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MATTs (Major Trauma Triage Tool Study):
Identification, development, validation and evaluation of major
trauma triage tools

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MATTS: Major Trauma Triage Tool Study

Contents

General information	5
Protocol amendments	6
Scientific Summary	7
Lay Summary	11
1. Introduction	12
2. Study Design	14
3. Aims and objectives	16
4. Phase One	17
5. Phase Two	20
6. Phase Three	25
7. Study supervision	33
8. Publication and dissemination	35
9. Finance	36
10. Ethics approval	37
11. Regulatory approvals	38
12. Indemnity / Compensation / Insurance	39
13. References	40

Abbreviations

AE	Adverse event
ASCOT	The American Association for the Surgery of Trauma
CI	Chief Investigator
CRF	Case report form
CTRU	Clinical Trials and Research Unit
DMEC	Data Monitoring and Ethics Committee
EMS	Emergency Medical Services (Ambulance services)
ENBS	Expected net benefit of sampling
EQ-5D-5L	European Quality of Life Measure (5 levels)
EVSI	Expected Value of Sample Information
GCP	Good Clinical Practice
HRA	Health Research Authority
HTA	Health Technology Assessment
LAS	London Ambulance Service
MTC	Major Trauma Centre
Non-MTC	Non-Major Trauma Centre
NHS	National Health Service
NIHR	National Institute of Health Research
NRES	National Research Ethics Service
PMG	Project Management Group
QALY	Quality adjusted life year
R&D	Research and development
REC	Research Ethics Committee
SAE	Serious adverse event
SAP	Statistical analysis plan
SSC	Study Steering Committee
STROBE	STrengthening the Reporting of OBservational studies in Epidemiology
SUSAR	Suspected unexpected serious adverse reaction
SWAST	South West Ambulance Service
TARN	Trauma Audit and Research Network
WMAS	West Midlands Ambulance Service
YAS	Yorkshire Ambulance Service

Definition of terms

Emergency Medical Services	Emergency services which treat illnesses and injuries that require an urgent medical response, providing out-of-hospital treatment and transport to definitive care. Also known as ambulance services or paramedic services.
Over-triage	Patients without major trauma incorrectly bypass a non-specialist trauma unit and are transported directly to a specialist major trauma centre. Taking patients with minor injuries to the major trauma centre could waste time, money and resources; denying treatment to those who require it by overstressing the capacity of the major trauma centre. It could also inconvenience patients and their families by taking them further from home.
Sensitivity	Sensitivity helps describe how well a test works. It reports how likely the test will be positive if a person has a disease. A sensitive test will help rule out a disease if the result is negative. If the test is highly sensitive and the test result is negative you can be confident that they don't have the disease.
Specificity	Specificity helps describe how well a test works. It reports how likely the test will be negative if a person does not have a disease. A specific test will help rule in a disease if the result is positive. If the test is highly specific and the test result is positive you can be confident that they do have the disease.
Triage	Prioritising of patients for treatment or transport according to their severity of injury. Over-triage occurs when a patient receives more advanced specialist care than necessary; they use costly, high level resources for a non-threatening condition. Under triage occurs when a severely injured patient fails to get the necessary specialist or advanced care.
Major Trauma	Major trauma describes serious and often multiple injuries where there is a strong possibility of death or disability. These might include serious head, chest, abdominal and skeletal injuries sustained as a result of accidents, sport or violence. Major trauma is the main cause of death for people under the age of 45 and is a major cause of debilitating long term injuries.
Major Trauma Network	Organised groups of health services and personnel, who serve a defined population and aim to reduce death and disability following injury. Integrates the organisations responsible for three overlapping phases (pre-hospital, in-hospital and rehabilitation) of a patient's journey. Incorporates defined patient pathways for different types of injury, ensuring that patients are treated at the time and place that most benefits them.
Local Emergency Hospital	The Local Emergency Hospital (LEH) is a hospital in a Trauma Network that does not routinely receive acute trauma patients (excepting minor injuries that may be seen in a minor injury unit). It has processes in place to ensure that should this occur patients are appropriately transferred to an MTC or TU. It may have a role in the rehabilitation of trauma patients and the care of those with minor injuries.

Major Trauma Centre	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. A major trauma centre (MTC) is part of a major trauma network.
Major Trauma Unit	A major trauma unit is a hospital that is part of the major trauma network providing care for all except the most severely injured patients. When it is not possible to get to the major trauma centre within a safe time period (commonly 60 minutes), or where a patient needs immediate stabilisation (e.g. uncontrolled haemorrhage, obstructed airway), the patient is taken to the nearest major trauma unit for immediate treatment and stabilisation before being transferred on to the major trauma centre. Once discharged from a major trauma centre, local trauma units also provide on-going treatment and rehabilitation for patients.
Under-triage	Patients with major trauma aren't recognised by ambulance services and instead of being taken directly to a specialist major trauma centre, are incorrectly transported to a non-specialist trauma unit. Failing to recognise serious injury could result in less effective treatment or increased harm.

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Changes to Scientific Summary

Changes to reflect the revised random sampling process for reference standard negative cases.

Changes to section 5.1 Validation Study

Changes to reflect the revised random sampling process for reference standard negative cases.

Changes to section 6.1 Service Evaluation Study

Changes to reflect the revised random sampling process for reference standard negative cases.

Scientific Summary

Background: The MATTS project is a comprehensive programme of research investigating pre-hospital triage tools for use in NHS major trauma networks. The project consists of 3 phases:

- Phase One: Identification and review of existing triage tools, and development of a new tool by expert consensus, for evaluation in subsequent phases.
- Phase Two: A prospective cohort study to validate triage tools from Phase One and identify an optimally performing candidate triage tool.
- Phase Three: Operational implementation and service evaluation of the candidate triage tool.

Aim: To develop an accurate, acceptable and usable pre-hospital triage tool to identify patients with major trauma who benefit from MTC care.

Design:

a) Phase One - Triage Tool Identification and Development

A series of sub-studies will identify existing triage tools; and develop a new tool for further evaluation, comprising:

- A systematic review and document analysis of current tools
- A retrospective cohort study, focus groups and surveys with clinicians to identify predictors of major trauma.
- Decision analytical modelling evaluating trade-offs between under/over-triage.
- Expert consensus and PPI process to define which patients should receive MTC care and develop a new major trauma triage tool.

b) Phase Two - Validation Study

- **Setting:** 4 major trauma networks within the West Midlands, Yorkshire, South Western and London Ambulance Services.
- **Study design:** Single gate diagnostic accuracy cohort study with a census sample of reference standard positive major trauma cases; and random sample of reference standard negative cases without major trauma.
- **Study population:** Patients attended by ambulance following injury. Sub-group analyses of children (<16 years) and elderly patients (≥65 years).
- **Study sample:**
 - *Reference standard positive cases:* Census sample of consecutive cases meeting MATTS reference standard /secondary reference standards, identified through augmented TARN processes.
 - *Reference standard negative cases:* Random sample of cases presenting to EMS with injury. Appropriate patients identified using injury related working impression codes, use of major trauma interventions, hospital trauma team pre-alerts, and call priority.

- **Data collection:**
 - Ambulance service data: fixed fields used as recorded in EPR. Free text fields coded by research paramedics blinded to reference standard.
 - TARN data: Fixed fields as recorded in TARN database. Additional MATTS required data fields completed by TARN data coordinators/research paramedics as required.
 - Data linkage: Research paramedics to review all reference standard positive cases and manually determine a definitive EMS identifier for deterministic linkage. Non-linked cases assumed to be reference standard negative.
 - Data governance: The proposed study design change does not affect data flows; and CAG and ethics approvals should be unaffected.

- **Index tests:** Existing and expert consensus-derived major trauma triage tools scored according to observed pre-hospital variables by blinded research paramedics. Identifiable data and reference standard classification withheld from research paramedics during triage tool coding.

- **Reference standard:** Patients with the potential to benefit from MTC care previously defined by independent expert consensus (clinicians, stakeholders) and Patient and Public Involvement (PPI) consultation. Secondary reference standards of Injury Severity Score (ISS) >15 and US consensus definition. Major trauma cases identified through augmented TARN case ascertainment process, supported by MATTS research paramedics.

- **Outcomes:** Sensitivity/specificity (corresponding to 1-Under/over-triage rates).

- **Sample size:** TARN/EMS data suggests approximately 200 major trauma cases (ISS>15) per 4 months per trauma network. Assuming a target sensitivity of 95% as per American College of Surgeons Committee on Trauma (ASCOT) guidance, the total of 800 reference standard positive cases would give a 95% confidence interval coverage of 2% for sensitivity. EMS data suggests approximately 25,000 patients presenting with injury over 4 months per trauma network (total 100,000 across all 4 of the participating trauma networks). Assuming a target specificity of 70% as per ASCOT guidance, coding 2000 reference standard negative cases (sampling fraction of 2%) would give a 95%CI coverage of 2% for specificity. The total sample size of 2,800 cases would equate to an approximate total of 700 patients (200 major trauma cases and 500 non-major trauma cases) per network. This should be a manageable work load for research paramedics (approximately 9 cases to code per working day), while providing sufficient statistical power.

The following table presents the precision achieved for a range of observed sensitivities and specificities with the proposed sample size:

MATTS Study

Estimated sensitivity	Precision	Level of confidence	LCL	UCL	Reference standard positive N=
0.97	0.0125	0.95	0.958	0.983	716
0.95	0.015	0.95	0.935	0.965	811
0.90	0.02	0.95	0.880	0.920	865
0.80	0.03	0.95	0.770	0.830	683
0.70	0.03	0.95	0.670	0.730	897
0.60	0.035	0.95	0.565	0.635	753
0.50	0.035	0.95	0.465	0.535	784
Estimated Specificity	Precision	Level of confidence	LCL	UCL	Reference standard negative N=
0.97	0.0075	0.95	0.963	0.978	1988
0.95	0.01	0.95	0.940	0.960	1825
0.9	0.0125	0.95	0.888	0.913	2213
0.8	0.0175	0.95	0.783	0.818	2007
0.7	0.02	0.95	0.680	0.720	2017
0.6	0.0225	0.95	0.578	0.623	1822
0.5	0.0225	0.95	0.478	0.523	1898

- **Outputs:** Optimally performing candidate triage tool identified by expert consensus, PPI and participating trauma networks.

c) Phase Three - Evaluation of System-Level Performance of Implemented Optimal Triage Tool.

A service evaluation characterising under/over-triage rates of the candidate triage tool when implemented operationally:

- Setting: Major trauma network within each of the West Midlands, Yorkshire, South Western and London Ambulance Services.
- Study population: Any patient attended by EMS following injury. Sub-group analyses of children (<16 years) and elderly patients (≥65 years).
- Study sample:
 - Reference standard positive cases: Census sample of consecutive cases meeting MATTS reference standard /secondary reference standards, identified through augmented TARN processes.

- Reference standard negative cases: Random sample of cases presenting to EMS with injury. Appropriate patients identified using injury related working impression codes, use of major trauma interventions, hospital trauma team pre-alerts, and call priority.

- Outcomes: Under/over-triage rates based on actual patient destinations and observed hospital pre-alerts.
- Data collection: Linkage of pre-hospital and hospital variables using prospective EMS and augmented TARN data.
- Sample size: EMS/TARN data suggests approximately 300 major trauma cases (ISS>15) per 6 months per trauma network. Assuming, based on ASCOT criteria, a triage tool requires sensitivity of 95%, the total of 1,200 major trauma cases would give a 95% confidence interval coverage of $\pm 1.0\%$ for the under-triage rate. EMS data suggests approximately 37,500 patients presenting with injury over 6 months per trauma network (total 150,000 across all 4 of the participating trauma networks). Assuming a target specificity of 70% as per ASCOT guidance, coding 3000 reference standard negative cases (sampling fraction of 2%) would give a 95%CI coverage of $\pm 1.5\%$ for specificity.

- Evaluation of acceptability and usability to patients, ambulance services, and other important stakeholders using mixed-methods
- Cost-effectiveness of alternative triage tools using decision analytical modelling.

Project timetable: 31 month funded 3-phase research programme.

- Phase 1 Development Work: Permissions and set up, systematic review, retrospective cohort study, clinician focus groups, decision analytical modelling, and expert consensus process (10m). Conducted prior to the Phase 2 validation and Phase 3 implementation studies primarily considered in the current protocol.
- Phase 2 Validation Study: Prospective data collection, linkage and analysis (8m);
- Phase 3 Service Evaluation: Triage tool implementation, mixed methods assessment of performance, acceptability and usability (7m);
- Close-out: cost-effectiveness modelling, analysis and write-up (6m).

Expertise: Highly experienced team with track record of successfully delivering challenging pre-hospital studies. Specialists in pre-hospital care, major trauma, health services research, data management and linkage, systematic reviews, statistics, health economics, and strong PPI input. Expert advisory group of methodologists, and key policy, ambulance service and clinical stakeholders.

Lay Summary

Serious injuries are a major health problem in England, responsible for 3,000 deaths and 8,000 disabilities each year. Treatment in specialist hospitals, called major trauma centres, can improve survival following such injuries. In order to benefit from this expert care, ambulance crews must first correctly identify suitable patients at the scene of injury and then transport them to a major trauma centre, potentially bypassing closer non-specialist hospitals.

The presence of serious injury is not always obvious and assessment can be difficult. Taking patients with minor injuries to the major trauma centre could waste time, money and resources; denying treatment to those who require it by overstressing the capacity of the major trauma centre. It could also inconvenience patients and their families by taking them further from home. In contrast, failing to recognise serious injury could result in less effective treatment or increased harm.

The term 'triage' means to sort patients in terms of priority. Ambulance crews currently use a 'triage tool' to help them to recognise whether a patient is seriously injured or not. The tool is a checklist of patient and injury features, for example the presence of low blood pressure, that indicate that care in a major trauma centre care might be beneficial. Unfortunately, research has suggested that current tools are not very accurate, as they could miss patients with serious injury and often unnecessarily direct patients with more minor injuries to a major trauma centre. This study aims to develop a new and more accurate tool that will help to ensure that the right patient gets to the right place at the right time.

We will carefully study existing triage tools used in England and world-wide. We will also use data already collected by ambulance services and the English national major trauma database (the Trauma Audit and Research Network, TARN) to investigate what factors are important for detecting serious injury at the scene of the incident. Additionally we will develop a computer model that simulates the costs and outcomes of using different triage tools. Together, we will take this information to a group of experts and ask them to develop a new triage tool.

We will then test the experts' triage tool, together with other existing tools, to see how they perform. In order to do this we will link data that is routinely collected by the Yorkshire, West Midlands, South Western and London Ambulance services, with hospital information collected by TARN. It has been suggested that identifying major trauma in older people is particularly difficult, so we will also specifically focus on this age group. We will then take the best-performing tool and introduce it into practice in an area of each ambulance service, to see how it works in real life. To find out about the experiences and views of patients, and paramedics using the tool, we will carry out interviews and focus groups. We will also consult with major trauma specialists, service managers and other stakeholders to assess the possible impact of the tool.

We have talked to patients affected by serious injury, and a group of patients involved in research about emergency care, while developing these research ideas. Members of these groups have agreed to join an advisory panel to help guide any future study. We have included a lay person with personal experience of major trauma as part of our research team alongside specialists in emergency medicine, pre-hospital practice, and major trauma. We have also consulted national specialist groups and gained support from participating ambulance services.

1. Introduction

Major trauma is an important and life-threatening condition caused by serious injury.[1] Correct pre-hospital identification of significant injuries with direct transportation to a specialist Major Trauma Centre (MTC) may improve outcomes.[2] The MATTS project is a comprehensive research programme that will develop an accurate, acceptable and usable pre-hospital triage tool for use in NHS trauma networks, to identify patients with major trauma that may benefit from MTC care, optimising under/over-triage.

What is the problem being addressed?

The MATTS project addresses the research questions outlined in the HTA commissioned research brief: a national pre-hospital major trauma triage tool/process. Major trauma is an important and life-threatening condition caused by serious injury.[1] It has a bimodal age distribution with a first peak in the under-20s, and a second peak in over-65s; an age group where the burden of trauma continues to increase.[3] In 2012 major trauma care in England was reconfigured with the introduction of regional networks, aiming to concentrate seriously injured patients in specialist MTCs.[4] The bypass of non-specialist local hospitals ('non-MTCs') with less experience, resources and expertise, has been associated with improved patient outcomes; the correct identification of appropriate patients who may benefit from specialist MTC care is therefore critical.[2, 5, 6] The recent NICE trauma guideline recommends that pre-hospital triage tools should be used by EMS (i.e. the ambulance service) to identify which patients should be sent to MTCs.[7] However, research has suggested that existing triage tools are inaccurate, particularly in elderly patients, and NICE were consequently unable to support a specific tool.[8] Further research was therefore recommended to develop and validate a national trauma triage tool.

Why is this research important?

Major trauma is a major public health problem responsible for 3,000 fatalities, 8,000 patients with severe disabilities, £0.4 billion of immediate treatment NHS costs, and a £3.5 billion loss in economic output each year in England.[1, 9] Improvements in the management of major trauma, therefore, have the potential to improve greatly both health, and individual and societal wealth. In England, an estimated 20% of the annual 6.3 million 999 calls requiring an EMS response are due to injury,[10] but only a small fraction represents major trauma and identification is not always obvious at the scene of injury. Bypassing of patients without potential to benefit from MTC care ('over-triage') may waste the time, money and resources of ambulance services and MTCs; and may inconvenience patients and their families. Conversely, failing to recognise appropriate patients with serious injury ('under-triage') could result in transport to non-specialist hospitals, resulting in less effective treatment, increased harm including higher rates of mortality, and poorer recovery.

What is currently known about major trauma triage?

Several narrative and systematic reviews have examined the performance of adult major trauma triage tools.[11-15] The most recent, valid and comprehensive review by van Rein et al. identified 21 predominantly North American studies, investigating 16 different triage tools in adults.[15] Sensitivity and specificity estimates were extremely heterogeneous, ranging from 9% to 100%; and were worse in elderly patients. Included studies were noted to be at high risk of bias, and poorer quality retrospective studies, with selected study populations, reported more optimistic results. The performance of the American College of Surgeons Committee on Trauma (ASCOT) triage tool,[16] on which many current UK instruments are based, was poor with sensitivity and specificity of 66% and 88% respectively. The evidence base for major trauma triage in children is less developed, but a further recent systematic review also suggests sub-optimal performance.[17-19] These findings suggest

that prospective validation of an existing tool is unlikely to be useful, supporting the development of a new tool. The epidemiology of major trauma in the UK is evolving, with the number of serious injuries in elderly patients increasing.[3] We will therefore specifically focus on this sub-group of patients where existing triage tools have consistently demonstrated unacceptable levels of under-triage.[20-22]

Narrative reviews have examined the role of paramedic judgement as an alternative method of triage for trauma patients.[12, 23, 24] They report poor quality studies, disparate reference standards and conflicting accuracy results, with sensitivity ranging from 29% to 98%, and heterogeneous specificity estimates between 60% and 96%. Using paramedic gestalt as an adjunct to major trauma triage tools, and the process by which paramedics reached their triage decisions, has not been previously investigated. Further investigation of paramedic judgement is therefore clearly warranted.

Few studies have examined the system-level, real-life, performance of triage tools when implemented in trauma networks. Both Newgard et al. and Voskens et al. have reported a marked discrepancy between triage tool results scored according to observed variables and actual transport destinations seen in practice.[25, 26] We will consequently examine triage tool implementation, usability and acceptability of an optimally accurate tool to explore real-life performance.

Conclusion

Major trauma is an important public health burden in the United Kingdom. Specialist management in MTCs may improve outcomes, but existing ambulance service triage tools appear to be sub-optimal, have a limited evidence base, and have not been investigated in the NHS setting. The development of new triage tools, NHS based validation of existing tools, and the evaluation of real-life triage tool performance is required to optimise outcomes of UK trauma networks.

2. Study Design

MATTS project overview

The MATTS project comprises a comprehensive programme of research work that will develop, validate and evaluate implementation of a new major trauma triage tool through primary and secondary research methods in a 3 phase study:

Phase One Triage Tool Identification and Development Study

In Phase One existing triage tools will be identified and a new expert-derived tool developed. Phase One comprises multiple sub-studies consisting of secondary research or qualitative work with clinicians and PPI representatives, comprising:

- 1) A systematic review and document analysis of current triage tools.
- 2) Document analysis and descriptive synthesis of existing trauma triage tools
- 3) A retrospective cohort study (using existing data)
- 4) Focus groups and surveys with clinicians to identify predictors of major trauma
- 5) Decision analytical modelling of major trauma triage, evaluating the trade-offs between under/over-triage.
- 6) An expert consensus process, informed by stages a) to d) above, to define which patients should receive MTC care and develop a new major trauma triage tool; including an expert consensus workshop and a final expert panel meeting to confirm the content of the new trauma triage tool.

No patients are involved in any of these sub-studies and no new patient data will be collected. Ethical approvals for individual studies within this work stream are therefore unnecessary, or will be confirmed separately with the University of Sheffield. Phase One sub-studies are summarised in Section 4. Phase One

Phase Two Validation Study

The Phase Two validation study is a prospective diagnostic accuracy cohort study. Major trauma triage tools identified and developed in Phase One will be validated using linked EMS and hospital data. Patients of any age will be included if attended following injury by EMS. Triage tools identified (systematic review, document analysis) and developed (expert consensus process) during Phase One, and paramedic judgement on the need for MTC care measured in Phase Two, will comprise the index tests. The primary reference standard will consist of the Phase One consensus definition of major trauma with the potential to benefit from MTC care. Secondary reference standards will include ISS>15, published consensus-based criterion standards for trauma centre need,[27, 28] and composite clinical outcome (death, ICU admission, urgent intervention or surgery). Under- and over-triage levels will be calculated and the most promising performing candidate triage tool will be identified by an expert panel, PPI and participating trauma networks. The study population, data collection, and analyses are detailed in

5. Phase Two- **Validation Study.**

Phase Three Service Evaluation Study

In Phase Three, the optimal candidate triage tool confirmed in Phase Two, will be implemented in participating trauma networks and a service evaluation conducted. Real life under/over-triage performance against the MATTS reference standard for major trauma will be calculated. Paramedic recognition of patients' eligible for triage and compliance with triage tool decisions will also be observed. The study population, data collection, and analyses are detailed in 6. Phase Three-**Service Evaluation.**

Additional qualitative investigation of the acceptability and usability of the triage tool, and a cost-effectiveness evaluation, will also be conducted as detailed in **Section 6: Phase Three Ancillary sub-studies.**

3. Aims and objectives

The MATTS project aims to develop an accurate, acceptable and usable pre-hospital triage tool to identify patients with major trauma who benefit from MTC care.

Specific objectives are to:

1. Define which patients should receive MTC care through literature review, expert consensus and PPI.
2. Undertake a systematic review and document analysis to identify current major trauma triage tools, and characterise their content and performance.
3. Analyse existing ambulance service and TARN data, conduct focus groups and surveys with clinicians managing major trauma, to identify predictors of under/over-triage.
4. Develop a decision analytic model to investigate the trade-offs between triage tool performance, costs and clinical outcomes.
5. Develop a new triage tool through expert consensus, informed by the preceding information.
6. Prospectively validate the diagnostic accuracy of expert derived and existing major trauma triage tools, and paramedic judgement, using linked ambulance service and augmented TARN data.
7. Identify a candidate triage rule with optimal performance.
8. Evaluate system-level performance of the implemented optimal triage tool, including identification of major trauma cases and compliance.
9. Determine the usability and acceptability of the optimal triage tool.
10. Evaluate the cost-effectiveness of alternative triage tools and future research in this area.

4. Phase One

Identification and Development of Major Trauma Triage Tools

In Phase One, a series of sub-studies will identify existing triage tools and inform the development of a new expert-derived tool for further investigation. No patients are involved in any of these sub-studies and no new patient data will be collected. Ethical approvals for individual studies involving staff within this work stream will be confirmed separately with the University of Sheffield. Written informed consent will be sought from individual participants where relevant. For completeness, individual Phase One sub-studies are summarised below.

4.1 Systematic review

The performance of triage tools can be considered at 3 levels:

- The relative contribution of constituent variables, including: i) mechanism of injury; ii) physiology; iii) suspected anatomical injury patterns; iv) patient factors (e.g. age, co-morbidities, alcohol); v) paramedic judgement.
- The theoretical diagnostic accuracy of complete tools based on observed pre-hospital data and rigidly applied to all injured patients.
- The real-life performance of implemented tools, accounting for whether a tool was applied, paramedic judgement, and compliance with the indicated tool result.

Recently published, valid, systematic reviews are available which have examined the relative contribution of prehospital physiology and level of consciousness in adults;[29, 30] diagnostic accuracy in adults and children;[15, 31] and real-life performance in adults.[26] There are also older reviews examining paramedic judgement and mechanism of injury.[23, 32] Elderly patients have not previously been considered specifically, but represent an increasingly important sub-group that might be subject to under-triage. A novel systematic review will therefore be performed to characterise the diagnostic accuracy and performance of existing tool in elders. Systematic reviews will be undertaken in accordance with guidelines published by the Centre for Reviews and Dissemination and the Cochrane Screening and Diagnostic Tests Methods Group.[33, 34] The protocol will be registered with the PROSPERO database.

4.2 Document analysis and descriptive synthesis

Different elements and characteristics of existing triage tools will be identified from existing systematic reviews, and those currently in use in UK ambulance services. The broad categories used will be identified (for example injury mechanism, patient characteristics, clinical findings, environmental factors) and the individual criteria used in each tool mapped to each category. The frequency with which each criteria is used will be recorded and a narrative summary constructed comparing and contrasting the different tools in terms of, for example, common features, the range in numbers of categories and criteria used and scoring systems. The findings will be tabulated as a spreadsheet map or graphic to summarise categories and criteria with supporting simple summary statements of the key themes identified by the narrative analysis.

4.3 Retrospective cohort study

A retrospective cohort study will be performed using existing, anonymous, ambulance service and TARN data to identify patient and injury characteristics associated with under/over-triage. The study population will comprise patients presenting with injury to the Severn Trauma network within SWAST in 2017, identified from patient records using diagnostic code and free text filters. Patients with major trauma (ISS>15) will be identified during the same time period from the TARN database. A matched dataset will be then be created by deterministic data linkage based on unique ambulance service identifiers. No patient-identifiable data will be used. Data will be analysed using descriptive statistics, focusing on the characteristics of false negative cases not transported to non-MTCs, and false positive cases incorrectly bypassed to MTCs. Multivariable analysis, with logistic regression or classification and regression trees, will then be used to identify which variables are independent predictors of major trauma. The findings of this sub-study will be presented to the expert advisory group and will inform development of a new consensus triage tool.

4.4 Clinician focus groups and surveys

The usefulness, or not, of trauma triage tools may be influenced by factors that are not identifiable by quantitative analyses of tool components. To supplement the quantitative analyses we will therefore also conduct an exploratory study with pre-hospital and hospital clinicians to capture their views on existing tools and how they think they might be improved. This will aim to use first-hand experience to identify any key issues that can be fed in to the consensus development work.

Several focus groups will be conducted, across different participating ambulance services, with 10-15 clinicians recruited in each. The sample will include paramedics, TU clinicians and MTC doctors. Focus groups will be conducted using a topic guide that initially focusses on eliciting views of the trauma triage tool in use but then broadens to explore wider issues that may be associated with on-scene triage decisions and which may need to be considered in the design of a new tool. Focus group proceedings will be digitally recorded and supplemented with hand written notes. Audio recordings will be transcribed verbatim by the approved University of Sheffield, SchARR transcribing service, in line with GDPR legislation. Transcriptions will be analysed using a simple framework analysis approach. Short summaries of key themes will be constructed and collated as a table suitable for use in the consensus development work.

Surveys will be distributed to clinicians as both paper and online forms and will cover the same topics as those included for the focus groups, but allow us to target a wider audience. Paper copies of the surveys will be distributed at conferences associated with EMS or trauma services, and the online survey link will be disseminated to trauma networks and relevant EMS organisations (via email/twitter/study website). The data will be entered into a spreadsheet and then analysed using a simple framework analysis approach. Short summaries of key themes will be constructed and collated as a table suitable for use in the consensus development work.

4.5 Decision analytical modelling

A decision analytic model will be developed to explore important features of different triage strategies. The model structure will be determined after conceptual modelling, literature review and in conjunction with clinical experts. Key events may include triage decisions, time to resuscitation, secondary transfer and definitive care, hospital management, and major trauma-related death and disability.

A population of individuals' representative of patients attended by EMS following injury will be investigated. A priori subgroups of interest will include children and elderly patients; isolated traumatic brain injury versus non-brain injury; and blunt versus penetrating trauma. Model inputs will be informed by literature reviews, and routine official data sources at low risk of systematic error. Evidence synthesis will be performed according to best practice when required.[63] Where relevant and unbiased published evidence is unavailable, expert opinion will be formally elicited.[64]

Model analysis will focus on exploring key determinants of clinical effectiveness (QALYs, deaths, severe disability and patient distribution within trauma networks). Triage tool accuracy estimates will be varied experimentally to investigate the trade-offs in under-/over-triage from increasing sensitivity and lowering specificity, and vice-versa. Multiple sensitivity analyses will subsequently be performed to identify the optimum target cut-points for sensitivity and specificity. Sensitivity analyses will explore which sub-groups of major trauma will accrue the most benefit from MTC care, based on specific patient or injury characteristics, or mortality risk. Together, this information will provide the expert consensus process with important information to define an appropriate reference standard and inform triage tool content.

4.6 Expert consensus process

4.6.1 Expert consensus derived reference standard

A reference standard will be developed through expert consensus, defining which patients should receive MTC care. This will be informed by preceding Phase One sub-study findings. Together, this information will be presented to a purposive sample of major trauma clinicians and policy stakeholders during a one-day face-to-face workshop. A consensus technique (e.g. nominal group technique, RAND/UCLA method, or facilitated roundtable meeting), appropriate to the decision problem and emerging data, will then be used to define a reference standard against which triage tools will subsequently be tested.[35] The meeting will be chaired by an independent and experienced facilitator/ researcher and will follow recommended principles for best practice in developing consensus. A PPI consultation will also be undertaken to ensure the reference standard aligns with patient values.

4.6.2 Expert consensus derived triage tool

The culmination of Phase One is the development of a new major trauma triage tool, designed to select patients who should receive MTC care, through expert consensus. Evidence from the systematic review, decision analytical modelling, clinician focus groups and retrospective cohort study will be presented to the expert panel at a second face-to-face workshop. Predictors of major trauma and the diagnostic accuracy of existing triage tools will be emphasised. The trade-offs in costs and outcomes between over- and under-triage, and optimal thresholds for triage tool sensitivity and specificity, will also be highlighted. Appropriate consensus methods, as described above, will be used to confirm the content of a new triage tool. This may incorporate criteria or modifications for different ages (e.g. children v elderly), settings (e.g. urban v rural), and types of trauma (e.g. blunt v penetrating).

5. Phase Two

5.1 Validation Study

The Phase Two validation study is a prospective diagnostic accuracy cohort study. Major trauma triage tools identified and developed in Phase One will be validated using linked EMS and hospital data.

Setting and study population

The MATTS Phase Two validation source population will be a single major trauma network, within each participating ambulance service:

- West Midlands Ambulance Service (WMAS)
- Yorkshire Ambulance Service (YAS)
- London Ambulance Service (LAS)
- South Western Ambulance Service (SWAST)

Patients of any age will be included in analyses if attended following injury by EMS within a participating regional Trauma Network. Patients transported to participating hospitals from non-study EMS, transported to out-of-area hospitals by participating EMS, or where record linkage would not be possible will be excluded. Patients from mass-casualty major incidents will also be excluded as special, non-standard, triage strategies are necessary in these scenarios. A census sample of consecutive patients will be enrolled over 4 months from WMAS, YAS, and SWAST in Phase Two; to allow achievable data collection from paper based records a representative cohort will be enrolled from the participating LAS Major Trauma Network using random sampling.

Collaborating EMS include a diverse range of settings and it will therefore be possible to investigate the influence of differing contexts on triage tool performance, for example, varying rates of blunt versus penetrating trauma and shorter versus longer transport times.

Identification of injured patients

Patients presenting with injury to ambulance services where major trauma could be expected will be identified from YAS, WMAS and SWAST electronic patient administrative systems, including computer aided dispatch records and patient report forms. Diagnostic codes for injury will be used where possible, with additional electronic searching of free text filters. Manual review of patient records will be performed in equivocal cases. LAS uses paper PRFs which are scanned with computerised extraction of basic demographic and clinical data. Identification of patients with injury in LAS will be performed by electronic searching for injury codes supplemented by direct review of paper records. To evaluate the completeness of patient identification a sub-sample of unfiltered records will be scrutinised by hand to detect the proportion of any missed cases.

Consent procedures

In Phase Two, routinely collected anonymised data will be used to score triage tools and patient care will be unaffected. We will therefore not seek individual participant consent, but will confirm approval from the HRA Confidentiality Advisory Group (CAG) and a NHS REC to link and analyse de-identified anonymised linked data.

Data collection - Index test / triage tool variables and decisions

Anonymised demographic, clinical and injury information will be collated from EMS electronic PRFs. Results of currently used triage tools (i.e. whether the currently used triage tool 'triggered') and hospital destination will also be collected. LAS paper PRFs are scanned with computerised extraction of basic demographic and clinical data; additional patient data, not extracted by scanning, will be abstracted manually by research paramedics. Collated EMS data will then be coded to score whether triage tools are positive or negative and allow calculation of under-/overtriage against the reference standard described below.

Data collection - reference standard / major trauma classification

The presence of major trauma in patients conveyed to hospital by EMS following injury will be determined by a comprehensive case finding process performed in conjunction with the English national trauma registry, TARN.

The TARN database collects information on patients with major injuries presenting to all trauma receiving hospitals in England. Patients are included in the TARN database if they sustain injury resulting in any of: hospital admission for >72 hours; critical care or high dependency unit admission; transfer for specialist care; or death. Patients with, simple isolated injuries (e.g. radius fracture), pubic rami or femoral neck fractures and aged over 65, pre-hospital deaths, or diagnosed as dead on emergency department arrival with no further management instigated, are excluded. The TARN registry therefore aims to include all patients requiring substantial treatment for non-trivial injuries sustained from meaningful trauma. During MATTS Phase One a definition of major trauma that will benefit from MTC care will be developed by expert consensus, which may differ from TARN inclusion criteria. Furthermore, TARN's current criteria do not include pre-hospital deaths and may miss rapidly discharged patients e.g. penetrating thoracic trauma in young patients. To meet this challenge, additional training will be provided to TARN data coordinators in participating hospitals on the MATTS major trauma case definition; research paramedics will offer additional support in applying this definition.

Admissible patients are identified by data coordinators in member hospitals. TARN standards of practice recommend that ED information technology systems and hospital patient administration systems are checked regularly to identify eligible patients based on recorded clinical information, diagnostic codes and discharge dates. To capture secondary transfers, screening of intensive care units, and orthopaedic, plastic surgery, paediatrics and other trauma speciality admissions is dictated. Individual hospitals may also employ additional ad hoc procedures for case recognition. Cases potentially eligible for TARN inclusion are subsequently confirmed by examination of clinical case notes. There may be incomplete major trauma case ascertainment into the TARN database. This is a particular concern for patients transported to non-MTCs. We will develop a comprehensive case-finding process, building on existing TARN practices, to identify incident cases of major trauma, including ambulance service and hospital patient administration systems. MATTS research paramedics will perform this process in all study hospitals; in conjunction with, and supporting, existing TARN data coordinators. We will also triangulate TARN submissions with HES data and local trauma registries (e.g. North West London trauma registry) to ensure complete enrolment of major trauma cases.

TARN data collectors in member hospitals collate demographic, injury, treatment, investigation, and outcome data for eligible patients. Data are gathered from all relevant patient records including ambulance records, radiology reports, post mortem reports, hospital notes, trauma sheets, operative notes, discharge summaries and clinical

information technology systems. Information is submitted to the trauma registry by a web based electronic Data Collection and Reporting system. Auto-generated unique submission numbers, field limiters, range limiters, drop lists and radio buttons are utilised to reduce input errors. MATTS research paramedics will support existing TARN data coordinators collating these data.

Completion of a core dataset including details of patient demographics, incident information, EMS identifiers, attendants, key observations, important clinical interventions injury descriptions and outcome is mandatory. An extended data-set is accessible including information on clinical assessment, transfers and specific treatments in the field, ED, ward and critical care.

Independent, trained, TARN injury coders centrally grade individual injuries for each case according to AIS (2008 revision) criteria based on clinical, radiological and post mortem information, and a subsequent ISS is assigned.[36] Only definite injuries are considered with possible, probable or suspected injuries excluded. All submissions are checked centrally for consistency with TARN inclusion criteria and completeness of the core data-set. Additional information may be requested from hospitals prior to final approval of each submission. Major trauma cases often undergo inter-hospital transfer during their patient journey and separate submissions for individual patients from separate hospitals are automatically linked where possible using incident date, date of birth, age, gender and patient name. Potential transfer matches are manually checked and linked by central TARN data validators who ensure that key fields such as demographics, pre-hospital details and injuries are consistent. Multiple submissions are linked to form a single unique case.

A TARN procedures manual provides standards of practice, defines data fields and provides guidance on electronic data entry. All data collectors in member hospitals receive initial and refresher training, including an overview of TARN structures, reporting facilities, trauma outcome process statistics and how to enter data into the web based collection system. Case ascertainment in member hospital is checked against HES data and is physically audited every five years by examination of hospital records.[34] Hospitals undergo additional audit every two to five years examining coding, data ranges and inconsistencies. Quality assurance is also performed on central AIS coding with a 1% sample of cases extracted and re-coded each month to test reproducibility.

Data linkage

Data linkage between a) MATTS major trauma cases collected by TARN, and b) EMS identified patients with injuries and will initially be conducted deterministically based on ambulance service unique identifiers (e.g. incident, CAD and call sign numbers), tailored to the context of each ambulance service. In cases where deterministic record linkage is not possible, a probabilistic TARN algorithm based on patient demographics, hospital destination, and incident date/time will be used. Unmatched major trauma cases where a confident match is not possible will be examined by hand and if a confident match cannot be made will be excluded. Matched major trauma patients will represent triage tool true positives and true negative cases. Data linkage will be performed without direct patient identifiers e.g. name, date of birth, address, and any indirect patient identifiers will be removed from the data set after successful linkage has taken place.

Any included EMS identified patients with injuries who are not identified as having major trauma, will be classified as reference standard negative, and will therefore not undergo any data linkage. These patients will represent false positive and true negative cases. We will

perform a detailed case note review by hand for a random sample of these cases to ensure we are not missing a significant number of major trauma cases.

Data handling and record keeping

The collaborating Ambulance Services and TARN will both check their data for any patients who have registered for the NHS 'National data opt-out', and remove any patients as necessary before the transfer of data. Non-identifiable EMS and TARN data will then be transferred to the University of Sheffield by secure NHS/University email accounts using encrypted, password protected, data files.

This information will then be entered into a secure University of Sheffield database. The CTRU, Study Manager, research assistant and the Data Management Team will work with research paramedics to ensure the quality of data provided. Validation reports will be run regularly to check the study data for completeness, accuracy and consistency. Discrepancies will be generated and managed to resolution. Data monitoring and audit will be conducted in accordance with the University of Sheffield CTRU SOP QU001 and DM009.

Patient identifiable data (names, date of birth, and contact details) will not be collected or stored. The study manager, data managers, CI, research paramedics and administrators will have access to anonymised data on the study database, through the use of usernames and encrypted passwords. The Sponsor will permit monitoring and audits by the relevant authorities, including the Research Ethics Committee. The CI will also allow monitoring and audits by these bodies and the Sponsor, providing direct access to source data and all study documentation. All data will be collected and retained in accordance with the Data Protection Act 1998, European Union General Data Protection Regulations (GDPR) 2018, HRA Confidentiality Approval Group (CAG) approvals, and University of Sheffield CTRU SOPs. Output for analysis will be generated in a format and at intervals to be agreed between Sheffield CTRU and the CI.

Sample size calculation

TARN/EMS data suggests approximately 200 major trauma cases (ISS>15) per 4 months per trauma network. Assuming a target sensitivity of 95% as per American College of Surgeons Committee on Trauma (ASCOT) guidance, the total of 800 reference standard positive cases would give a 95% confidence interval coverage of 2% for sensitivity. EMS data suggests approximately 25,000 patients presenting with injury over 4 months per trauma network (total 100,000 across all 4 of the participating trauma networks). Assuming a target specificity of 70% as per ASCOT guidance, coding 2000 reference standard negative cases (sampling fraction of 2%) would give a 95%CI coverage of 2% for specificity. The total sample size of 2,800 cases would equate to an approximate total of 700 patients (200 major trauma cases and 500 non-major trauma cases) per network. This should be a manageable work load for research paramedics (approximately 9 cases to code per working day), while providing sufficient statistical power.

Statistical analyses

Full details of planned analyses will be contained in a specific statistical analysis plan (SAP), which will conform to Sheffield CTRU SOP ST001. Sample derivation and data linkages will be presented with a STROBE flow diagram.

The Phase Two validation study will be conducted, reported and presented according to the latest STARD 2015 guidelines for diagnostic accuracy studies.[37, 38] Under-triage is defined as the proportion of patients who could benefit from specialist care not transported to a

MTC, this corresponds to $1 - \text{sensitivity}$. Over-triage is defined as the proportion of patients incorrectly transported to the MTC, this corresponds to $1 - \text{specificity}$. We will summarise the baseline demographic and clinical characteristics of participants with appropriate summary statistics. The primary analysis will examine the protocol-based diagnostic accuracy of triage tools based on recorded EMS data, regardless of actual hospital destination using the primary reference standard. Under/over-triage, sensitivity, specificity, predictive values, and c-statistics with their 95% confidence intervals (95% CI), will be calculated for all included index tests. Differences in test performance will be tested using De Long's method for comparing c-statistics.

A secondary analysis will similarly evaluate the actual performance of triage tools currently used in participating trauma networks according to transport destination. Sensitivity analyses will be performed to explore the influence of missing data (including multiple imputation and scenario analyses where appropriate) and different gold standards (secondary reference standards e.g. $\text{ISS} > 15$). Pre-specified sub-group analyses will include children (<16 years) and elderly patients (≥ 65 years); urban versus rural environments; and blunt versus penetrating trauma. Results of the Phase Two validation study will be presented to the expert advisory, participating trauma networks and PPI groups, and an optimally performing candidate triage tool chosen for refinement, implementation, and further investigation in the Phase Three service evaluation study.

Safety reporting

In the MATTS Phase Two validation study, routinely collected anonymised data will be used to remotely score non-operational triage tools and patient care will be unaffected. Safety reporting is therefore not relevant.

6. Phase Three

6.1 Service Evaluation Study

The Phase 3 Service Evaluation will assess the real-life operational performance of the candidate triage tool, selected at the end of Phase Two, based on actual transport destinations.

Study setting and population

In Phase Three the most optimally performing candidate triage tool, determined from Phase Two, will be voluntarily implemented operationally in a major trauma network within each ambulance service. System-level accuracy, compliance, and usability will be evaluated. Consecutive patients of any age will be included if attended by EMS following injury over the 6 month study period. Patients transported to participating trauma networks from non-study EMS, transported to out-of-area hospitals, or where record linkage would not be possible will again be excluded. Patients from mass-casualty major incidents will again be excluded.

Implementation of the candidate triage tool

Introduction of the candidate triage tool will be conducted in partnership with participating trauma networks. Training will be provided to all relevant ambulance service staff using standard methods for implementing protocol changes within ambulance services (e.g. face-to-face sessions or on-line teaching packages). Major Trauma Centres and Trauma Units will be informed of changes to pre-hospital triage tools in advance.

Identification of injured patients and data collection

EMS and hospital data collection will be performed as described for Phase Two.

Data linkage, handling and record keeping

Data linkage, data handling and record keeping will be performed as described for Phase Two.

Consent procedures

In Phase Three an optimal candidate trauma triage tool will be selected by trauma networks for implementation. A service evaluation will subsequently be performed using routinely collected data to evaluate real life performance and compliance. As no additional data will be collected, and the triage tool will be applied to all patients presenting with injury, we will not obtain individual patient consent, but we will seek ethical approval from an NHS research ethics committee and CAG to analyse anonymised linked data.

Sample size calculation

Participating ambulance services estimate 150,000 calls for injury per 6 months across the included trauma networks, with TARN data suggesting that approximately 1,200 of these cases represent major trauma (ISS>15). Assuming, based on ASCOT criteria, a triage tool requires sensitivity of 95%, this sample size would provide a 95% confidence interval coverage of $\pm 1.0\%$ for the under-triage rate. Assuming a target specificity of 70% as per

ASCOT guidance, coding 3000 reference standard negative cases (sampling fraction of 2%) would give a 95% confidence interval coverage of $\pm 1.5\%$ for the over-triage rate.

Statistical analyses

The implemented triage tool will be scored using observed data, the presence of a trauma pre-alert recorded, and the actual transport destination collected. Compliance and real life performance of the implemented triage tool will subsequently be assessed. The reference standard will be the MATTS expert consensus definition of trauma with the potential to benefit from MTC care. Under/over-triage, sensitivity, specificity, predictive values, and c-statistics with their 95% confidence intervals (95% CI), will be calculated. The compliance of paramedic transport decisions with triage protocol results will be examined as a proportion with 95% CI. A priori sub-group analyses will examine tool performance in children and the elderly; and in penetrating and urban injury victims.

Safety reporting

In the MATTS Phase Three service evaluation study an optimal candidate triage tool will be voluntarily implemented by participating trauma networks. Adverse changes in the health of patients will be defined, monitored, recorded and reported according to CTRU SOP PM004 and Health Research Authority guidance for non-CTIMP studies. Adverse events (AEs) and serious adverse events (SAEs) related to major trauma triage will be recorded and reported. Table 1 details the definitions used.

Identification

Adverse health changes will be identified by paramedics during implementation of the triage tool and by research paramedics' review of EMS and hospital records. AEs will also be detected through review of ambulance service, hospital and trauma network incident reporting processes. Furthermore local investigators will report any additionally identified adverse health changes.

Management

All adverse health changes will be assessed for severity by an appropriately qualified member of the MATTS research team, or local clinician. It is their responsibility to review all documentation (e.g. patient records, laboratory and diagnostic reports) related to the event and determine seriousness according to the definitions stated in Table 1.

By definition, major trauma is a life threatening illness that will result in hospitalisation, disability, or incapacity, and these outcomes will therefore not be classified as SAEs.

If an AE is classed as non-serious, these will be recorded by the MATTS research team, and reported on aggregate to CTRU on a monthly basis.

If the AE is classed as serious, an SAE report form must be completed by the MATTS research team and sent to the CTRU within 24 hours of its discovery. The CI will then review causality, and expectedness to determine whether the SAE is related and/or is unexpected. Additional information may be requested from local research team members, research site staff, or GP, at a later date.

Documentation

SAE's deemed unrelated to the triage tool or study procedures will be recorded in the TMF only, and no further action will be taken.

All identified related SAE's will be documented in the participant's source medical records (if relevant) and entered into the study database, and followed up until resolution. A SAE form will be completed for each identified SAE and signed by the CI. This will be kept in the study

master file and a copy sent to the research site for filing in the investigator site file. If further information is obtained at a later date regarding a SAE, the SAE report form will be updated.

Reporting

Reporting requirements are dependent on the seriousness of the adverse health change and categorisation as expected or unexpected:

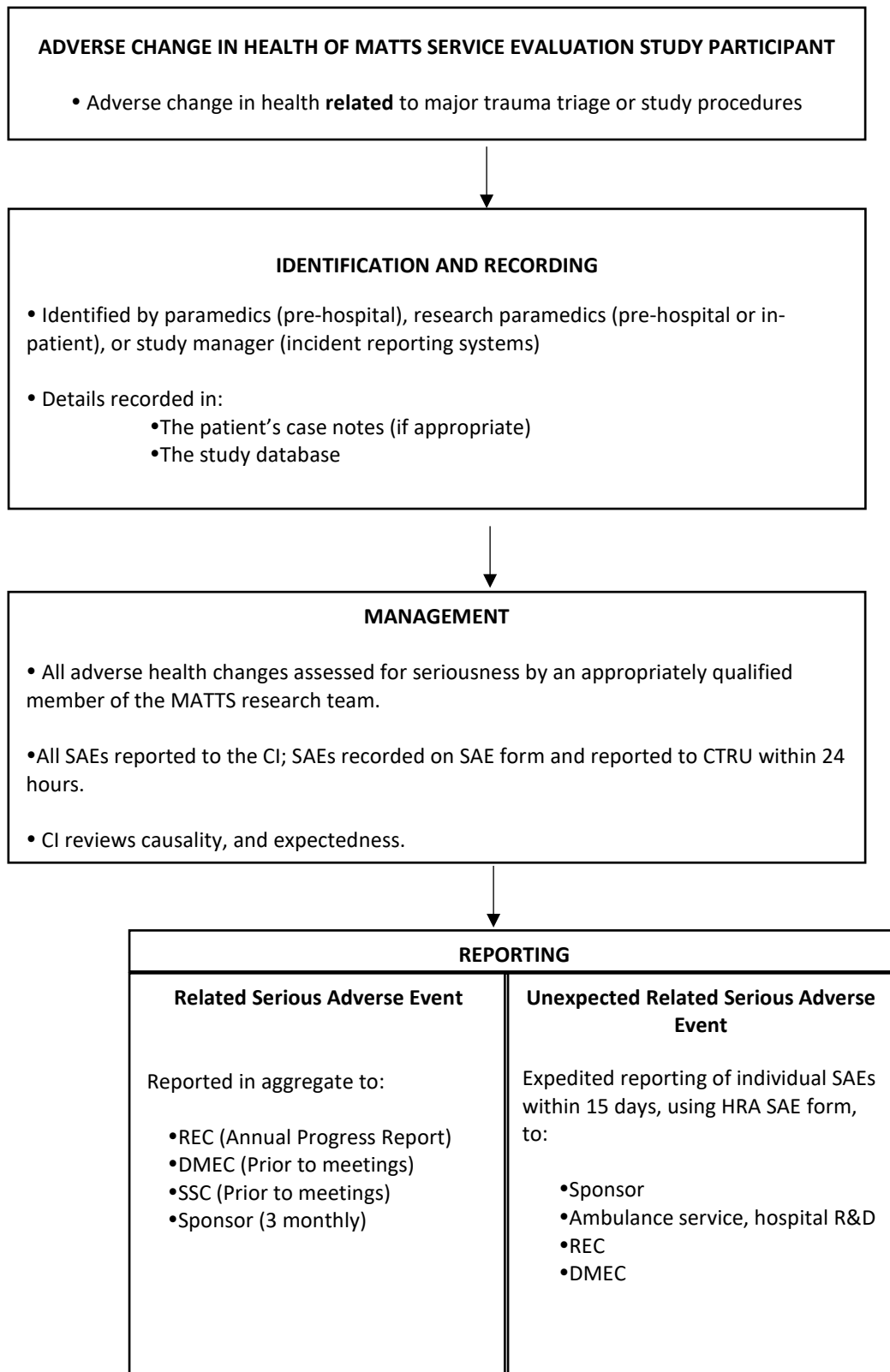
- Related expected SAEs, will be reported in aggregate to the PMG, SSC and DMEC prior to each meeting; to the sponsor every 3 months; and to the REC in the Annual Progress Report. Expected SAEs will include: false negative and false positive triage tool results; changes in clinical status during prehospital transportation; expected disease progression (e.g. deteriorating level of consciousness following traumatic brain injury); normal symptoms of underlying injury (e.g. pain, bleeding, nausea); or death and disability from underlying major trauma unrelated to the MATTS triage tool.
- Unexpected SAEs related to the triage tool or study procedures require expedited reporting. The trial manager will inform the sponsor and relevant NHS R&D department; trauma network and will also inform the REC and DMEC within 15 days of notification using the Health Research Authority (HRA) serious adverse event form.

Figure 3 summarises the safety reporting procedures. SAE data will be reported to the trial governance groups and the Sponsor as aggregated data periodically. This will be monitored at management meetings and, if required, action in regards to safety will be decided. A DMEC will also monitor adverse event data and make recommendations to the Study Steering Committee (SSC) on whether there are any ethical or safety reasons why the study should not continue.

Adverse Health Change Terminology*	Definition
Seriousness	
Adverse Event (AE)	An adverse change in health that occurs while a patient is taking part in a study
Serious Adverse Event (SAE)	Any adverse event occurring while a patient is taking part in a study, that results in: <ul style="list-style-type: none"> • Death • Prolongation of Hospitalisation • Other significant medical event
Causality	
Unrelated	An adverse change in health that occurs while a patient is taking part in a study which is not caused by or related to study interventions or procedures.
Related	An adverse change in health that occurs while a patient is taking part in a study, which is caused by or related to study interventions. An AE or SAE is considered related if the relationship between the event and trial treatments is: <ul style="list-style-type: none"> • Possible - There is some evidence to suggest a causal relationship. However, the influence of other factors may have contributed to the event (e.g. the participant’s clinical condition, other concomitant treatments). • Probable - There is evidence to suggest a causal relationship and the influence of other factors is unlikely, or • Definite - There is clear evidence to suggest a causal relationship and other possible contributing factors can be ruled out.
Expectedness	
Unexpected	Any adverse health change that is NOT consistent with the known and expected adverse events of trial treatments i.e. it is not listed in the protocol or related documents/literature as an expected occurrence.
Expected	Any adverse health change that IS consistent with the known and expected adverse events of study interventions.
Severity*	
Mild	An adverse health change that does not interfere with routine activities
Moderate	An adverse health change that interferes with routine activities
Severe	An adverse health change that makes it impossible to perform routine activities

Table 1. Classification of adverse events *The term ‘severity’, is used to describe the intensity, and should not be confused with ‘serious’ which is based on participant/event outcome or action criteria. For example, a headache may be severe but not serious, while a minor stroke is serious but may not be severe.

Figure 3. Flow chart detailing safety reporting procedures for the MATTS study



6.2. Phase Three - Ancillary Sub-Studies

6.2.1 Cost Effectiveness Evaluation

Background

A decision analytical model will be developed during Phase One of the MATTS project to inform the expert consensus process in defining an appropriate reference standard and developing a clinically and cost-effective new triage tool. In Phase Three, an economic evaluation will be performed to evaluate the costs incurred and expected benefits of a fully implemented new national major trauma triage tool strategy, compared to other triage tools/strategies. The overall aim is to structure and parameterise a model that reflects the costs and consequences of different pre-hospital triage strategies in patients with major trauma.

Decision problem and Model scope

The scope of the decision model is informed by the decision problem specified in the HTA commissioning brief and the base case principles for economic evaluations outlined in the NICE Guide to the Methods of Technology Appraisal.[39] The model setting will be an English major trauma network. Any triage tool strategy that could be feasibly be implemented in the NHS will be considered. The model will take the perspective of the English NHS, and thus include direct medical costs and costs arising from personal and social services. As major trauma may result in death or long term disability, costs and consequences will be examined over a life-time horizon. In line with the NICE reference case productivity losses, costs to patients and families, and resource use in non-health sectors will not be considered.

Model structure and study population

An individual patient simulation will be developed to estimate the clinical and cost-effectiveness of different pre-hospital major trauma triage strategies.[40] A patient level model was chosen over a cohort model to fully explore sub-groups and non-linearity in results arising from heterogeneous major trauma populations. The precise model structure will be determined after conceptual modelling, literature review and in conjunction with clinical experts. Key events may include triage decisions, secondary transfer and definitive care, hospital management, and major trauma-related death and disability. A base-case population of individuals representative of patients attended by EMS following injury will be investigated. Patient characteristics will be determined by representative data sources e.g. existing ambulance service and TARN data. A priori subgroups of interest will include children and elderly patients; isolated traumatic brain injury versus non-brain injury; and blunt versus penetrating trauma.

Model parameterisation

Model inputs will be informed by literature reviews, routine official data sources at low risk of systematic error, and prospective MATTS data. Evidence synthesis will be performed according to best practice when required.[41] Where relevant and unbiased published evidence is unavailable, expert opinion will be formally elicited.[42] Each model input will be assigned an average or most likely value, and a probability distribution representing a credible range and the relative likelihood of possible values for the uncertainty in this estimate defined. Distributional choices will be chosen based on theoretical considerations, logical constraints, and the parameter estimation process. Where the data exists, correlation between model inputs, costs and outcomes will be accounted for using appropriate co-

variances. Outcomes will include death, disability and quality-adjusted life years (QALYs) accrued by each triage tool strategy. Costs for EMS management, initial hospital assessment and ongoing hospital management will be estimated using NHS reference costs. Appropriate rehabilitation and long term care costs will also be assigned.

Model implementation and analysis

Simul8 software (Simul8 Corporation, Boston, USA) will be used to track the progression of heterogeneous patients with the accumulating history of each individual determining: the probability of, and time to, events; costs; and health outcomes. Internal testing will be performed throughout model development to ensure that mathematical calculations accurately represent model specifications and are correctly implemented. Debugging techniques will include: null and extreme input values; setting equal values across strategies; fixed distributions; and code breaks with line by line checking of syntax. The model will be also be independently verified by a second modeller. Model validation will be performed by comparing model outputs with published estimates from the literature.[40]

Outcomes

The main outcome measure for the Phase 3 economic modelling is the incremental cost-effectiveness ratio (ICER) for each triage tool strategy.[40] A full incremental analysis will be conducted comparing the new implemented triage tool with all other feasible strategies, according to established principles of strong and extended dominance. The ICER will be compared to a maximum acceptable ICER range of £20,000 to £30,000 per QALY gained, in line with decision making processes by NICE.[61] An initial base case deterministic analysis, with parameters fixed at their mean or mostly likely values, will estimate the mean expected costs and QALYs gained per patient for each triage strategy. In order to account for the uncertainty in model inputs and non-linearity within the model a base case probabilistic sensitivity analysis (PSA) will also be conducted using Monte Carlo simulation to randomly sample from the inverse cumulative distribution function of each model parameter's probability density function.[43] Mean ICERs for each management strategy, calculated from the average expected costs and effects over all model runs, will be recalculated and compared with cost-effectiveness thresholds to inform adoption decisions.

Model uncertainty due to variability, heterogeneity, parameter uncertainty and structural uncertainty will be fully explored in sensitivity analyses. Investigation of variability arising from random differences between individuals with similar characteristics is facilitated by the individual patient sampling design. Heterogeneity will be examined in the pre-specified subgroup analyses. Univariate, threshold and scenario sensitivity analyses will be performed on model parameters thought to be important or uncertain. Structural uncertainty in methodological choices and assumptions (e.g. varying the discount rates for costs and effects) will also be also examined. The exact sensitivity analyses will be formulated post hoc informed by input from an expert clinical group, model structuring, evidence synthesis and emerging results.

Value of information analysis will also be conducted to examine if further research into the cost-effectiveness of the strategies is an efficient use of resources from the health care system perspective, and determine the overall gain associated with: removing all uncertainty from the decision problem (Expected Value of Perfect Information); removing all uncertainty from a subset of parameters (Expected Value of Partial Perfect Information); and if these values are sufficiently large, the expected value of conducting future research assuming finite sized trials (Expected Value of Sample Information).[44] The exact focus of such analyses would be determined during the research but candidate studies could include a cluster-randomised trial of new versus existing triage tools, or the collection of further evidence to validate the adoption decision advocated by current evidence.

6.2.2 Acceptability and usability of implemented triage tool

The acceptability and usability of the triage tool implemented in the Phase Three service evaluation study will be investigated using mixed qualitative and quantitative methods.[45] Barriers to triage tool implementation, and targets to improve future performance, will also be identified. Three approaches will be used:

- **Trauma triage tool use:** An important question is, of all eligible trauma patients, in how many cases was the tool used? To assess this we will measure what proportion of eligible patients (identified using the MATTS expert consensus definition) were recorded as assessed using the trauma triage tool in the ambulance service records in each study area. Overall and individual service rates will be calculated to establish if there are any between service differences. For cases identified as eligible but where the tool was not applied we will conduct descriptive analyses of patient, incident type and injury variables to assess if there are any common characteristics which may help further refine the tool.
- **Online Survey:** We will conduct an electronic survey of all participating clinicians using the tool in Phase Three to elicit their views on the usefulness and practical application of the tool.[46] Study information will be provided at the beginning of the survey and informed consent for completion and data collection obtained. A questionnaire will be designed using open and closed questions to explore factors including ease of use; relevance of criteria; confidence in decisions; improvement in function compared to previous tools; redundant or missing criteria; design or content issues that could further improve the tool. Closed questions with multiple choice answers will be coded and analysed using descriptive statistics. Frequencies of responses will be tabulated and presented as aggregated data for all services combined and individual services. Open questions using free text responses will be transcribed in to tables and data scrutinised to identify within and between question themes to identify which elements of the tool worked well, and which could be improved with further refinement. The findings of the survey will be triangulated with the themes identified during the Phase One clinician focus groups to map whether potential barriers and facilitators have been adequately addressed or if there are still unresolved issues that require further work.[47]
- **Dissemination and development workshop:** We will conduct a workshop with a range of stakeholders including clinicians (pre-hospital and hospital), patients, commissioners, service providers, senior NHS management and policy makers. The results of the Phase Two and Phase Three will be presented and will summarise what has worked well and where there are still potential gaps in successful implementation. We will then facilitate a structured discussion of the findings and explore issues of acceptability, usefulness and suggestions for further improvement from different stakeholder perspectives.[48] Outputs from these discussions will be presented by each group to all participants and collated as themes. Where potential areas for improvement are identified a consensus decision will be sought on importance and priority for subsequent further development. The findings from each of these activities will be collated and developed in to a practical “toolkit” to support further implementation of the trauma triage tool in other services if the tool is established as a viable alternative to existing tools.

7. Study supervision

Study Steering Committee

A Study Steering Committee will be convened during study set up. This group will provide overall supervision of the MATTS project in general, and the Phase 2 validation and Phase 3 service evaluation studies specifically, on behalf of the trial sponsor (University of Sheffield) and funder (National Institute of Health Research, NIHR). The SSC will ensure that the study is conducted according to principles of Good Clinical Practice (GCP), with specific tasks including:

- Approval of the study protocol
- Review of study progress
- Monitoring adherence to study protocol
- Ensuring patient safety
- Consideration of new information relevant to the research question
- Scrutiny of protocol amendments and extension requests
- Recommend appropriate actions such as changes to the protocol, additional patient information, stopping or extending the study.

The composition of the SSC is detailed in Table 3. The SSC will receive information from the Project Management Group and the DMEC. SSC meetings will be convened by the CI approximately annually. Representatives of the trial sponsor and funder may also be invited to participate. The SSC chairperson will provide advice to the CI, sponsor (University of Sheffield), host institutions (Ambulance services and trauma networks), and funder (NIHR). The SSC will have the power to prematurely close the study if necessary due to safety concerns, futility, or lack of convincing clinical effectiveness.

Table 3. Composition of Study Steering Committee

SSC roles	DMEC roles
<p>Members: Independent chair Lay representative Independent statistician Independent paramedic Independent clinician Chief Investigators</p>	<p>Members: Independent chair Independent clinician Independent statistician</p>

Project Management Group

A Project Management Group (PMG) will oversee day-to-day management of the MATTS validation and service evaluation studies, in accordance with CTRU SOP GOV001. Specific roles will include:

- Ensuring adherence with the study protocol
- Ensuring ethical and GCP standards are met
- Monitoring data quality
- Developing and reviewing paperwork
- Responding to queries from the host institutions

- Developing the study protocol in response to operational challenges
- Review of results
- Dissemination of study findings

The PMG will comprise the CI, study manager, co-investigators, trial statistician, research paramedics, ambulance service Research and Development, paramedic, data manager and lay representatives. The PMG will meet frequently during trial set up and approximately quarterly thereafter.

Data Monitoring and Ethics Committee

An independent DMEC will be organised during the study set up period in accordance with CTRU SOPs. The DMEC will review emerging data and adverse event reports and will ensure that the safety, rights and well-being of study participants are upheld throughout the study. Specific roles will include:

- Approval of the study protocol
- Review and approval of the SAP
- Evaluate interim data
- Review data collection, data linkage, and loss to follow up rates
- Consider emerging evidence from relevant studies
- Advise the SSC on whether there are any ethical or safety reasons why the study should not continue or protocol should be amended
- Advise the SSC on release of interim data

DMEC composition (Table 3) and conduct will be in accordance with CTRU SOP GOV003. An initial meeting will be held prior to the start of the trial and then approximately 6 monthly thereafter. No formal interim analyses are planned.

Patient and Public Involvement (PPI)

A public and patient advisory group will be enlisted for collaboration throughout the study. This group will be consulted on all aspects of study conduct, and help with specific tasks such as developing research materials and dissemination. The CI will liaise and mediate between the advisory group and the trial oversight groups, providing support where needed.

8. Publication and dissemination

The study protocol will be registered with an international research registry (ClinicalTrials.gov) and will be made available in the open access University electronic repository. Results of the study will be disseminated in high profile peer-reviewed scientific journals and relevant academic conferences. Authorship will include funded co-applicants, clinical collaborators, research paramedics and the study manager, according to International Committee of Medical Journal Editors (ICMJE) guidelines.

Details of the study, including regularly updated progress reports, will be available on a dedicated study website hosted by the CTRU. Plain English study progress reports will be provided to collaborators, patient advocacy groups, local PPI panels and our service user advisory group. Study developments will also be communicated through social media including twitter. The lay SMG member and service user advisory group will contribute to writing any scientific publications, particularly plain English summaries and conference presentations.

At the end of the study a report will be submitted to the trial funders with full details of study progress and study findings. It is anticipated that this report will be independently peer reviewed and the final accepted report published as a “gold” open access monograph in the *Health Technology Assessment* journal.

9. Finance

The study is funded by the NIHR Health Technology Assessment Programme (grant number 17/16/04). Details have been drawn up in a separate agreement.

10. Ethics approval

Phase 1 sub-studies, and Phase 3 sub studies on acceptability and usability of implemented triage tool do not involve patients and ethical approval will be confirmed with the University of Sheffield.

Phase 2 and 3 of the study will be conducted subject to a favourable opinion from a Local Research Ethics Committee (LREC), organised through the central National Research Ethics Service allocation system. An approval letter from the ethics committee will be registered with the CTRU before initiation of the study. Local research governance approvals will be sought from all participating research sites via the Health Research Authority (HRA). The study will be conducted in accordance with Good Clinical Practice Guidelines and CTRU SOPs.

11. Regulatory approvals

The MATTS validation and service evaluation studies will be conducted in compliance with a predefined protocol, HRA, CAG and REC approvals, Good Clinical Practice, CTRU SOPs, and the NHS research framework. Local research governance approvals will be sought from all participating research sites.

12. Indemnity / Compensation / Insurance

The MATTS project is sponsored by the University of Sheffield. The University holds insurance covering liabilities arising from negligent harm caused by poor protocol design by the Chief Investigator and researchers employed by the University. The participating ambulance services are covered by NHS indemnity for liabilities arising from clinical negligence, or other negligent harm to individuals taking part in the study where a duty of care is owed.

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