a stated 'confidence' (conventionally 95%) that it contains the true value. The interval is calculated from sample data, and straddles the sample estimate. The 'confidence' value means that if the method used to calculate the interval is repeated many times, then that proportion of intervals will actually contain the true value.
Confounding	In a study, confounding occurs when the effect of an intervention (or risk factor) on an outcome is distorted as a result of one or more additional variables that are able to influence the outcome, and that also have an association with the intervention (or risk factor). Association with the intervention (or risk factor) generally means an imbalance in the confounder across intervention (or risk factor) groups. For example, a sample of coffee drinkers may be observed to have more heart disease than a sample of non-coffee drinkers. If the coffee drinker sample are much older than the non-coffee drinker sample, then differing age may explain the outcome rather than coffee consumption, assuming greater age increases heart disease risk.
Consensus methods	Techniques that aim to reach an agreement on a particular issue. Consensus methods may be used when there is a lack of strong evidence on a particular topic.
Constant-Murley shoulder Outcome Score	A commonly used outcome measure for assessing the outcomes of the treatment of shoulder disorders.
Control group	A group of people in a study who do not receive the treatment or test being studied. Instead, they may receive the standard treatment (sometimes called 'usual care') or a dummy treatment (placebo). The results for the control group are compared with those for a group receiving the treatment being tested. Without a control group it is impossible to know the extent to which a change in outcome in the intervention group is due to the treatment effect or to intervening effects such as the placebo effect , practice effect or natural history effect. However if a control group has very similar characteristics to the treatment group then it can be assumed that it will be exposed to very similar intervening effects. Therefore taking the difference between group outcomes (or the ratio if the outcome is bivariate) allows the intervening effects to largely cancel out, leaving only the differential between-group treatment effect.

Term	Definition
Cosmesis	The surgical correction of a disfiguring physical defect.
Cost benefit analysis	A type of economic evaluation where both costs and benefits of healthcare treatment are measured in the same monetary units. If benefits exceed costs, the evaluation would recommend providing the treatment.
Cost-consequences analysis (CCA)	A type of economic evaluation where various health outcomes are reported in addition to cost for each intervention, but there is no overall measure of health gain.
Cost-effectiveness analysis (CEA)	An economic study design in which consequences of different interventions are measured using a single outcome, usually in 'natural' units (For example, life-years gained, deaths avoided, heart attacks avoided, cases detected). Alternative interventions are then compared in terms of cost per unit of effectiveness.
Cost-effectiveness model	An explicit mathematical framework, which is used to represent clinical decision problems and incorporate evidence from a variety of sources in order to estimate the costs and health outcomes.
Cost-utility analysis (CUA)	A form of cost-effectiveness analysis in which the units of effectiveness are quality-adjusted life-years (QALYs).
Credible Interval	The Bayesian equivalent of a confidence interval.
Crush injury	An injury by an object that causes compression of the limb or body.
Cryoprecipitate	A source of fibrinogen, vital to blood clotting.
Damage control surgery	A technique of surgery for critically ill patients involving other sub-specialty services in addition to the trauma surgeon. This technique places emphasis on preventing the "lethal triad", rather than correcting the anatomy. The patient will be stabilised before definitive treatment.
Debridement	The whole process of opening up of a wound, or pathological area (for example, bone infection), together with the surgical excision of all avascular, contaminated, infected, or other undesirable tissue.
Decision analysis	An explicit quantitative approach to decision making under uncertainty, based on evidence from research. This evidence is translated into probabilities, and then into diagrams or decision trees which direct the clinician through a succession of possible scenarios, actions and outcomes.
Deep infection	Deep incisional surgical site infections must meet the following three criteria: • Occur within 30 days of procedure (or one year in the case of implants) • are related to the procedure • involve deep soft tissues, such as the fascia and muscles. In addition, at least one of the following criteria must be met: • Purulent drainage from the incision but not from the organ/space of the surgical site. • A deep incision spontaneously dehisces or is deliberately opened by a surgeon when the patient has at least one of the following signs or symptoms - fever (>38°C), localised pain or tenderness - unless the culture is negative. • An abscess or other evidence of infection involving the incision is found on direct examination or by histopathologic or radiological examination. • Diagnosis of a deep incisional SSI by a surgeon or attending physician.
Definitive closure	The final surgical closing of a wound by suture or staple.
Definitive cover	Final closure of the open fracture wound, using a local flap of skin, or skin grafted from another part of the body.

Term	Definition
Definitive (internal or external) fixation	The final surgical implantation of internal or external metalwork for the purposes of repairing a bone and fixing it into place.
Definitive haemorrhage control	A surgical procedure to completely stop bleeding following trauma.
Definitive treatment	A final treatment, which may conclude prior preparatory stages, which aims to achieve a specific therapeutic effect.
Delayed bone healing	A fracture that takes longer to heal than expected.
Detection bias	Bias relating to the way in which data is collected. The most common cause of detection bias results from failure to blind outcome assessors. If outcome assessors know the group allocation of a participant this may influence the way that the measurement is carried out.
Diagnostic RCT	A randomised controlled trial that compares outcomes from groups allocated to two or more different forms of diagnostic assessment. Diagnostic RCTs are a pragmatic way of assessing how well diagnostic tests affect outcome through their ability to determine appropriate management of patients. In contrast to diagnostic accuracy studies, they can encompass issues like the duration or comfort of a test, which may be important considerations in the decision concerning which diagnostic test should be used.
The Disabilities of the Arm, Shoulder and Hand (DASH) Score	A patient reported questionnaire to inform on functional capacity of the arm.
Disability rating index	A patient reported clinical tool for assessing physical disability, mainly intended for clinical settings.
Discounting	Costs and perhaps benefits incurred today have a higher value than costs and benefits occurring in the future. Discounting health benefits reflects individual preference for benefits to be experienced in the present rather than the future. Discounting costs reflects individual preference for costs to be experienced in the future rather than the present.
Discrete Event Simulation	A type of model (also known as time-to-event model) based on patient-level simulation where 'time to event' is the key parameter as opposed to 'probability of event occurring' like in a Markov model.
Dislocation	Displacement of one or more bones at a joint.
Dominance	An intervention is said to be dominated if there is an alternative intervention that is both less costly and more effective.
Drop-out	A participant who withdraws from a trial before the end.
Dynamic fluoroscopy	Imaging technique which uses an X-ray tube and a fluoroscopic screen with an image intensifier to create a real-time image of moving objects.
Economic evaluation	Comparative analysis of alternative health strategies (interventions or programmes) in terms of both their costs and consequences.
Effect (as in effect measure, treatment effect, estimate of effect, effect size)	The observed association between interventions and outcomes or a statistic to summarise the strength of the observed association.
Effectiveness	See 'Clinical effectiveness'.
Efficacy	See 'Clinical efficacy'.
Embolization	Therapeutic introduction of a substance into a blood vessel in order to occlude it and prevent active bleeding following trauma.
Emergent phenomena	A stage in recovery from general anaesthesia that includes a return to spontaneous breathing, voluntary swallowing and normal consciousness.
Epidemiological study	The study of a disease within a population, defining its incidence and prevalence and examining the roles of external influences (For example,

Term	Definition
	infection, diet) and interventions.
EQ-5D (EuroQol-5D)	A standardise instrument used to measure a health outcome. It provides a single index value for health status and measures quality of life
Evidence	Information on which a decision or guidance is based. Evidence is obtained from a range of sources including randomised controlled trials, observational studies, expert opinion (of clinical professionals and/or patients).
Exclusion criteria (literature review)	Explicit standards used to decide which studies should be excluded from consideration as potential sources of evidence.
Exclusion criteria (clinical study)	Criteria that define who is not eligible to participate in a clinical study.
Extended dominance	If Option A is both more clinically effective than Option B and has a lower cost per unit of effect, when both are compared with a do-nothing alternative then Option A is said to have extended dominance over Option B. Option A is therefore more efficient and should be preferred, other things remaining equal.
Extended Focused Assessment with Sonography for Trauma (eFAST)	Extends the viewing area of FAST to include other assessments . It is often used to image the thorax.
External fixation	External fixation involves the placement of pins or screws into the bone on both sides of the fracture. The pins are then secured together outside the skin with clamps and rods, forming an external frame.
Extrapolation	In data analysis, predicting the value of a parameter outside the range of observed values.
Fascia iliaca compartment block	Fascia iliaca block is a low-tech alternative to a femoral nerve or a lumbar plexus block. The mechanism behind this block is that the femoral and lateral femoral cutaneous nerves lie under the iliacus fascia.
Fasciotomy	The surgical division the investing fascial wall of an osseo-fascial muscle compartment, usually to release pathologically high intra-compartmental pressure.
Fibrinolysis	A process within the body that prevents blood clots that occur naturally from growing and causing problems.
Focused assessment with sonography for trauma (FAST)	A rapid bedside ultrasound (see definition) examination performed as a screening test for blood around the heart (pericardial effusion) or abdominal organs (hemoperitoneum) after trauma.
Flap failure	When a mass of tissue used for grafting, only partially removed so that it retains its own blood supply during transfer to another site, does not fully re-vascularise.
Follow-up	Observation over a period of time of an individual, group or initially defined population whose appropriate characteristics have been assessed in order to observe changes in health status or health-related variables.
Frankel classification	Precursor to ASIA scoring system to assess spinal function.
Fresh frozen plasma	The remaining serum of human blood that is frozen after the cellular component has been removed for blood transfusion
Full-body computed tomography (CT)/whole-body CT	A CT scan from the head to below the hips with a form of X-ray imaging that produces cross-sectional images.
Generalisability	The extent to which the results of a study based on measurement in a particular patient population and/or a specific context hold true for another population and/or in a different context. In this instance, this is the degree to which the guideline recommendation is applicable across both geographical and contextual settings. For example, guidelines that suggest substituting one

Term	Definition
	form of labour for another should acknowledge that these costs might vary across the country.
Glasgow coma scale (GCS)	A rating scale devised to assess the level of consciousness following brain damage. The scale assesses eye, verbal and motor responses. The GCS grades on a scale of 1–15, the lower score indicating the greater neurologic impairment.
Glasgow outcome scale (GOS)	A system for classifying the outcome of persons who survive. The scale has eight outcome categories and relates to functional independence and not residual deficits.
Gold standard	See 'Reference standard'
Gustilo Anderson Grade	The Gustilo Anderson Grade open fracture classification system comprises: Type I: clean wound smaller than 1 cm in diameter, appears clean, simple fracture pattern, no skin crushing. Type II: a laceration larger than 1 cm but without significant soft-tissue crushing, including no flaps, degloving, or contusion. Fracture pattern may be more complex. Type III: an open segmental fracture or a single fracture with extensive soft-tissue injury. Also included are injuries older than 8 hours. Type III injuries are subdivided into three types: Type IIIA: adequate soft-tissue coverage of the fracture despite high-energy trauma or extensive laceration or skin flaps. Type IIIB: inadequate soft-tissue coverage with periosteal stripping. Soft-tissue reconstruction is necessary. Type IIIC: any open fracture that is associated with vascular injury that requires repair.
Haematoma block	An analgesic technique used to allow painless manipulation of fractures avoiding the need for full anaesthesia.
Haemodynamic instability	Patients who are non-responders or transient responders to intravenous fluid therapy.
Haemodynamically unstable	A patient requiring frequent interventions to maintain Heart Rate, Blood Pressure, or oxygenation.
Haemodynamic status	The status of blood flow in the circulation, the sum result of cardiac output and blood pressure. Stable haemodynamic status occurs when the circulatory supply of oxygen maintains organ perfusion.
Harms	Adverse effects of an intervention.
Health economics	The study of the allocation of scarce resources among alternative healthcare treatments. Health economists are concerned with both increasing the average level of health in the population and improving the distribution of health.
Health-related quality of life (HRQoL)	A combination of an individual's physical, mental and social well-being; not merely the absence of disease.
Heterogeneity	The term (or 'lack of homogeneity') is used in meta-analyses and systematic reviews when the results or estimates of effects of treatment from separate studies seem to be very different. This can be in terms of the different size of treatment effects or even to the extent that some studies indicate beneficial treatment effects and others suggest adverse treatment effects. Such results may occur as a result of differences between studies in terms of the patient populations, outcome measures, definition of variables or duration of follow-up, although there is also a small probability they may due to random sampling error.
High-energy fracture	A fracture resulting from a direct impact of sufficient energy to cause disruption of bone in anyone regardless of their health or comorbidities.

Term	Definition
	Examples are a motor vehicle accident, a high-height fall, or an industrial accident.
Image intensifier	A medical device that converts X-rays into visible light at higher intensity than fluorescent screens do.
Immobilised	The process of holding a joint or bone in place with a splint, cast or brace. This is done to prevent an injured area from moving while it heals.
Imprecision	Results are imprecise when they have wide confidence intervals around the estimate of effect. This may be partly due to studies including relatively few patients. It also arises as a result of high intrinsic variability in continuous outcome, or a low event rate.
Inclusion criteria (literature review)	Explicit criteria used to decide which studies should be considered as potential sources of evidence.
Incomplete injury	If a person with a spinal cord injury has either some sensation and/or some movement below the level of their spinal cord lesion, their injury is said to be incomplete
Incontinence	Loss of control of bowel or bladder.
Incremental analysis	The analysis of additional costs and additional clinical outcomes with different interventions.
Incremental cost	The mean cost per patient associated with an intervention minus the mean cost per patient associated with a comparator intervention.
Incremental cost effectiveness ratio (ICER)	The difference in the mean costs in the population of interest divided by the differences in the mean outcomes in the population of interest for one treatment compared with another.
Incremental net benefit (INB)	The value (usually in monetary terms) of an intervention net of its cost compared with a comparator intervention. The INB can be calculated for a given cost-effectiveness (willingness to pay) threshold. If the threshold is £20,000 per QALY gained then the INB is calculated as: (£20,000 x QALYs gained) – Incremental cost.
Indirectness	The available evidence is different to the review question being addressed, in terms of the population, intervention, comparison or outcome.
Initial surgery	A patient's first surgical intervention after injury
Injury Severity Score (ISS)	A clinical scale from 1 to 75 (higher score being more serious) which can classify patients following a traumatic incident. Those scoring above 15 are defined as having suffered from major trauma. ISS of 9-15 have moderately severe trauma.
International normalised ratio (INR)	A laboratory test measure of blood coagulation based on prothrombin time.
Intention to treat analysis (ITT)	A strategy for analysing data from a randomised controlled trial. All participants' data are analysed in the arm to which they were allocated, regardless of whether participants received (or completed) the intervention given to that arm or not. Intention-to-treat analysis reflects real-world adherence to the protocol and also prevents bias caused by the loss of participants' data from analysis. (see attrition bias)
Intervention	Healthcare action intended to benefit the patient, for example, drug treatment, surgical procedure, psychological therapy.
Interventional radiology (IR)	Defined by the British Society for Interventional Radiology (IR) it refers to a range of techniques which rely on the use radiological image guidance (X-ray fluoroscopy, ultrasound, computed tomography [CT] or magnetic resonance imaging [MRI]) to precisely target therapy. Most IR treatments are minimally invasive alternatives to open and laparoscopic (keyhole) surgery.
Intramedullary fixation	A surgical technique in which a metal nail provides stability to the bone.

Term	Definition
Intraoperative	The period of time during a surgical procedure.
Intraosseous (IO) access	The process of injecting directly into the marrow of a bone to provide a non-collapsible entry point into the systemic venous system
Intraperitoneal	Intraperitoneal means within or administered through the peritoneum. The peritoneum is a thin, transparent membrane that lines the walls of the abdominal (peritoneal) cavity and contains and encloses the abdominal organs, such as the stomach and intestines
Intravenous	A drug, nutrient solution, or other substance administered into a vein.
Intubation	Insertion of a tube into the trachea for purposes of anaesthesia, airway maintenance and lung ventilation.
Ischaemic damage	Damage caused to tissue or an organ due to insufficient supply of blood to an organ.
Kappa statistic	A statistical measure of inter-rater agreement that assesses the probability that the agreement occurred by chance.
Kendrick Extrication Device (KED)	A device used for extricating and immobilizing patients from auto accidents and other confined spaces.
Laparotomy	A surgical procedure to open the abdomen for diagnosis or in preparation for surgery.
Length of stay	The total number of days a participant stays in hospital.
Lesion	Site of injury or wound to the spinal cord.
Licence	See 'Product licence'.
Life-years gained	Mean average years of life gained per person as a result of the intervention compared with an alternative intervention.
Likelihood ratio	The likelihood ratio combines information about the sensitivity and specificity. It tells you how much a positive or negative result changes the likelihood that a patient would have the disease. The likelihood ratio of a positive test result (LR+) is sensitivity divided by 1- specificity.
Limb salvage	A surgical procedure to maintain a limb following a traumatic incident.
Log roll	Method of turning a patient without twisting the spine.
Long-term care	Residential care in a home that may include skilled nursing care and help with everyday activities. This includes nursing homes and residential homes.
Loss to follow-up	Loss to follow up is usually caused by failure of participants to attend for follow-up outcome assessments, though it can also occur if researchers exclude participants from a study for non-compliance (see 'intention to treat'). Loss to follow up may cause bias if the reason for non-attendance could have affected outcomes. For example, if non-attendance at follow-up is due to the treatment having made the condition worse, then such harm from the treatment is not captured during follow up and thus analysis, making the treatment seem better than it really is.
Low energy fracture	A fracture resulting from mechanical forces that would not ordinarily lead to the bone to fracture, for example, a fall from a standing height. Low-energy fractures may be more common in individuals with bone fragility (e.g. individuals with osteoporosis)
Lumbar	Lower-level area of the spine, lying below the thoracic spine and above the sacral spine. Lumbar nerves are responsible for innervation of the abdomen, parts of the perineum and most of the lower limbs.
Magnetic resonance imaging (MRI)	A medical imaging technique used for medical diagnosis, staging of disease and for follow-up without exposure to ionizing radiation. MRI scanners use magnetic fields and radio waves to form images of the body.
Major haemorrhage	Loss of more than one blood volume within 24 hours (around 70 mL/kg,

Term	Definition
	>5 litres in a 70 kg adult), a 50% of total blood volume lost in less than 3 hours, or bleeding in excess of 150 mL/minute.
Major trauma	Major trauma is defined as a potentially life threatening injury or injuries with the potential to cause the loss of a major limb
Major Trauma Centre (MTC)	A specialist hospital responsible for the care of major trauma patients across the region. It is a specialist hospital responsible for the care of the most severely injured patients involved in major trauma. It provides 24/7 emergency access to consultant-delivered care for a wide range of specialist clinical services and expertise. It is optimised for the definitive care of injured patients. In particular, it has an active, effective trauma Quality Improvement programme. It also provides a managed transition to rehabilitation and the community. It takes responsibility for the care of all patients with Major Trauma in the area covered by the Network. It also supports the Quality Improvement programmes of other hospitals in its Network. It provides all the major specialist services relevant to the care of major trauma, that is, general, emergency medicine, vascular, orthopaedic, plastic, spinal, maxillofacial, cardiothoracic and neurological surgery and interventional radiology, along with appropriate supporting services, such as critical care. The Royal College of Surgeons cite research advising that such centres should admit a minimum of 250 critically injured patients per year
Major Trauma Network	A collaboration between the providers commissioned to deliver trauma care services in a geographical area. A trauma network includes all providers of trauma care: pre-hospital services, other hospitals receiving acute trauma admissions (Trauma Units), and rehabilitation services. The trauma network has appropriate links to the social care and the voluntary/community sector. While individual units retain responsibility for their clinical governance, members of the Network collaborate in a Quality Improvement programme.
Malunion	Consolidation of a fracture in a position of deformity.
Markov model	A method for estimating long-term costs and effects for recurrent or chronic conditions, based on health states and the probability of transition between them within a given time period (cycle).
Multi-detector computed tomography (MDCT) scan	A form of computed tomography (CT) technology for diagnostic imaging. In MDCT, a two-dimensional array of detector elements replaces the linear array of detector elements used in typical conventional and helical CT scanners. The two-dimensional detector array permits CT scanners to acquire multiple slices or sections simultaneously and greatly increase the speed of CT image acquisition
Meta-analysis	A statistical technique for combining (pooling) the results of a number of studies that address the same question and report on the same outcomes to produce a summary result. The aim is to derive more precise and clear information from a large data pool. It is generally more likely to confirm or refute a hypothesis than the individual trials.
Methaemoglobinaemia	Methaemoglobin (MetHb) is an altered state of haemoglobin (Hb), reducing its ability to release oxygen. It can be acquired following admission of anaesthesia.
Minimal load bearing	Load-bearing only as much as is required to maintain the best level of independence achievable.
Minimal weight bearing	Weight-bearing only as much as is required to maintain the best level of independence achievable.
Motor function	Ability to perform functional tasks.

Term	Definition
Motor recovery	Recovery of the strength and co-ordination of voluntary movement.
Multidisciplinary team (MDT)	Group of experts providing optimal management following Spinal Cord Injury. Teams can consist of Medics, Nurses, Surgical Team Physiotherapists, General Practitioner, Speech and Language Therapist.
Multivariable model	A statistical model for analysis of the relationship between two or more predictor (independent) variables and the outcome (dependent) variable.
Muscle/joint contracture	A permanent shortening of a muscle or joint.
Myoglobinuria	Myoglobinuria is a condition usually the result of rhabdomyolysis or muscle destruction which can be detected by the detection of myglobin in the urine.
National Emergency X Radiography Utilization Study (NEXUS)	Guideline detailing Low-Risk Criteria to rule-out cervical spine injury in patients following acute trauma.
Necrosis	The death of most or all of the cells in an organ or tissue due to disease, injury, or failure of the blood supply.
Neer Classification	The Neer classification of proximal humeral fractures is probably the most frequently used along with the AO classification of proximal humeral fractures. The classification has been variably adapted by multiple authors into 4 main areas: • One-part fracture - fracture lines involve 1-4 parts none of the parts are displaced (that is, <1 cm and <45 degrees). These undisplaced/minimally displaced fractures account for approximately 70-80% of all proximal humeral fractures and are almost always treated conservatively 6-7. • Two-part fracture - fracture lines involve 2-4 parts, one part is displaced (that is, >1 cm or >45 degrees). Four possible types of two-part fractures exist (one for each part): surgical neck, greater tuberosity, anatomical neck, lesser tuberosity: uncommon • Three-part fracture - fracture lines involve 3-4 parts, two parts are displaced (that is, >1 cm or >45 degrees) • Four-part fracture -fracture lines involve parts, three parts are displaced (that is, >1cm or >45 degrees) with respect to the 4th.
Negative predictive value (NPV) [In screening/diagnostic tests:]	A measure of the usefulness of a screening/diagnostic test. It is the proportion of those with a negative test result who do not have the disease, and can be interpreted as the probability that a negative test result is correct.
Neuropathic/spinal cord pain	Neuropathic pain is a problem experienced following Spinal Cord Injury. A sharp pain is the result of damage to the spine and soft tissue surrounding the spine.
Neuroprotective agents	Medications that protect the brain and spinal cord from secondary injury caused by stroke or trauma.
Neurovascular compromise	Injury occurring when vessels and nerves are be disrupted or distorted by a fracture or dislocation and require urgent reduction.
Non-union	Non-union is failure of bone healing. A fracture is judged to be un-united if the signs of non-union are present when a sufficient time has elapsed since injury, during which the particular fracture would normally be expected to have healed by bony union. That period will vary according to age, fracture location and patho-anatomy.
Normotension	Fluid resuscitation with the aim of increasing systemic blood pressure to normal blood pressures.
No weight bearing	Not allowed to walk/stand.
Number needed to treat (NNT)	The number of patients that who on average must be treated to cause a single occurrence of the positive outcome of interest.

Term	Definition
Oblique fracture	A fracture with an angled pattern.
Observational study	Retrospective or prospective study in which the investigator observes the natural course of events with or without control groups; for example, cohort studies and case–control studies.
Occlusive dressing	A dressing that seals the wound from air or bacteria
Odds ratio	The odds of an event is the ratio of the number of events occurring (for example, the number of people dying) to the number of non-events (for example, the number of people not dying) within a single group. Odds are distinct from risks (see risk ratio) and are therefore not strictly a measure of probability. Odds are normally compared across two groups as an odds ratio (OR). For example the OR of dying in smokers compared to non-smokers would be calculated by dividing the odds of death in smokers by the odds of death in non-smokers. An odds ratio of 1 would show that the odds of the event is the same for both groups. An odds ratio greater than 1 means the odds of event are greater in the first group. An odds ratio less than 1 means that the odds of the event are less likely in the first group. Sometimes odds can be compared across more than 2 groups – in this case, one of the groups is chosen as the 'reference category', and the odds ratio is calculated for each group compared with the reference category. For example, to compare the odds of dying from lung cancer for non-smokers, occasional smokers and regular smokers, non-smokers could be used as the reference category. Odds ratios would be worked out for occasional smokers compared with non-smokers and for regular smokers compared with non-smokers. See also ‘relative risk’ and ‘risk ratio’.
Open fracture	The skin may be pierced by the bone or by a blow that breaks the skin at the time of the fracture. The bone may or may not be visible in the wound. This term is synonymous with ‘compound fracture’.
Open pneumothorax	When there is a pneumothorax associated with a chest wall defect, such that the pneumothorax communicates with the exterior. Usually caused by gunshot or knife wounds to chest.
Open reduction and internal fixation (ORIF)	A method of surgically repairing a fractured bone. Generally, this involves either the use of plates and screws or an intramedullary (IM) rod to stabilize the bone.
Opiates	A class of drugs that includes heroin, morphine, and codeine.
Opportunity cost	The loss of other health care programmes displaced by investment in or introduction of another intervention. This may be best measured by the health benefits that could have been achieved had the money been spent on the next best alternative healthcare intervention.
Osteomyelitis	An acute or chronic inflammatory condition affecting bone and its medullary cavity, usually the result of bacterial (occasionally viral) infection of bone.
Ottawa ankle rules	Ottawa ankle rules are a set of guidelines for clinicians to help decide if a patient with foot or ankle pain should be offered X-rays to diagnose a possible bone fracture.
Outcome	Measure of the possible results that may stem from exposure to a preventive or therapeutic intervention. Outcome measures may be intermediate endpoints or they can be final endpoints. See ‘Intermediate outcome’.
P-value	The probability that an observed difference could have occurred by chance, assuming that there is in fact no underlying difference between the means of the observations. If the probability is less than 1 in 20, the P value is less than 0.05; a result with a P value of less than 0.05 is conventionally considered to

Term	Definition
	be 'statistically significant'.
Paralysis	Injury or disease to a person's nervous system can affect the ability to move or feel.
Paraplegia	Loss of function and paralysis below the cervical area of the neck; generally, the upper body retains motor and sensory function.
Partial weight bearing	A small amount of weight may be supported by the limb.
Pelvic packing	Pelvic packing is an invasive surgical procedure, used to tamponade sources of pelvic bleeding. Absorbent packs are placed within the preperitoneal and retroperitoneal spaces and must be removed, usually within 48 hours.
Performance bias	Bias resulting from differences in the way different groups are treated, apart from the actual treatment under investigation. This may occur if those caring for participants are not blinded to group allocation. For example, participants in the 'favoured' group may be given better care. Performance bias also relates to participant beliefs about a treatment's efficacy. For example, if a participant knows he/she is in the intervention group then they may experience a placebo effect, which might not be felt by those in a non-treatment group.
Perioperative	The period from admission through surgery until discharge, encompassing the pre-operative and post-operative periods.
Permissive hypotension	The use of restrictive fluid therapy, specifically in the trauma patient, that increases systemic blood pressure without reaching normal blood pressures.
Picture Archiving and Communications Systems (PACS)	PACS enables X-ray and scan images to be stored electronically and viewed on screens.
Pilon	The distal end of the tibia – from the French for a stump, or a pestle. Fractures of the distal tibial metaphysic caused by axial load failure are called "pilon fractures".
Placebo	An inactive and physically identical medication or procedure used as a comparator in controlled clinical trials.
Plantar aspect	Relating to the sole of the foot.
Platelets	Blood cells whose function (along with coagulation factors) is to stop bleeding.
Pneumothorax	A collection of air or gas in the pleural cavity which can cause the lung(s) to collapse.
Polypharmacy	The use or prescription of multiple medications. Polypharmacy is often defined as taking 5 or 10 medications at the same time/
Polytrauma	Patients with associated injury (i.e. two or more severe injuries in at least two areas of the body), or with a multiple injury (i.e. two or more severe injuries in one body area). Also known as multisystem trauma.
Positive predictive value (PPV)	In screening/diagnostic tests: A measure of the usefulness of a screening/diagnostic test. It is the proportion of those with a positive test result who have the disease, and can be interpreted as the probability that a positive test result is correct.
Postoperative	Pertaining to the period after patients leave the operating theatre, following surgery.
Post-test probability	For diagnostic tests. The proportion of patients with that particular test result who have the target disorder
Post-traumatic arthritis	Post-traumatic arthritis is caused by the wearing out of a joint that has had

Term	Definition
	any kind of physical injury. Such injuries can damage the cartilage and/or the bone, changing the mechanics of the joint and making it wear out more quickly.
Power (statistical)	The ability to demonstrate an association when one exists. Power is related to sample size; the larger the sample size, the greater the power and the lower the risk that a possible association could be missed.
Preoperative	The period before surgery commences.
Pressure sore	Skin breakdown due to unrelieved pressure.
Pre-test probability	For diagnostic tests. The proportion of people with the target disorder in the population at risk at a specific time point or time interval. Prevalence may depend on how a disorder is diagnosed.
Primary amputation	A primary amputation is one that is carried out immediately on admission without any attempt to salvage the limb.
Primary care	Healthcare delivered to patients outside hospitals. Primary care covers a range of services provided by general practitioners, nurses, dentists, pharmacists, opticians and other healthcare professionals.
Primary outcome	The outcome of greatest importance, usually the one in a study that the power calculation is based on.
Product licence	An authorisation from the MHRA to market a medicinal product.
Prognosis	A probable course or outcome of a disease. Prognostic factors are patient or disease characteristics that influence the course. Good prognosis is associated with low rate of undesirable outcomes; poor prognosis is associated with a high rate of undesirable outcomes.
Prophylactic antibiotics	The prevention of infection complications using antimicrobial therapy (most commonly antibiotics).
Prospective study	A study in which people are entered into the research and then followed up over a period of time with future events recorded as they happen. This contrasts with studies that are retrospective.
Protected load bearing	Encouraged to use limb within load limit set by clinician.
Protected weight bearing	Patient encouraged to walk as normal, but with the use of a walking aid.
Prothrombin complex concentrate (PCC)	A combination of blood clotting factors II, VII, IX and X, as well as protein C and S, prepared from fresh-frozen human blood plasma used to reverse the effects of oral anticoagulation therapy in an actively bleeding patient.
Publication bias	Also known as reporting bias. A bias caused by only a subset of all the relevant data being available. The publication of research can depend on the nature and direction of the study results. Studies in which an intervention is not found to be effective are sometimes not published. Because of this, systematic reviews that fail to include unpublished studies may overestimate the true effect of an intervention. In addition, a published report might present a biased set of results (e.g. only outcomes or sub-groups where a statistically significant difference was found.
Quadriplegia	Scientifically known as tetraplegia; paralysis affecting all four limbs.
Quality of life	See 'Health-related quality of life'.
Quality-adjusted life year (QALY)	An index of survival that is adjusted to account for the patient's quality of life during this time. QALYs have the advantage of incorporating changes in both quantity (longevity/mortality) and quality (morbidity, psychological, functional, social and other factors) of life. Used to measure benefits in cost-utility analysis. The QALYs gained are the mean QALYs associated with one treatment minus the mean QALYs associated with an alternative treatment.
Randomisation	Allocation of participants in a research study to two or more alternative groups using a chance procedure, such as computer-generated random

Term	Definition
	numbers. This approach is used in an attempt to ensure there is an even distribution of characteristics across groups, which should minimise selection bias.
Randomised controlled trial (RCT)	A comparative study in which participants are randomly allocated to intervention and control groups and followed up to examine differences in outcomes between the groups.
Rapid Sequence Induction of anaesthesia and intubation (RSI)	A medical procedure prompt involving a prompt administration of general anaesthesia and subsequent intubation of the trachea. The procedure results in rapid unconsciousness (induction) and neuromuscular blockade (paralysis) and is used to maintain a patient's airway following a traumatic incident.
RCT	See 'Randomised controlled trial'.
Receiver operated characteristic (ROC) curve	A graphical method of assessing the overall accuracy of a diagnostic test at several different thresholds of the index measure. Sensitivity is plotted against 1 minus specificity. A perfect test will have a vertical line that extends from the origin to the top left point of the graph, continuing as a horizontal line to the top right portion of the graph. A good test will be somewhere close to this ideal.
Reduction	The replacement or realignment of a body part in normal position or restoration of a bodily condition to normal.
Reference standard	The test that is considered to be the best available method to establish the presence or absence of the outcome – this may not be the one that is routinely used in practice.
Regional nerve block	A deliberate interruption of signals traveling along a nerve, often for the purpose of pain relief
Rehabilitation	Set of services intended to restore maximum function -- physical, psychological, vocational and social - to a person with a disability.
Relative risk (RR)	Risk and probability are synonymous. The risk of an event is the ratio of the number of events occurring (for example, the number of people dying) to the total number of events and non-events (for example, the total number of people dying and staying alive) in a group. Risks are distinct from odds (see odds ratio). Risks are normally compared across two groups as a relative risk, which is also known as a risk ratio (RR). For example the RR of dying in smokers compared to non-smokers would be calculated by dividing the risk of death in smokers by the risk of death in non-smokers. A RR of 1 would show that the risk of the event is the same for both groups. RR ratio greater than 1 means the risk of the event are greater in the first group. A RR less than 1 means that the risk of the event are less likely in the first group. Sometimes risks can be compared across more than 2 groups – in this case, one of the groups is chosen as the 'reference category', and the RR is calculated for each group compared with the reference category. For example, to compare the risk of dying from lung cancer for non-smokers, occasional smokers and regular smokers, non-smokers could be used as the reference category. RRs would be worked out for occasional smokers compared with non-smokers and for regular smokers compared with non-smokers. See also 'odds ratio'.
Reporting bias	See publication bias.
Rescue board	A robust and light construction board for placing patients on following injury. Rescue boards are particularly useful for water rescues but can be also used on land.

Term	Definition
Resource implication	The likely impact in terms of finance, workforce or other NHS resources.
Respiratory compromise	An impairment of normal pulmonary gas exchange. If this leads to an arterial PaO2 of <8Kpa this signals the onset of respiratory failure. Respiratory compromise could be due to respiratory depression (see 'respiratory depression') or other causes such as fluid in the lungs.
Respiratory depression	Respiratory depression: Occurs when ventilation is compromised below the level required for normal gas exchange. This is related to both rate (<10 breaths per minute) and depth of breathing. This can be induced by many causes such as excessive analgesia, head injury, intoxication or cervical spine injury.
Restricted weight bearing (active/passive range)	Restricted to range specific to a joint.
Retroperitoneal	The space between the peritoneum and the posterior abdominal wall that contains especially the kidneys and associated structures, the pancreas, and part of the aorta and inferior vena cava.
Retrospective study	A retrospective study deals with the present/ past and does not involve studying future events. This contrasts with studies that are prospective.
Revascularisation	The restoration of perfusion to a body part or organ that has suffered ischemia following surgical intervention.
Review question	In guideline development, this term refers to the questions about treatment and care that are formulated to guide the development of evidence-based recommendations.
Rigid non-removable cast	A non-removable off-bearing cast which is generally made from fibreglass or plaster of Plaster of Paris.
Scoop stretcher	The scoop stretcher is a device used specifically for casualty lifting. It is most frequently used to lift supine patients from the ground, either due to unconsciousness or in order to maintain stability in the case of trauma, especially spinal injury.
Secondary amputation	An amputation that is carried out after an attempted salvage of the limb.
Secondary outcome	An outcome used to evaluate additional effects of the intervention deemed a priori as being less important than the primary outcomes.
Selection bias	A systematic bias in selecting participants for study groups, so that the groups have differences in prognosis and/or therapeutic sensitivities at baseline. Randomisation (with concealed allocation) of patients protects against this bias. In non-randomised studies a multivariable analysis helps to partially adjust for selection bias.
Selective imaging	An imaging method following trauma in which scanning is limited to areas suspected of having injury. Imaging can be undertaken using ultrasound, CT or X-ray.
Selective immobilization	Immobilization following the use of a prediction soon.
Sensitivity	Sensitivity or recall rate is the proportion of true positives which are correctly identified as such. For example in diagnostic testing it is the proportion of true cases that the test detects. See the related term 'Specificity'
Sensitivity analysis	A means of representing uncertainty in the results of economic evaluations. Uncertainty may arise from missing data, imprecise estimates or methodological controversy. Sensitivity analysis also allows for exploring the generalizability of results to other settings. The analysis is repeated using different assumptions to examine the effect on the results. One-way simple sensitivity analysis (univariate analysis): each parameter is varied individually in order to isolate the consequences of each parameter on

Term	Definition
	the results of the study. Multi-way simple sensitivity analysis (scenario analysis): two or more parameters are varied at the same time and the overall effect on the results is evaluated. Threshold sensitivity analysis: the critical value of parameters above or below which the conclusions of the study will change are identified. Probabilistic sensitivity analysis: probability distributions are assigned to the uncertain parameters and are incorporated into evaluation models based on decision analytical techniques (For example, Monte Carlo simulation).
Significance (statistical)	A result is deemed statistically significant if the probability of the result occurring by chance is less than 1 in 20 ($p < 0.05$).
Skeletal maturity	Skeletal maturity is relevant to the consideration of fractures for many reasons. The term is used frequently in the guideline. The anatomy of immature bone is different from mature bone; most obviously in the presence of growth plates, but also in the different pattern of blood supply. Immature bones break in a way different to mature bone, consequent upon the presence of growth plates and the quality of the bone itself. Immature bone tend to heal more rapidly. The initial injury or its treatment may interfere with normal bone growth. For the whole person the skeleton is mature once all growth plates are closed. For an individual injury skeletal maturity is when the growth plates in the bones under consideration have closed. Clinical judgement is required during the transition period from immaturity to maturity as to how the bone should be regarded for clinical management purposes.
Skeletal stabilisation	Stabilising an unstable limb, part of limb or pelvis by a method which involves attaching something to the bone. This can be definitive or temporary. Definitive skeletal stabilisation (also referred to as definitive skeletal fixation) will be left in situ throughout the planned healing process, and therefore is durable and precisely applied. Temporary skeletal stabilisation is replaced by a definitive solution before the healing process is complete, and so can be done more quickly, may cross joints, and may not involve such precise reduction.
Softcast	A lightweight splint that is removal and can be applied for immobilisation.
Specificity	The proportion of true negatives that a correctly identified as such. For example in diagnostic testing the specificity is the proportion of non-cases incorrectly diagnosed as cases. See related term ‘Sensitivity’. In terms of literature searching a highly specific search is generally narrow and aimed at picking up the key papers in a field and avoiding a wide range of papers.
Spinal Cord Injury (SCI)	An injury to the spinal cord interferes with messages between the brain and the body and results in paralysis and sensory loss below the level of the injury. The location at which the cord is injured and the severity of the injury determines the physical limitations the person will have.
Spinal shock	Often occurring soon after spinal cord injury, this is a loss of reflexes below the level of injury with associated loss of sensorimotor functions. This condition can last for several hours to days after initial injury.
Stakeholder	Those with an interest in the use of the guideline. Stakeholders include manufacturers, sponsors, healthcare professionals, and patient and carer groups.

Term	Definition
Subcutaneous	An injection in which a needle is inserted just under the skin.
Supraglottic device	Medical device that when applied facilitates unobstructed access of respiratory gases to the glottic opening by displacing tissue and sealing off the laryngeal area.
Surgical site infection (SSI)	Defined as being present when pathogenic organisms multiply (SSI) in a wound giving rise to local signs and symptoms, for example heat, redness, pain and swelling, and (in more serious cases) with systemic signs of fever or a raised white blood cell count. Infection in the surgical wound may prevent healing taking place so that the wound edges separate or it may cause an abscess to form in the deeper tissues. The definitions of SSI may vary between research studies but are commonly based on those described by the Centers for Disease Control and Prevention (CDC) although other valid measures have been used, for example the ASEPSIS scoring method for postoperative wound infections and some studies that have focused only on the more serious deep and organ/space infections for which less subjective measures are available. Differences in case definitions should be taken into account when comparing reported rates of SSI.
Surgical wound classification	*Clean* – an incision in which no inflammation is encountered in a surgical procedure, without a break in sterile technique, and during which the respiratory, alimentary and genitourinary tracts are not entered. *Clean-contaminated* – an incision through which the respiratory, alimentary or genitourinary tract is entered under controlled conditions but with no contamination encountered. *Contaminated* – an incision undertaken during an operation in which there is a major break in sterile technique or gross spillage from the gastrointestinal tract, or an incision in which acute, non-purulent inflammation is encountered. Open traumatic wounds that are more than 12–24 hours old also fall into this category. *Dirty or infected* – an incision undertaken during an operation in which the viscera are perforated or when acute inflammation with pus is encountered during the operation (for example, emergency surgery for faecal peritonitis), and for traumatic wounds where treatment is delayed, and there is faecal contamination or devitalised tissue present.
Systems model	A problem-oriented representation of a complex system where parts of the system and their interactions that are relevant to the decision problem are explicitly set out.
Systematic review	Research that summarises the evidence on a clearly formulated question according to a pre-defined protocol using systematic and explicit methods to identify, select and appraise relevant studies, and to extract, collate and report their findings. It may or may not use statistical meta-analysis.
Telemedicine	Delivery of health services via remote telecommunications. This includes interactive consultative and diagnostic services.
Tension band	A format for orthopaedic wiring of fracture fragments either alone or with a screw or Kirschner wire to force fragments together in compression.
Tension pneumothorax	A tension pneumothorax occurs when intrapleural air accumulates progressively in and leads to significant impairment of respiration and/or blood circulation. It is a life threatening occurrence requiring rapid recognition and treatment is required if cardiorespiratory arrest is to be avoided.
Test and treat studies	See ‘diagnostic RCT’.
Thoracic	Portion of the spinal column in the chest, between the cervical and lumbar areas.

Term	Definition
Thoracostomy	The construction of an artificial opening through the chest wall, usually for the drainage of fluid or the release of an abnormal accumulation of air. Used to treat pneumothorax.
Tiered team response	Tiered trauma systems aim to better match the personnel and resources of the trauma team to the immediacy of the patients need for care
Time horizon	The time span over which costs and health outcomes are considered in a decision analysis or economic evaluation.
Tracheal intubation	A medical procedure in which a tube is placed into the windpipe (trachea), through the mouth or the nose. In most emergency situations it is placed through the mouth.
Transverse fracture	This type of fracture has a horizontal fracture line.
The Trauma Audit & Research Network (TARN)	An independent monitor of trauma care in England and Wales that is committed to making a real difference to the delivery of the care of those who are injured. They promote improvements in care through national comparative clinical audit.
Trauma coordinator	Typically a nurse recruited into MTCs with experience of trauma care
Trauma Unit (TU)	A hospital that is part of the major trauma network providing care for all except the most severe major trauma patients. When it is not possible to get to the major trauma centre within 45 minutes, or where the patient needs to be stabilised quickly, the patient is taken to the nearest hospital with a local trauma unit for immediate treatment and stabilisation before being transferred on to the major trauma centre.
Traumatic Brain Injury	A non-degenerative, non-congenital insult to the brain from an external mechanical force, possibly leading to permanent or temporary impairment of cognitive, physical, and psychosocial functions, with an associated diminished or altered state of consciousness.
Treatment allocation	Assigning a participant to a particular arm of the trial.
Triage	Triage is the process by which people are classified according to the type and urgency of their symptoms/condition/situation. The aim is to get someone in need to the right place at the right time to see an appropriately skilled person/team.
Ultrasound	Diagnostic ultrasound, also called sonography or diagnostic medical sonography, is an imaging method that uses high-frequency sound waves to produce images of structures within your body.
Univariate	Analysis which separately explores each variable in a data set.
Unrestricted load bearing	Encouraged to use limb as normal.
Unrestricted mobility	Encouraged to use limb as normal.
Unrestricted weight bearing	Encouraged to walk as normal.
Unstable fracture	A fracture with a tendency to displace after reduction.
Utility	A measure of the strength of an individual's preference for a specific health state in relation to alternative health states. The utility scale assigns numerical values on a scale from 0 (death) to 1 (optimal or 'perfect' health). Health states can be considered worse than death and thus have a negative value.
Vacuum mattress	A vacuum mattress is a medical device used for the immobilisation of patients, especially in the case of vertebra, pelvis or limb trauma. The atmospheric pressure enables the mattress to become rigid securing the patient.
Vitamin K antagonist (VKA)	A group of substances that reduce blood clotting by reducing the action of vitamin K.

Term	Definition
Whole-Body CT	A scanogram (vertex to toes) followed by a CT scan from vertex to mid-thigh.
Wound photographs	A digital photograph of the wound to kept along kept as documentation with the patients note.
X-ray	A photographic or digital image of the internal composition of something, especially a part of the body, produced by X-rays being passed through it and being absorbed to different degrees by different materials .Structures that are relatively radiopaque (allow few X-rays to pass through), such as bones and cavities filled with a radiopaque contrast medium, cast a shadow on the film

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