STUDY PROTOCOL

Conservative Management in Traumatic Pneumothoraces in the Emergency Department (CoMiTED): A Randomised Controlled Trial

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This protocol has regard for the HRA guidance

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CONTENTS

GLOSSARY OF ABBREVIATIONS

AE	Adverse Event
AR	Adverse Reaction
BTC	Bristol Trials Centre
CI	Chief Investigator
CONSORT	Consolidated Standards of Reporting Trials
COVID-19	Coronavirus
CRF	Case Report Form
CTIMP	Clinical Trial of an Investigational Medicinal Product
DPA	Data Protection Act
DSA	Data Sharing Agreement
ED	Emergency Department
EEA	European Economic Area
GCP	Good Clinical Practice
GDPR	General Data Protection Regulation
GP	General Practitioner
HEAP	Health Economic Analysis Plan
HRA	Health Research Authority
ICU	Intensive Care Unit
I.D	Identification
ISF	Investigator Site File
ISRCTN	International Standard Randomised Controlled Trials Number
ISS	Injury Severity Score
ITT	Intention to treat
MCA	Mental Capacity Act
NHS	National Health Service
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health and Care Research
PI	Principal Investigator
PIS	Participant Information Sheet
PPE	Personal Protective Equipment
PPI	Patient and Public Involvement
PROMS	Patient reported outcome measures
PSS	Personal social services
QALY	Quality-Adjusted Life Year
RCT	Randomised Controlled Trial
R&D	Research & Development
RDSF	Research Data Storage Facility
REC	Research Ethics Committee
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan

SAR	Serious Adverse Reaction
SD	Standard Deviation
SEAR	Screened, Eligible, Approached, Randomised
SOP	Standard Operating Procedure
SUSAR	Suspected Unexpected Serious Adverse Reaction
TARN	Trauma and Audit Research Network
TERN	Trainee Emergency Medicine Research Network
TMF	Trial Master File
TMG	Trial Management Group
TSC	Trial Steering Committee
UKCRC	UK Clinical Research Collaboration
UoB	University of Bristol

1 STUDY SUMMARY

Title	Conservative Management in Traumatic Pneumothoraces in the Emergency Department (CoMiTED).
Study Location	NHS Hospitals (Emergency Departments [EDs]) in England and Wales.
Study Question	Is initial conservative management of significant traumatic pneumothoraces non-inferior to invasive management in terms of subsequent emergency pleural interventions, complications, pain, breathlessness, and quality of life?
Study Objectives	**a)** To establish if initial conservative management is non-inferior to invasive management regarding subsequent emergency pleural intervention over 30 days (or until death if sooner). **b)** To determine whether conservative management improves health-related quality of life and other patient reported outcomes. **c)** To determine the clinical and cost effectiveness of conservative management versus invasive management of traumatic pneumothoraces by measuring resource use, mortality and costs over the six months following injury. **d)** To assess acceptability of initial conservative management to patients and clinicians.
Study Design	Multicentre, parallel group, individually randomised controlled non-inferiority trial with an internal pilot, economic evaluation and integrated qualitative study.
Main inclusion criteria	• Patients presenting with traumatic pneumothoraces • who are (believed to be) 16 years and over, and • in whom the treating clinician(s) are uncertain if a chest drain is required.
Main exclusion criteria	• Treating clinician(s) believe injuries are incompatible with life • Respiratory arrest • Haemothorax (associated with pneumothorax) requiring a chest drain in the opinion of the treating clinician(s) • Clinical or imaging evidence of tension pneumothorax • Prisoners, and • Retrospective paediatric exclusion if patient confirmed to be less than 16 years.
Planned sample size	750 participants (confirmed to be aged 16 years and over) and approximately 25 patient (participant) interviews at two timepoints for the integrated qualitative study.

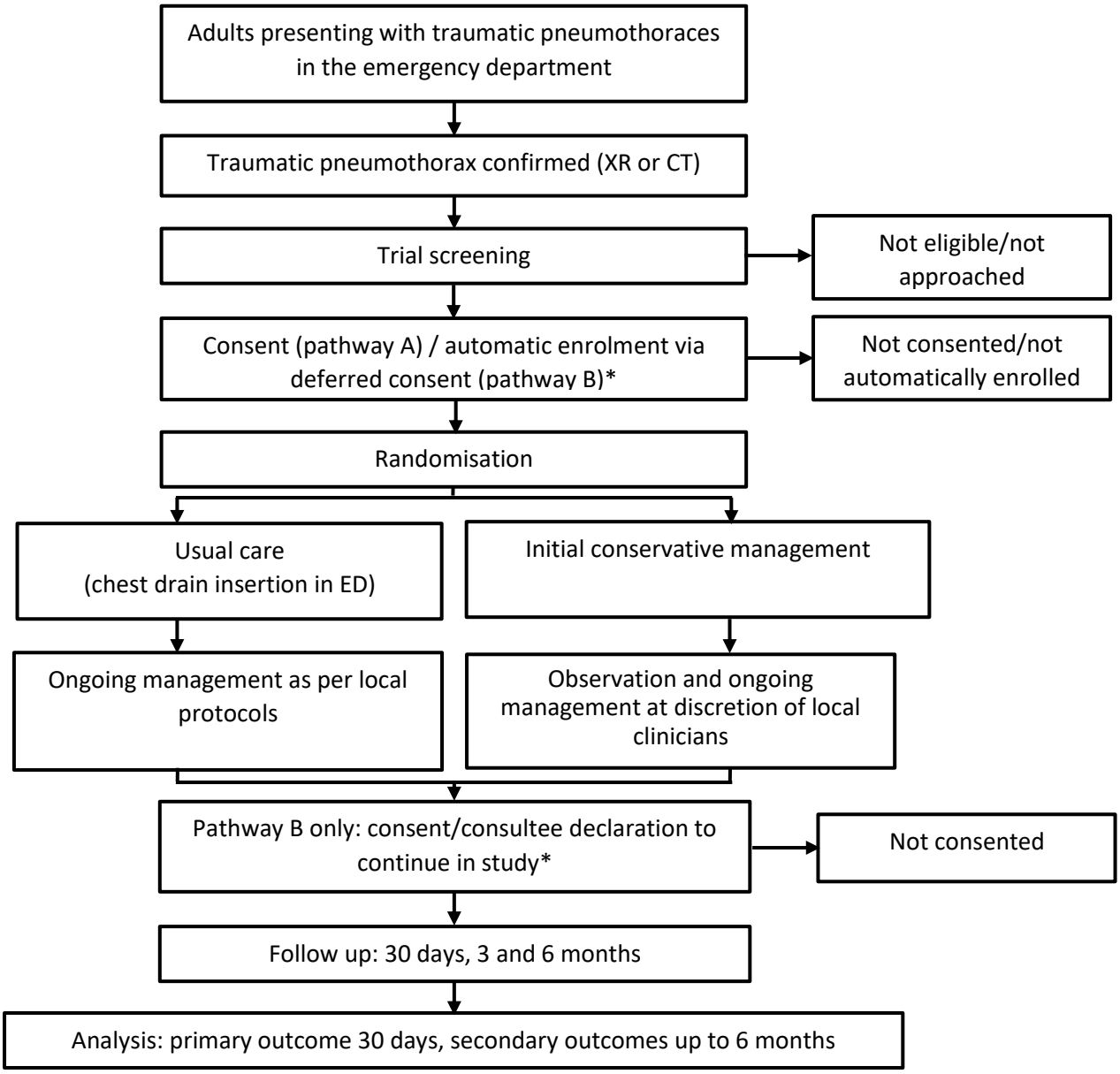
Study interventions	
Control arm	Chest drain insertion in the ED.
Intervention arm	Initial conservative management (i.e. no immediate chest drain).

Summary of objectives and outcome measures		
	Objectives	**Outcome measures**
Primary Outcome	Need for one or more subsequent emergency pleural interventions (excluding chest drain insertion in the ED) up to 30 days.	Binary measure of the need. Patient records /electronic patient tracking systems.[A]
Secondary Outcomes (at specified timepoints	**a)** All pleural interventions (including chest drain insertion in the ED) up to 30 days.	Patient records /electronic patient tracking systems.[A]
	b) All complications of pleural intervention up to 30 days.	Patient records /electronic patient tracking systems. [A]

post-randomisation)	**c)** Total days of pleural drainage up to 30 days.	Patient records /electronic patient tracking systems. [A]
	d) Patient-reported pain, function and breathlessness at "baseline"[B], 30 days, 3 and 6 months	Validated Brief Pain Inventory (1) and MRC dyspnoea scale (2) (Patient Reported Outcome Measures [PROMS]).
	e) Quality of life at "baseline"[B], 30 days, 3 and 6 months.	EQ-5D-5L questionnaire (3). Impact of Events Scale-Revised (IES-R) (4) (at 30 days, 3 and 6 months only).
	f) Total length of stay (hospital, critical care admission (including HDU) and readmission) up to 30 days.	Patient records/electronic patient tracking systems. [A]
	g) Adjudicated mortality at 30 days (pneumothorax or chest injury related).	Patient records /electronic patient tracking systems.
	h) All-cause mortality at 6 months.	Patient records /electronic patient tracking systems. [A]
	i) Cost per quality-adjusted life year (QALY) at 6 months.	Combines data collected in secondary outcomes 'a, b, d, e, f, g and h' supplemented by a study-specific patient resource use questionnaire (5). Methods to be outlined in separate Health Economic Analysis Plan (HEAP). (We are also collecting routinely recorded trauma timelines where available. Review of these timelines will be used to confirm the costing approach and validate assumptions, and is not intended as a key source of data collection).
	j) Patient views and experiences of conservative management/chest drain.	Qualitative interviews with patients or personal consultees.
	k) Clinician views of conservative management/chest drain.	Qualitative interviews with clinicians.
	Notes: ***A.*** *During the internal pilot phase, data will be collected via both the Trauma Audit Research Network (TARN) registry (routinely collected on all patients with severe traumatic injuries) and study-specific Case Report Forms (CRFs) utilising patient records (/electronic patient tracking systems). This is to inform the data collection methods for the remainder of the full trial. See section 17.2 (Data Collection) for further details.* ***B.*** *For this trial, "Baseline" Patient Reported Outcome Measures (PROMS) can be collected from as soon as feasible following randomisation and treatment delivery (where appropriate) and up to 7 days post-randomisation or until point of discharge from hospital (whichever is sooner). Participants will be asked to complete them according to how they feel at the time of completion, rather than retrospectively.*	
Study schedule		
Schedule	• Start date (contracting began): 01 October 2021.	

	• Proposed duration: 36 months (subject to change). • Proposed end date: 30 September 2024 (subject to change).

2 PATIENT FLOW DIAGRAM



** See section 7 for more details about screening and recruitment, including approach and consent pathways.*

Figure 1 Patient Flow Diagram

3 BACKGROUND AND RATIONALE

Injury is a leading cause of death among adults aged <45 years (6). Traumatic pneumothoraces (lung collapse) are present in 1 in 5 victims of severe trauma (7, 8). In 2019 over 50,000 patients were diagnosed with traumatic pneumothoraces in hospitals in England and Wales (unpublished data from Trauma and Audit Research Network [TARN]: a patient-level audit of all patients admitted to hospitals following major trauma in the England and Wales). It is a condition that affects not only victims of accidents such as motor vehicle crashes but also a diverse range of underserved groups including young victims of knife crime and older patients who suffer chest injuries after falls.

We estimate from our prior observational and survey work (9, 10) that around half of patients admitted to hospital with traumatic pneumothoraces will be treated with the insertion of a tube (or chest drain) into the chest. Current guidelines advise chest drain insertion for any traumatic pneumothorax, although very small pneumothoraces can be managed with observation at the treating physician's discretion (11, 12). For some patients with very large pneumothoraces, chest drain placement can reduce the risk of cardiorespiratory compromise (13). However, there remains a large proportion of patients in whom there is clinical uncertainty as to whether an immediate chest drain is required (9). Insertion is usually done in the emergency department (ED) and is one of the most invasive procedures undertaken outside of an operating theatre. Chest drains carry a high-risk of complications such as bleeding and infection in 15-30% of patients (14). There is no robust evidence to inform practice, and the default to invasive treatment may cause potentially avoidable patient pain, distress and complications.

In our analysis of >600 patients with traumatic pneumothoraces from TARN data, 90% of patients treated without a chest drain did not require subsequent intervention (10), suggesting a potential role for conservative management. However, in this analysis, a remaining 50% of patients were initially treated with a chest drain and there was considerable clinical variation in those selected for this invasive procedure. We have also conducted an international survey of 222 emergency physicians (9) utilising clinical vignettes of larger traumatic pneumothoraces, and over 60% of clinicians would elect to insert a chest drain in ED, even without clinical compromise.

Therefore, based on the observational studies and lack of robust data, we propose a randomised controlled trial (RCT) to assess the clinical and cost-effectiveness of an initial conservative approach to the management of patients with traumatic pneumothoraces. If we demonstrate that this approach is effective, it will reduce the use of a painful, invasive and potentially harmful management strategy.

3.1 Evidence explaining why this research is needed now

We searched Medline for systematic reviews, and Medline, Embase, Cochrane Central, ClincalTrials.gov and the WHO trials registry for trials published from any time until January 15th 2021. One systematic review from 2010 evaluated three small (total n=101) RCTs examining the safety of conservative management in small occult traumatic pneumothoraces (13). These occult cases are not relevant to the broader range of participants within this trial, in whom clinical uncertainty remains. However, this review suggested that conservative management may be at least as safe and effective as chest drain insertion.

We have identified one multicentre RCT of small pneumothoraces in severely injured patients in Canada which concluded in 2021 (15). These patients were all on ventilators (receiving positive

pressure ventilation) and current guidelines suggest chest drain insertion in all patients undergoing ventilation (7, 9). Reassuringly, the results showed no difference in mortality or intensive care unit (ICU) or hospital length of stay between patients who were conservatively managed or who had chest drains inserted. The authors concluded that small traumatic pneumothoraces may be safely observed in patients undergoing ventilation and that the complications of chest drains remain unacceptably high. Similarly, our prior observational work found no evidence that ventilation was associated with a failure of conservative management (8). The Canadian trial results are underpowered to provide conclusive evidence as to which treatment strategy is beneficial (142 of an anticipated 300 participants were recruited). Importantly, by including only patients undergoing ventilation (which is around 30% of the traumatic pneumothorax population in the UK (10)), the Canadian study did not fully address conservative management in the broader trauma population, as we propose to do in this trial.

4 AIMS AND OBJECTIVES

4.1 Aim

The aim of this study is to establish whether initial conservative management of significant traumatic pneumothoraces is non-inferior to invasive management in terms of subsequent emergency pleural interventions, complications, pain, breathlessness, and quality of life.

4.2 Objectives

Specific objectives of the trial are:

- **a)** To establish if initial conservative management of significant traumatic pneumothoraces is non-inferior to invasive management regarding subsequent emergency pleural intervention over 30 days post-randomisation.
- **b)** To determine whether conservative management improves health-related quality of life and other patient reported outcomes such as pain and breathlessness over the six months following injury (post-randomisation).
- **c)** To determine the clinical and cost effectiveness of conservative management versus invasive management of traumatic pneumothoraces by measuring resource use, mortality and cost-effectiveness over the six months following injury (post-randomisation).
- **d)** To assess the acceptability of initial conservative management or chest drain insertion to patients and clinicians.

4.3 Primary outcome

The primary outcome is a binary measure of the need for one or more subsequent emergency pleural interventions (such as chest drain insertion/re-insertion/video-assisted thoracoscopy/thoracotomy) from the point of randomisation and within 30 days of the initial injury (post-randomisation, excluding chest drain insertion in the ED for those allocated to the chest drain [control] group). The primary outcome will be adjudicated as detailed in section 4.5. It is important to recognise that the intervention is INITIAL conservative management. Some participants randomised to the intervention will therefore undergo subsequent chest drain insertion during their routine care (e.g. due to anaesthetic concern prior to a period of prolonged anaesthesia). If this subsequent intervention is undertaken outwith an emergency (independently adjudicated) it will be recorded but will not meet the primary outcome.

Reasons for subsequent emergency chest drain insertion may include (but are not limited to): clinically significant symptoms persisting despite adequate analgesia; chest pain or breathlessness preventing activity; a patient is unwilling to continue with conservative treatment; the patient's condition becomes physiologically unstable presumed secondary to pneumothorax; repeat chest radiograph shows an enlarging pneumothorax with physiological instability. Reasons for subsequent emergency pleural intervention will be determined by local practice and will be recorded but not controlled.

Further justification for this primary outcome, and the decision to exclude initial chest drain insertion in the ED (for those in the control group), is based on the complication rate for chest drain insertion, of which over 10% require subsequent pleural intervention within 30 days (10, 14).

A 30-day (post-randomisation) endpoint has been chosen because chest drains remain in place for an average of 6 days (14), and 30 day follow-up is therefore expected to capture all complications related to insertion in the control group.

Figure 2 (below) illustrates the anticipated outcomes in terms of initial treatment allocation and rates of primary outcome between groups.

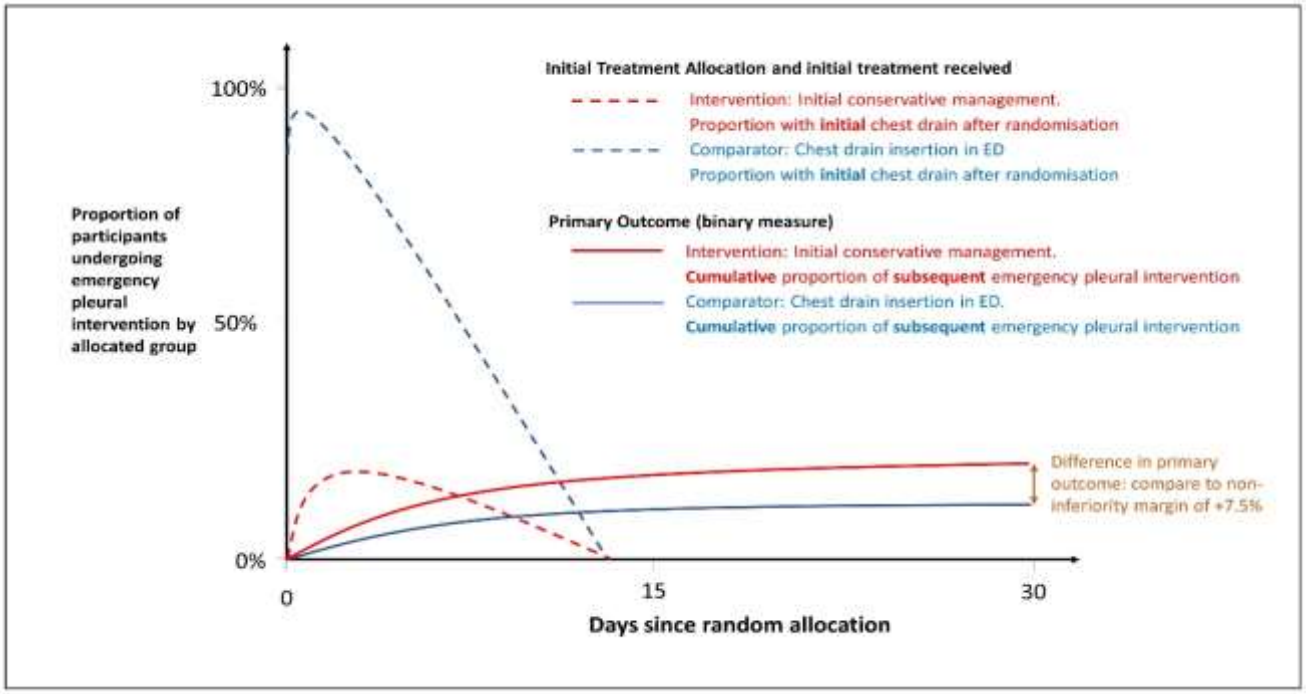


Figure 2 Schematic diagram of initial emergency department treatment received and primary outcomes by randomised treatment groups

4.4 Secondary outcomes

The secondary outcomes will capture the possible advantages of the intervention for patients in terms of reduced pain, complications and improved health-related quality of life in the short to medium term, as well as inform a formal cost-effectiveness analysis. All secondary outcomes will be measured at the time intervals (post-randomisation) indicated in the summary table below (Table 1). Data collection is also detailed in section 10.

Table 1 Summary of secondary outcomes and measures (tools).

Outcome	Measure / Tool
Secondary outcomes (all time intervals specified are 'post-randomisation')	
a) All pleural interventions (including chest drain insertion in the ED) up to 30 days.	Patient records /electronic patient tracking systems.[A]
b) All complications of pleural intervention up to 30 days.	Patient records /electronic patient tracking systems. [A]
c) Total days of pleural drainage up to 30 days.	Patient records /electronic patient tracking systems. [A]

d) Patient-reported pain, function and breathlessness at "baseline"[B], 30 days, 3 and 6 months	Validated Brief Pain Inventory (1) and MRC dyspnoea scale (2) (Patient Reported Outcome Measures [PROMS]).
e) Quality of life at "baseline"[B], 30 days, 3 and 6 months.	EQ-5D-5L questionnaire (3). Impact of Events Scale-Revised (IES-R) (4) (at 30 days, 3 and 6 months only).
f) Total length of stay (hospital, critical care (including HDU) admission and readmission) up to 30 days.	Patient records/electronic patient tracking systems. [A]
g) Adjudicated mortality at 30 days (pneumothorax or chest injury related).	Patient records /electronic patient tracking systems.
h) All-cause mortality at 6 months.	Patient records /electronic patient tracking systems. [A]
i) Cost per quality-adjusted life year (QALY) at 6 months.	Combines data collected in secondary outcomes 'a, b, d, e, f, g and h' supplemented by a study-specific patient resource use questionnaire (5). Methods to be outlined in separate Health Economic Analysis Plan (HEAP). (We are also collecting routinely recorded trauma timelines where available. Review of these timelines will be used to confirm the costing approach and validate assumptions, and is not intended as a key source of data collection).
j) Patient views and experiences of conservative management/chest drain.	Qualitative interviews with patients or personal consultees.
k) Clinician views of conservative management/chest drain.	Qualitative interviews with clinicians.

Notes:

A. *During the internal pilot phase, data will be collected via both the Trauma Audit Research Network (TARN) registry (routinely collected on all patients with severe traumatic injuries) and study-specific Case Report Forms (CRFs) utilising patient records (/electronic patient tracking systems). This is to inform the data collection methods for the remainder of the full trial. See section 17.2 (Data Collection) for further details.*

B. *For this trial, "Baseline" Patient Reported Outcome Measures (PROMS) can be collected from as soon as feasible following randomisation and treatment delivery (where appropriate) and up to 7 days post-randomisation or until point of discharge from hospital (whichever is sooner). Participants will be asked to complete them according to how they feel at the time of completion, rather than retrospectively.*

4.5 Adjudication of outcomes

4.5.1 Adjudication of the primary outcome

Where possible, we will adjudicate the primary outcome for all participants recruited during the internal pilot phase, during which time we will review and finalise the adjudication process for the remainder of the trial. Images may be requested if required.

The adjudication panel will be made up of independent expert members (e.g. emergency clinician, respiratory clinician, intensive care clinician and thoracic surgeon). They will be blinded to group allocation and presented with clinical and imaging vignettes of what happened to each participant and subsequently asked to determine whether in their opinion any subsequent pleural intervention that occurred within 30 days of randomisation was required due to an emergency.

Separate trial specific guidance will be provided to the adjudication panel to outline potential reasons for emergency intervention and consensus agreement should be obtained by two members of the panel.

4.5.2 Adjudication of mortality data (up to 30 days)

All deaths will be recorded in the study CRFs as detailed in sections 10 and 13. During the pilot phase, deaths occurring within the 30 day follow up period will be adjudicated (pneumothorax or chest injury related), where possible. During this time we will review and finalise the adjudication process for the remainder of the trial. Deaths will only be adjudicated where cause of death is not immediately apparent from information provided at site level (e.g. death certification/notes record). The adjudication panel may adjudicate the cause of death from blinded (to group allocation) evaluation of the clinical data provided by site teams via CRFs to determine whether this may have been pneumothorax and/or chest injury related.

5 TRIAL DESIGN

5.1 Summary of trial design and setting

A multicentre, parallel group, individually randomised controlled non-inferiority trial with an internal pilot, an economic evaluation and integrated qualitative study.

The trial will recruit patients from approximately 25 Major Trauma Centres and Trauma Units across England and Wales (potentially subject to change).

5.2 Project timetable

This project (contracting) started 01 October 2021. The project duration is expected to be 36 months, through to 30 September 2024 (potentially subject to change).

5.3 Internal Pilot

Following set-up, we will carry out an internal pilot for up to six months, at approximately five sites. In this pilot, we aim to confirm the feasibility of the trial processes including, recruitment of participants, randomisation, and adherence to the allocated intervention arm. Detailed information will be gathered during the internal pilot from both the qualitative and quantitative elements of the study to inform optimisation and refinement of study processes. Completeness of TARN data and number of randomised trial patients who are eligible for TARN inclusion will be established during the internal pilot to streamline data collection for the main trial.

The pilot will be evaluated using quantitative progression criteria (Table 2) and a qualitative exploration of the acceptability of the trial (as detailed in section 11, Integrated Qualitative Research). Participants recruited to the internal pilot will be included in the final analysis.

Table 2 Pilot phase criteria for trial progression after 6 months

	Red (if any of)	Amber (if any of)	Green (if all of)
Average patient recruitment per site per month	<1	1-<3	≥3
Number of sites opened	3	4	5
Total number of participants recruited	<60	60-90	>90
Adherence to allocated treatment	<70%	70-85%	>85%

The following actions will be taken in response to the progression criteria, in close consultation with the trial Data Monitoring Committee (DMC), Trial Steering Committee (TSC), Sponsor and the funder (i.e. the National Institute for Health and Care Research [NIHR]):

Green (if all of): The study will proceed. Refinements to enhance recruitment and adherence will be implemented by the study team.

Amber (if any of): The study team will discuss modifications to improve recruitment and adherence. The trial will continue if effective modifications to research processes can be agreed and made with regular reviews.

Red (if any of): The study team will discuss any mitigating circumstances with the TSC and the funder (NIHR). If the study does not prove feasible, a closure plan will be agreed.

5.4 Planned recruitment

On progressing to the main trial recruitment period, we will immediately extend recruitment to approximately 20 additional sites for a further 12 months recruitment.

A total of 750 participants (confirmed to be aged 16 years and over) will be recruited to the trial over a total of 18 months (with a 10% loss to follow-up for the primary outcome).

Each site will need to recruit an average of 28 participants during the main recruitment period to allow us to reach our overall sample size. This means that sites will have to recruit approximately 40% of eligible patients that present.

5.5 Blinding

Only researchers evaluating outcomes for the analyses can be blinded to treatment group allocation, except where otherwise specified. For example, two statisticians based at the University of Bristol (UoB) will support this trial. The senior (lead) statistician will be blinded throughout the trial. The second trial statistician will perform all disaggregated analyses according to a pre-specified Statistical Analysis Plan (SAP) and will attend closed (DMC) meetings as required. In addition, the health economist(s) (UoB/Warwick) will be blinded when cleaning data and preparing the analysis plan, but unblinded when conducting the analysis. Furthermore, to enable the conduct and analysis of the qualitative interviews (section 11), it is not feasible for the qualitative researcher(s) to be blinded to intervention group allocation.

5.6 Mitigation of bias in the chest drain (control) group

To mitigate bias against the chest drain (control) group (there is concern that the sensitivity to a benefit of a chest drain will be reduced if a proportion of patients do not follow their group allocation), we will evaluate adherence to the allocated treatment in our internal pilot. If adherence falls <70%, progression will be discussed with the funder and oversight committees. The oversight committees will oversee adherence throughout the trial, and we will address any areas where poor adherence occurs, including variance in management by specialist teams after admission to a ward. Analysis of the primary outcome will be by intention to treat. We will also explore the underpinning reasons for any possible bias in the chest drain arm in our qualitative study through clinician interviews (see section 11, Integrated Qualitative Research).

6 ELIGIBILITY CRITERIA

The screening and recruitment of patients, delivery of intervention and recording of outcomes will be carried out within participating EDs in England and Wales. * *See section 7 for more details about screening and recruitment, including approach and consent pathways.*

Figure 1 depicts the patient flow (see page 13).

6.1 Participant population

Adults presenting with traumatic pneumothoraces. Our study population broadly includes three different groups: young victims of knife crime; older patients who suffer chest injuries following a fall; and victims of polytrauma (serious injury in more than one body region). However, all potential patients, irrespective of injury mechanism will be approached. Potential participants will be identified once traumatic pneumothoraces are confirmed during routine care.

6.2 Inclusion criteria

Potential participants must satisfy the following criteria to be enrolled in this study:

- Patients presenting with traumatic pneumothoraces***1*2**
- Aged, or believed to be aged, 16 years and over, and
- In whom the treating clinician(s) are uncertain if a chest drain is required.***3**

6.3 Exclusion criteria

Potential participants who meet any of the following criteria will be excluded from participation:

- Treating clinician(s) believe injuries are incompatible with life
- Respiratory arrest
- Haemothorax (associated with pneumothorax) requiring a chest drain in the opinion of the treating clinician(s)
- Clinical or imaging evidence of tension pneumothorax
- Prisoners (**NB:** "prisoners" does not include those in police custody; only those detained in prison establishments), and
- Retrospective paediatric exclusion if patient confirmed to be less than 16 years.

***1If bilateral pneumothoraces are present:**

If one side qualifies then the patient can be enrolled, providing no exclusion criterion is present (in which case they are excluded). Treatment of the eligible side then follows the randomisation assignment with follow-up as usual. The other side is treated according to usual practice.

If both sides qualify then both sides receive the same treatment according to the randomisation assignment, with follow-up as usual.

***2Pre-hospital thoracostomies:**

Potential participants who have received pre-hospital thoracostomies may still be enrolled provided they fulfil inclusion/exclusion criteria. Where a participant who has received a pre-hospital thoracostomy is randomised to conservative management it is advised that a chest seal is placed over the wound and delayed wound closure is undertaken. However, this should follow local practice.

***[3]Clinical uncertainty:**

Our survey of clinicians suggests ongoing uncertainty around the need for chest drain insertion (9). However, it also suggests that some clinicians will already manage patients with smaller pneuomothoraces conservatively. Patients with smaller pneumothoraces are therefore unlikely to meet these uncertainty criteria and will not be recruited into the trial. Similarly, patients with very large pneumothoraces are unlikely to be recruited due to a lack of equipoise.

Victims of trauma are usually managed by a multidisciplinary team of senior clinicians from specialties including, but not limited to; Emergency Medicine, Intensive Care and Trauma Surgery. The uncertainty around chest drain insertion, in practical terms, is a multidisciplinary decision based upon individual patient variables (such a pneumothorax size and oxygen levels) and clinical practice at a site level. Our pragmatic approach to inclusion in this trial will allow robust evaluation of a cohort of patients in whom clinical uncertainty exists. This methodology has been adopted by emergency care trials that have led to rapid changes in clinical practice, e.g. CRASH-3 (16).

Separate trial specific guidance will be provided in relation to the conduct and evaluation of clinical (un)certainty, together with bespoke training material provided to sites and discussion at Site Initiation meetings/visits.

6.4 Inclusivity

Every effort will be made to include people from under-served groups (that is groups that are underrepresented in medical research). This includes, for example, making reasonable attempts to source translation services in the ED (and if taking part in a qualitative interview) for those unable to speak (communicate in) the English language. Where feasible, we will also offer key patient information materials and PROMS in other languages. During the internal pilot we will attempt to establish the need for translation of study specific materials for use during the definitive trial. In this trial, being unable to speak/understand the English language is not a specific exclusion criteria.

Additional examples of inclusivity are outlined throughout this protocol (and/or other trial-related documents and delivery), including the involvement of patients who lack capacity to consent for themselves, patients of varying age groups and consideration for other key factors, such as (but not limited to) social and economic factors.

6.5 Co-enrolment to other studies

Co-enrolment will be considered on a study by study basis, decisions around co-enrolment will consider participant burden and will consider whether the randomised interventions are distinct from those in this trial (e.g. blood product transfusion trials in trauma). Where trials with overlapping inclusion criteria are identified we will work with the Clinical Research Networks

(CRNs) and CIs and/or Principal Investigators (PIs) to ensure co-enrolment is in the best interest of patients.

7 SCREENING AND RECRUITMENT

7.1 Identification of participants

Recruitment will be undertaken 24 hours a day, 7 days a week by trained ED clinical staff or research staff (e.g. Research Nurses). Recruitment during out of normal research nursing hours, will be facilitated through targeted training of emergency clinicians at participating sites, supported by members of the Trainee Emergency Medicine Research Network (TERN) and the NIHR Associate Principal Investigator Scheme.

Patients will present to the ED through multiple routes and, where a traumatic pneumothorax is suspected, initial imaging (CT scan or Chest X-ray) will be performed usually within the first hour of their attendance. Imaging to identify traumatic pneumothoraces will be undertaken at the discretion of local clinical teams and will include X-ray or CT. This will form part of routine care and will not be altered for trial purposes.

Potentially eligible participants will be identified after a confirmed diagnosis of traumatic pneumothorax on the initial imaging in the ED by clinical staff or research nurses. Full eligibility must be assigned by an appropriately trained clinician.

Potential participants transferred from non-recruiting sites can be approached for recruitment. If a participant is recruited at a recruiting site and later transferred elsewhere, their participation in the trial will be ongoing and the initial recruiting site will remain responsible for follow-up.

7.2 Screening

Hospital staff will complete a trial-specific screening Case Report Form (CRF) for each patient that presents with a confirmed Traumatic Pneumothorax (data collected on this form are detailed in section 10.3). This CRF will be developed in line with the SEAR (Screened, Eligible, Approached, Randomised) framework (17), which will enable us to record the flow of potential participants through the recruitment process, in line with recommended Consolidated Standards of Reporting Trials (CONSORT) reporting guidelines (18, 19), and monitor equipoise for the trial duration. Each potential participant screened will be allocated a unique screening number. Participants who go on to be randomised will additionally be allocated a unique study identification (I.D) number. Where possible, the screening CRF will include reason(s) for non-participation.

Given the setting of this trial (i.e. the ED, 24 hours a day, 7 days a week), it is acknowledged that completion of a screening CRF may not be feasible at all times. Thus, a pragmatic approach to the screening CRF will be taken and trial-specific guidance will be provided to participating sites.

7.3 Approach and consent details

A summary of the various study invitation and consent (/advice) pathways are shown in Figure 3, directly below. Further supporting details then follow.

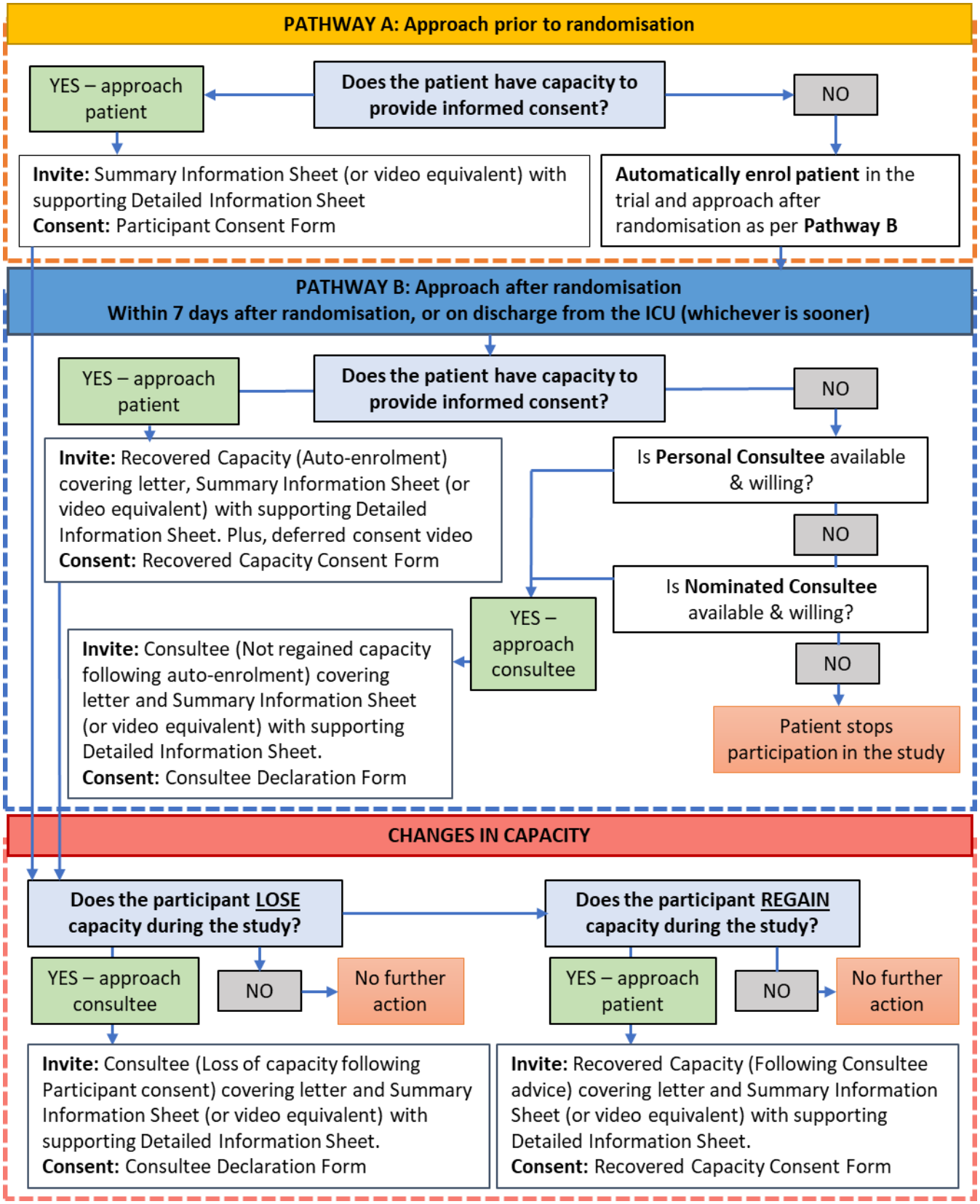


Figure 3 Study invitation and consent pathways depending on capacity status.

7.3.1 Pathway A - Approach prior to randomisation

Following a confirmed diagnosis of traumatic pneumothorax and eligibility assessment, eligible patients will undergo a capacity assessment from a suitably trained clinical staff member (all senior ED clinicians and research nurses have training in capacity assessment). If at this point the patient has capacity, they will be approached in the ED for their consent to take part in the study;

see Figure 3, 'Pathway A'. Further details about the provision of information about the trial are presented separately in section 7.4.

Where, upon the initial capacity assessment, patients are judged to be *unable* to provide informed consent for themselves at the time a decision or action needs to be taken (under some circumstances, loss of capacity may be due to stress or pain related to their traumatic injuries), then patients will be automatically enrolled in the study and approached after randomisation via 'Pathway B', see Figure 3). The decision to automatically enrol an incapacitated eligible patient will be made by two doctors (one independent of the trial) who will consider any known preferences of the patient regarding participation in the study; if relatives are present their views will be considered. The deferred consent model is based upon the HRA guidance on research of this type in the emergency setting. The HRA guidance (20) states that in England and Wales, the law allows adults not able to consent for themselves to be recruited into other intrusive research (i.e. research other than Clinical Trials of Investigational Medicinal Products) without prior advice from a consultee, in emergency situations if:

- Treatment needs to be given urgently;
- It is not reasonably practicable to seek advice from a consultee;
- The procedure is approved by a NHS Research Ethics Committee; and
- A consultee is consulted as soon as possible to seek advice on the participant's likely views and feelings.

Where patients are incapacitated upon initial assessment and are accompanied by a relative or friend, (for example): the clinician/appropriate member of the research team will introduce the trial and explain to the person accompanying the patient that, where considered appropriate, the patient will be enrolled in the trial as permitted within the remit of emergency research. Brief supporting information about the study will also be provided to them. This will be an extremely stressful time for friends or relatives and so further information will only be provided upon request. Furthermore, direct advice from the accompanying person about enrolling the patient in the trial will not be sought given the difficult circumstances (i.e. it is not reasonably practicable). If, however, the accompanying person expresses their objection to the patient's inclusion in the trial, their views will be considered by the clinician/member of the research team when deciding whether to enrol the patient. This approach has been used in other emergency research trials (16) and is supported by members of the PPI group.

7.3.2 Pathway B - Approach after randomisation (deferred consent)

Patients who regain capacity within 7 days post-randomisation*: If a patient regains capacity during the 7 days following randomisation*, or on discharge from the ICU (whichever is sooner), they will be approached by a member of the research team and provided information about the trial (see section 7.4) that will explain what has (likely) happened so far. Where feasible, they will also be shown (provided access to) a short video explaining what deferred consent is and why it wasn't possible to seek informed consent before they were auto-enrolled in the trial (https://youtu.be/P--SEfQOd3w). Patients will be asked to provide consent to continue in the trial; they may wish to continue active involvement in the trial (e.g. will complete questionnaires) or passive involvement (e.g. no questionnaires but allow continued access to medical records and TARN data only). If a patient decides that they do not wish to continue in the trial (i.e. withdraws

from the trial), their ongoing participation will stop. However, permission will be sought to retain and analyse any data already collected as detailed in section 15.2.

Patients who do not regain capacity within 7 day post-randomisation*: If a patient does not regain capacity within 7 days after randomisation*, or on discharge from the ICU (whichever is sooner), a suitable member of the research team will take reasonable steps to seek advice from a Personal Consultee (e.g. their partner, or a particular friend who is not seeking renumeration for doing so or acting in a professional capacity), regarding their likely willingness to continue in the study as per the Mental Capacity Act (MCA) 2005 (21). A consultee should be consulted as soon as possible after the 7-days post-randomisation timepoint.

If reasonable steps to contact a Personal Consultee have failed (e.g. where no family member or friend is willing and able to act as consultee, or where the family or friend live a long distance away, and/or are unable to at least discuss the information sheet(s) within adequate time), and/or a Personal Consultee becomes unavailable during the study, or is no longer willing to undertake the role, then a Nominated Consultee will be approached to advise the researcher about the participation of the person who lacks capacity. For this trial, a Nominated Consultee may include a member of the care team as long as they are not directly connected with the project to avoid potential conflict; the CI and locals PIs are therefore excluded. If a Nominated Consultee cannot be found within adequate time (e.g. up to five working days after the 7-days post-randomisation timepoint), the patients ongoing participation will stop but data collected up to this point will be retained and analysed as detailed in section 15.3.

*if day 7 falls on a weekend, complete capacity assessment on the following working day.

7.3.3 Process of approaching Consultees (where applicable):

The majority of hospitals within the UK have imposed visitor restrictions in light of the (ongoing) COVID-19 pandemic. In order to facilitate timely and appropriate participant recruitment with Personal Consultee approval, discussion of the trial will be made via telephone (or alternative method if requested by the Consultee and where it is appropriate and feasible, e.g. Sponsor/NHS-approved video/tele-conference platforms) in the first instance, appropriate documentation will be made available through the study website to view and download by the Consultee, or sent by email if required. If someone declines the invitation to be a Personal Consultee, they will not be asked to sign anything, however the research team will record, in the relevant study documentation and patient records, that the person was asked and said no; this is so that they are not asked again about this role in the future.

If the Consultee is present at the hospital, then appropriate information materials can be provided, and recording of advice obtained, in-person.

Advice from a Consultee about whether the named patient would wish to be included in the trial or not will be documented by completing the appropriate Consultee Declaration Form with a member of the research team as detailed in section 7.5.

Where appropriate, the research team will invite collaboration of the Consultee in the completion of any questionnaires.

If at any point in the trial, the Consultee advises the research team that the participant should stop taking part in the study, the research team must stop their participation in the study, but any data

collected up to that point will be retained.

7.3.4 Patients with fluctuating capacity (after the 7 day post randomisation period)

A summary of the various study invitation and consent pathways are shown in Figure 3.
The capacity status of an individual will be assumed to remain constant for the trial period unless established otherwise, in which case the following process will be followed.

If an individual regains capacity after the initial 7 day post-randomisation period: If an individual regains capacity to consent during the trial period, then they will be provided with the appropriate information (see section 7.4) that explains what has (likely) happened so far and what we are seeking their consent for. Where feasible, no further trial assessments and/or procedures outside of usual care will take place until after consent from the individual has been obtained. If they wish to continue their involvement in the study the participant will be asked to complete the appropriate consent form using the methods described in section 7.5. If they advise that they no longer want to take part in the study, the individual's participation in the study will be stopped. Consultees will be informed of this consent process.

Patients may wish to continue active involvement in the study (e.g. will complete questionnaires) or passive involvement (continued access to medical records and TARN only). If a patient decides that they do not wish to continue in the study, their ongoing participation will stop. See section 15, Changes in Participation for further information.

If an individual, who had capacity in the ED, later loses capacity during the trial: For individuals who have capacity at the time of consent, but who later lose capacity during the trial, the following process will apply; the consent obtained prior to loss of capacity will not endure the loss.

As soon as feasible following confirmed loss of capacity, an appropriate member of the research team will identify and approach a Personal Consultee (or, if not available, a Nominated) about the individuals' continuing participation in the trial, according to the provisions of the MCA 2005.

If a Consultee is not available or is unwilling or advises that the participant should no longer take part in the trial after they have lost capacity, then the participant will stop their participation but data already collected up to the point of loss of capacity will be retained. See section 15, Changes in Participation.

Advice from a Consultee about whether the individual would wish to be included in the trial or not, will be obtained in the same way described below (see section 7.5). Patients will be informed of this process at the outset via the participant study information materials they were originally provided.

7.3.5 Patients who decline to be randomised into the trial

If a potentially eligible patient with capacity to consent for themselves is invited to take part but decides that they do not want to participate (e.g. Pathway A), or a patient with initial incapacity was enrolled but decides not to continue taking part when subsequently approached (Pathway B), a member of the research team will (where appropriate) ask them about why they declined. Patients will only be asked for their reasoning at one single time point, which will be soon after

they decline. However, patients do not have to provide a reason if they do not wish to. The researcher will record relevant information on the study screening CRF.

As detailed in section 11 (Integrated Qualitative Research), where appropriate, patients who decline to join the trial will also be asked whether they would like to be contacted about taking part in a qualitative interview about why they declined. This will help to understand reasons for not participating and to identify potential misconceptions or misunderstandings about the trial.

7.3.6 Unknown patients

ED staff may not be able to identify some patients who present in the ED for example due to being unconscious or in a critical condition. For the purpose of the trial, the unknown patient will have a screening CRF completed and screening number allocated (and study I.D, if randomised) (as per section 7.2 above). Every effort will be made to retrieve the patient identifiers once the unknown patient is identified.

7.3.7 Patients who die before consent can be taken

It is possible that some patients who are enrolled in the trial under the emergency research remit will die before consent (advice) to continue taking part in the trial can be obtained. This will be a distressing time for friends and family of the patient, whereby informing them directly about the patient's involvement in the study may further heighten their distress. In these circumstances, the patient's involvement will have stopped and treatment will have already been received and therefore notifying friends or relatives would only be for the purposes of transparency. Similar to in other research studies in the emergency setting (22), we believe that the risk of potentially distressing relatives by providing study information after the patient's death would distress the family unduly and we will not actively attempt to do this. We will however ensure posters about the study are displayed in waiting rooms (areas) in EDs and intensive care units.

7.4 Information provision

We recognise our target population is heterogeneous, which poses challenges in terms of information provision and receiving consent. Patient information material will therefore be available in a variety of formats (for example, but not limited to, paper, electronic, and video formats), as advised by our patient groups to facilitate maximal participation across all potentially eligible patients.

Patients and/or Consultees will be given sufficient time to read/view the information material and ask any questions they may have about the trial. The amount of time available to consider taking part (or to continue participation) will vary. When considering participating in the ED for example, due to the nature of EDs and assessment pathways, patient consideration-time is estimated to be from 1 to 4 hours; as per other ED-based research.

Once a potentially eligible patient (with capacity) has been identified, a member of the clinical team and/or research nurse will present (and/or discuss) the patient with a Summary Participant Information Sheet (Summary PIS, or equivalent Summary Video (v)PIS) and, where appropriate, the full (written) Information Pack (Detailed PIS) (e.g. the patient has read/viewed/discussed the Summary (v)PIS and requested further information and/or is suitably comfortable and able to read

both elements at that time). Ideally patients will have read (/discussed/viewed) both the Summary (v)PIS and Detailed PIS before providing informed consent. We recognise, however, that it may not be appropriate or feasible for some patients (e.g. due to being in pain) to read/view both documents, or at least not the Detailed PIS in full, prior to providing informed consent. In these circumstances, patients who have read (/discussed/viewed) at least the Summary (v)PIS and are willing and eligible to take part will be asked to provide informed consent, as outlined below, and asked to read the supporting Detailed PIS in full as soon as appropriate. Informed consent will remain unless the individual requests to change or stop their participation (or loses capacity), in which case the relevant procedures will be followed; see section 15, Changes in Participation.

Information provision for Consultees is outlined in section 7.3.3 above.

7.5 Documenting informed consent/advice

The informed consent process (for both Pathway A and Pathway B) will be undertaken by an appropriately-trained attending clinician, or other member of the local (site) research team, who is identified on the Site Delegation Log.

Written informed consent/advice will be via a paper (wet ink) Consent Form signed by the patient/consultee, dated, and countersigned by the staff member receiving informed consent or via an equivalent study-approved online eConsent Form/eDeclaration form (via the study database system) that is signed electronically by the patient/consultee. EConsent does not need to be followed up with a paper (wet ink) consent form as an electronic signature constitutes documented informed written consent.

Five copies of the completed consent/declaration form are required (paper and/or electronic). A copy should be: (1) provided to the patient/consultee; (2) filed with a copy of the Summary, and Detailed, PIS in the participant's ED records; (3) filed in the investigator site file (ISF); (4) provided to the central trial team (University of Bristol (UoB)); and (5) provided to the patient's General Practitioner (GP; see section 8).

When an eConsent/eDeclaration Form is completed, a copy can be automatically emailed via the database system to the patient/consultee and/or person receiving informed consent if they choose this method and provide an email address. Additional copies can be obtained via the eConsent database system; these should be provided/filed (as required) at the earliest opportunity. We acknowledge that if a participant/consultee does not request an automatic email, and/or the patient is discharged from hospital before a printed copy is available, then a research nurse (or delegate) will send them a copy (e.g. by post).

When a patient has capacity but is unable to indicate their consent by marking a consent form, then they may give their informed consent verbally in the presence of at least one witness (any clinician on duty, nurse or doctor). The witness will indicate on the (e)Consent Form that they are completing (part of) it on behalf of the patient.

Besides completing the consent form (which includes the study title and date of consent), sites should record key details of the informed consent process in the patient's medical record. Patients are not required to provide reasons for taking part in the trial, or not, but if reasons are given, then they should also be documented in their notes.

Randomisation (as detailed in section 8), to inform the clinicians which treatment strategy to follow, can *only* take place once consent is recorded (or the patient is confirmed to have been automatically enrolled via Pathway B).

8 RANDOMISATION

Patients will be randomised in the ED immediately after traumatic pneumothorax has been diagnosed and consent has been given or deferred consent has been applied and suitably recorded. Participants will be allocated in a 1:1 ratio to either "initial conservative management (intervention group)" or "chest drain insertion in the ED (control group)" (see section 9, Trial Strategies for further details). Randomisation will be carried out using an online system and the randomisation sequence will be generated by the company called "Sealed Envelope™" (23). Appropriate staff at all sites, as delegated by the PI, will be provided with log-in details for the secure online randomisation system, and study database where applicable.

Randomisation will be minimised by three factors; 'study site', 'currently ventilated' and 'penetrating injury' at the point of randomisation.

Current ventilation is a key clinical variable for which to minimise by, since traditionally it has been taught that ventilation confers higher risk in developing a life-threatening pneumothorax and chest drainage is routinely advised in this patient group (11, 12). However, our recent observational study found no evidence to support this assertion (10). We anticipate that patients requiring ventilation will make up approximately 30% of our recruited population.

8.1 How to randomise

To randomise a participant, the recruiting doctor or appropriate research staff will access the secure online randomisation system and enter brief participant details (e.g. eligibility, study site, date of birth, date of initial consent/auto-enrolment, and 'currently ventilated' and 'penetrating injury') at point of randomisation. Once the process is complete, the randomisation system will allocate the participant's unique study I.D and indicate to the user whether the participant has been randomised to the intervention (initial conservative management) or control group (usual care – chest drain insertion in the ED).

Site staff will place a relevant pre-prepared 'treatment allocation group' sticker in the patient's ED records (where feasible). The online randomisation system will automatically send an email to relevant users with 'notifications enabled' confirming the randomisation. Appropriate site staff will place a record (electronic or print out) of the allocation generated by the randomisation system in the participant's ED (/medical) notes and in the ISF.

Once a participant has been randomised, they are enrolled in the study and treatment (initial conservative management or chest drain) can proceed. Hospital (site/equivalent research) staff should proceed to complete and send a study approved letter to the participant's GP (e.g. via post or secure email), including a copy of their patient's completed consent form (or declaration form where appropriate), informing the GP that their patient has entered the trial; a copy of this letter should also be filed in the ISF.

Medical case notes containing source data or other trial-related information should also be identified by a label (or equivalent for electronic notes, where feasible), e.g. "Keep until at least dd/mm/yyyy" where the date given is at least five years after the end of the trial.

9 TRIAL STRATEGIES

As detailed in section 8, patients who are deemed eligible to take part and have either provided informed consent in the ED (where possible, e.g. approach and consent as per Pathway A), or have automatically been enrolled due to the patient's inability to provide informed consent themselves in the ED (e.g. deferred consent via Pathway B) will immediately be randomised in the ED to either initial conservative management (intervention group) or chest drain insertion in the ED (control group) (1:1). All participants will undergo clinical assessment, initial management of other injuries, analgesia, monitoring and oxygen as required according to usual care at that site.

9.1 Intervention group (initial conservative management)

In the intervention (initial conservative management) group, the treating clinician will be advised to manage the participant without chest drain insertion and undertake observation and admission to a hospital ward or ICU. Given the pragmatic nature of this trial, all subsequent interventions and further imaging such as X-rays to evaluate pneumothorax resolution after the point of randomisation will be at the discretion of the treating clinical teams.

9.2 Control group (standard clinical management)

In the control group (chest drain insertion in the ED), it is assumed that all patients in the control arm will have a chest drain inserted. It is standard practice for chest drains to be inserted immediately after an imaging diagnosis in the ED. This is done aseptically, under monitored conditions and with a combination of sedation, intravenous analgesia and local anaesthetic at the insertion site. We anticipate chest drain insertion will be undertaken using a "blunt dissection" technique in the majority of participants as this is standard practice in trauma patients. However, where local practice dictates this may be done using a "seldinger" chest drain. Specific details of the procedure (including but not limited to anaesthesia and insertion technique) will be at the discretion of treating clinicians.

9.3 Standard protocol for both groups

Analgesia and sedation: All study participants will be provided with analgesia and sedation (if required) according to local guidelines and protocols. This will not be altered for trial purposes.

Antibiotic prophylaxis: Antibiotic prophylaxis should be prescribed according to local practice and not altered for trial purposes.

Chest drain removal: The decision to remove chest drains (where inserted) should follow usual practice (according to local protocols-where in place) and should not be altered for trial purposes.

COVID-19: Local policies in terms of Personal Protective Equipment (PPE) and infection control should be followed. Participants who test positive for COVID-19 may still be approached for recruitment.

9.4 Ensuring standardisation of standard clinical management (performance bias)

All professionals involved in delivery of chest drains will already be fully trained in the procedures, as these are specialist major trauma centres or trauma units. We will rely on quality of service delivery as scrutinised by the local trauma Morbidity and Mortality review (or equivalent) process. We do not propose to give procedural training as part of the trial.

10 DATA COLLECTION

Demographic, clinical and other study-related data will be collected and recorded by participating site team members, which will be supplemented by TARN registry data where feasible (see section 10.2, below). During our internal pilot phase, we will test TARN registry data content through duplicate data collection (e.g. via both CRF and TARN registry data collection) with a view to streamlining the CRFs for the remainder of the trial.

Table 3 summarises essential data proposed to be collected from each participant for the trial duration, where feasible. Some baseline and follow-up assessments will not be possible on all participants due to the nature of injuries sustained (e.g. patient reported questionnaires). However, we will be able to collect demographics and the information required for randomisation and primary outcome data for all participants, including for those who are incapacitated.

Data will be recorded into paper (and/or online) questionnaires and CRFs and either entered into a trial specific database at site by delegated clinical/research site staff, or sent securely (electronically or by post) to the Central Trial Team (Study Office, UoB) for database entry; this excludes data provided by the TARN registry which will be requested by, and provided directly to, the Central Trial Team (Study Office, UoB). See section 17 for further details about data management.

10.1 Schedule of assessments and outcome data collection

Table 3 depicts the key assessments/outcome measures and participant-related procedures scheduled at various trial timepoints. Further details are provided in this section, below.

To summarise, participants in the trial will undergo:

- Screening, Consent and Randomisation
- Assessments and data collection (where possible) at baseline
- Treatment (as per randomisation allocation) at baseline
- Follow up at 30 days (+10 days) post-randomisation (primary outcome), and approximately at 3 months and 6 months post-randomisation.
- Some participants/personal consultees will also be invited to take part in a qualitative interview around 30 days and 6 months (post-randomisation).

Table 3 Schedule of essential data capture and participant-related procedures

Data collection timepoint (→)	In the Emergency Department (ED)		Post-Randomisation Follow Ups		
Data capture / key trial procedure (↓)	**Recruitment**	**Post-Recruitment (Baseline)**	**30 days**	**3 months**	**6 months**
Screening, Consent & Randomisation	X				
Case Report Form including safety reporting (CRF)	X	X	X	X	X
Sociodemographic Details*		X			
Injury Details*		X			
Injury Severity Score*		X			
Comorbidities*		X			
National Early Warning Score (routinely collected)		X			
PROMS; Pain (Brief Pain Inventory)** α		X	X	X	X
PROMS; Function (Brief Pain Inventory)**		X	X	X	X
PROMS; Breathlessness (MRC dyspnoea scale)**		X	X	X	X
PROMS; Quality of life (EQ-5D-5L)** α		X	X	X	X
PROMS; Impact Events Scale (IES-R)			X	X	X
Patient completed resource use questionnaire				X	X
Pleural interventions*			X		
Complications*			X		
Days of pleural drainage*			X		
Length of stay (hospital and critical care (including HDU) admission, and readmission)*			X		
Mortality*			X		X
Qualitative interviews			X		X

Trauma timelines as detailed by scribes* **		X			

Key: PROMS, Patient Reported Outcome Measures. TARN, Trauma Audit Research Network.

*Data will be retrieved from TARN registry where applicable; **Where possible to obtain; *** For a sample of patients (up to n≤50) in the pilot study only - trauma timelines are routinely collected by trained scribes as part of clinical care, this may include operating theatre records. Data will be anonymised before scanning and upload to the trial database. [α] The University of Bristol is the license holder for the Brief Pain Inventory questionnaire and EQ-5D-5L.

10.2 TARN data

The TARN registry will be used to obtain data on standard in-patient clinical treatments and to process secondary outcome measures and other details relating to the participant's injury. This includes (for example) demographic information, data related to the injury and details of chest drain insertion in the ED (including timings), comorbidities, baseline National Early Warning Scores (NEWS2), mortality and secondary healthcare resource use. TARN data is routinely collected by trained trauma practitioners for every major trauma patient admitted to hospital for >72 hours.

During the pilot phase, data will be collected both in the study CRFs and via TARN reports linked via NHS number. This will establish TARN content and allow us to justify data collection for the definitive trial. Additionally, this will establish what proportion of recruited patients are not eligible for TARN to refine bespoke data collection in these patients. During the main phase of the trial, for participants who are ineligible for TARN data collection (e.g. did not remain in hospital for >72 hours), a separate set of CRFs will be used for sites to collect data which would otherwise have been collected through the TARN registry.

10.3 Screening data

A screening CRF will be completed for each patient that presents with a confirmed Traumatic Pneumothorax in the ED (as detailed in 7.2). Pneumothorax size measurements (assessed by local PIs using study specific guidance) will be collected within the screening CRF to allow monitoring of clinical equipoise and clinician uncertainty among all screened patients. Data capture on this CRF will include (but is not limited to):

- Age (years at time of approach)
- Sex
- Preferred language
- Eligibility details
- Capacity status of patient, approach and consent details (participant/automatic enrolment), if applicable
- Pneumothorax size (maximum difference between lung edge and chest wall edge)
- Haemothorax size (maximal depth from chest wall edge to edge of effusion (24))
- Initial chest drain interventions
- Ventilated or unventilated
- Type of injury

10.4 ''Baseline'' data

''Baseline'' data collection will take place after initial enrolment (randomisation) in the ED has taken place. In terms of the PROMS, however, it is acknowledged that it may not be feasible, or appropriate, to complete the questionnaire straight away (e.g. the patient does not have capacity or they are experiencing stress following a procedure). For this trial, "baseline" PROMS can be collected from as soon as feasible following randomisation and after treatment delivery (where appropriate) up to 7 days post-randomisation (or until point of discharge from hospital, whichever is sooner). Participants will be asked to complete the questionnaire according to how they feel at the time of completion, rather than retrospectively. The questionnaire may be completed with the assistance of a researcher/member of the clinical team (or person with caring responsibility, e.g. family member, if/where feasible). If the participant does not have capacity, then a consultee will be asked to complete the questionnaire on the participant's behalf (proxy versions may be used where possible). If it is not feasible for the participant to complete (part of) the questionnaire, site staff should record this (e.g. in the baseline CRF and/or questionnaire).

Questionnaire (participants): Participants (/consultee) will be asked to complete the Baseline study questionnaire (via paper copy or online) which contains (at least) the following PROMS:

- EQ-5D-5L (3)
- Brief Pain Inventory (1)
- MRC dyspnoea scale (2)

CRF (site staff): A research nurse, or other delegated site staff member, will complete the Baseline CRF. CRF contents are derived from outcome measures and demographic information, and as such we propose including (but content is subject to change*):

- Patient name and contact details
- NHS number
- Capacity status of patient and consent details (participant/consultee)
- Patient demographics, including (confirmed) date of birth, ethnicity and gender
- GP (Practice) contact details
- Details of Personal and/or Nominated Consultee (if relevant, including those who decline an invitation to be a Consultee)
- Injury Details
- Medical treatment received
- Admission details
- Comorbidities
- Pleural interventions in the ED
- Clinical observations
- Injury Severity Score (ISS) (25). The ISS may be calculated retrospectively after validation on the TARN database
- Rockwood frailty scale for patients aged >65 years (26)
- National Early Warning Score (routinely collected from clinical observations)

** As previously noted, during our internal pilot phase we will test TARN registry data content through duplicate data collection (e.g. via both CRF and TARN registry data collection) with a view to streamlining*

the CRFs for the remainder of the trial. Thus, CRF content highlighted here, and at other timepoints, is subject to change.

10.5 Follow up data (30 days, 3 months and 6 months post randomisation)

10.5.1 30 days

Participant questionnaire: Participants will be contacted at 30 days (+10 days*) following randomisation to complete a follow up study questionnaire (responses may be outside of this time frame but date of completion will be captured), which will include questions about pain and function (Brief Pain Inventory (1)), breathlessness (MRC dyspnoea scale (2)), quality of life (EQ-5D-5L (3)) and the impact of events scale (4).

Follow up at 30 days will be the responsibility of site staff. Where feasible, prior to contact, the relevant site staff, and/or researcher will check that the patient is still alive to mitigate any risk (plus capacity status**).

Participants who remain in hospital at 30-days post-randomisation (+10 days):

A member of the site research team will ask these participants to complete the 30-day study questionnaire (paper booklet or online equivalent if preferred and feasible).

For patients who have mild/moderate cognitive impairment (e.g. due to dementia or after head injury), the questionnaire may be completed with the assistance of a researcher/member of the clinical team (or person with caring responsibility if/where feasible); if in such participants it becomes unfeasible to complete the questionnaire (or elements of it), site staff should record this (e.g. in the 30-day CRF and/or questionnaire).

Participants who have transferred to a different hospital or who have been discharged from hospital at 30-days post-randomisation (+10 days):

Follow up will be completed remotely using a range of available methods to ideally suit the participant's preference (e.g. online, via telephone or alternative method if requested and where it is appropriate and feasible). In line with the Mental Capacity Act 2005, where data are collected via remote questionnaires (i.e. not in-person), consent (and capacity) is typically implied by return of the questionnaire, so the researcher need not proactively monitor capacity.

If the participant does not have capacity, where possible, then a consultee (and/or person with caring responsibility) will be asked to complete the questionnaire on the participant's behalf (proxy versions may be used where possible). If it is not feasible for the participant to complete (part of) the questionnaire, site staff should record this in the appropriate CRF and/or questionnaire.

If a participant response is not received within a reasonable time (e.g. ~2-3 weeks), then a researcher will try contacting the participant (and/or consultee) to complete the questionnaire, and/or resend another pack if appropriate/requested. For each follow up, the researcher will make (up to) three contact attempts (initial sending, plus two reminders) on different occasions (allowing at least 7 days between contacts). If no response is received after the third attempt, the

relevant questionnaire will be marked as missing. We will, however, continue to send the next follow up questionnaire as planned, unless the participant requests/confirms that they no longer want to complete them; a similar model has been successfully used in multiple studies conducted by the Bristol Trials Centre (BTC, UoB).

**While researchers are expected to complete hospital screening, CRFs, and send initial questionnaires within the desired timeframe (30 ±10days), we anticipate the need for flexibility regarding participant responses, especially if they have been discharged from hospital. Therefore, we foresee that participant responses may be outside this period.*

***Capacity status in participants who have already been discharged will be checked via medical notes, where feasible. It is also possible that a person with caring responsibility may inform the research team of any changes. If it becomes apparent that a participant who did not originally have capacity has potentially regained capacity, the patient will be contacted directly by a member of the hospital (site) research team. The researcher will formally assess capacity and capture consent if appropriate, which can be done remotely in such cases.*

CRF (site staff): A research nurse, or other delegated site staff member, will complete the 30-day CRF. CRF contents are derived from outcome measures and will be collected up until 30 days following randomisation from medical notes and GP records (where available electronically). Content includes (but is not limited to):

- Change in participant's capacity status (if applicable)
- All pleural interventions (which occurred post-ED)
- All complications of pleural intervention
- Total days of pleural drainage
- Hospital discharge details, including discharge destination and support requirements (where relevant)
- Total length of hospital stay up to 30 days
- Mortality data (during the pilot phase deaths up to 30 days are adjudicated as detailed in section 4.5.2)
- Resource use e.g. critical care (including HDU) length of stay to include initial admission and any additional readmission within 30 days
- Adverse events (as per requirements, see Section 13 Safety).

10.5.2 3 and 6 months

Participant questionnaires: participant questionnaires at 3 months and 6 months (± 10 days) will be managed centrally by the Central Trial Team (UoB) (responses may be outside of this time frame but date of completion will be captured). The 3 and 6 month questionnaire will include questions about pain and function (Brief Pain Inventory (1)), breathlessness (MRC dyspnoea scale (2)), quality of life (EQ-5D-5L (3)), the impact of events scale (4) and health resource use questionnaire ModRUM (5).

The content of the questionnaires and process for obtaining a questionnaire at each of the timepoints will be similar to that detailed for the 30 day follow up above. Noting, however, that no

further patient-completed questionnaires are expected after the final, 6 month data collection timepoint.

CRFs (site staff): A research nurse, or other delegated site staff member, will complete the 3 and 6 month CRFs. CRF contents are derived from outcome measures and will be collected 3 and 6 months (post-randomisation) from medical notes and GP records (where available electronically). Content includes (but is not limited to):

- All cause mortality at 6 months (data will be retrieved from TARN registry where applicable)
- Adverse events (as per requirements, see Section 13 Safety).

11 INTEGRATED QUALITATIVE RESEARCH

The qualitative research will consist of two phases: 1) rapid qualitative evaluation during the internal pilot phase and 2) more in-depth and comprehensive qualitative research during the main trial phase.

11.1 Phase 1: Internal Pilot phase

The main aim of the qualitative research during the pilot phase will be to support and optimise recruitment and trial implementation. Semi-structured interviews with patients recruited into the trial (or a personal consultee if appropriate) and clinicians, together with observations of investigator and site training meetings, will explore: equipoise; reasons for potential bias in clinicians; acceptability of the consent and randomisation processes; potential adherence to allocation.

Ongoing findings will be reported back to the trial team as the pilot study progresses, which may result in modification of the study processes and/or feedback to aid implementation at sites. Purposive sampling will be used to gain maximum variation and include a range of participants and meetings. We anticipate approximately 5 clinician and 10 participant/consultee interviews (via telephone (or alternative method if requested and where it is appropriate and feasible, e.g. Sponsor/NHS-approved video/tele-conference platforms) and approximately 6 investigator meeting observations (in person/via telephone (or alternative method if requested and where it is appropriate and feasible, e.g. Sponsor/NHS-approved video/tele-conference platforms). Meetings to be observed may include Trial Management Meetings, Site Initiation Visits or other investigator meetings where recruitment to the trial may be discussed. The qualitative researcher will attend these meetings and make field notes about factors influencing trial feasibility and recruitment.

11.2 Phase 2: Main trial

To provide a comprehensive and in-depth understanding of the acceptability of initial conservative management versus chest drain to patients and clinicians we will conduct further semi-structured interviews during the main trial phase.

11.2.1 Qualitative interviews

We will interview willing trial participants (or a personal consultee if appropriate) at two time points (approximately 30 days and 6 months after randomisation). Interviews will explore patient views and experiences of conservative management or chest drain insertion in the short to medium term including impact on their daily life, positive and negative aspects of the treatment, including pain, post-procedure recovery, subsequent treatments and return to activities.

To enhance the understanding of clinician acceptability of initial conservative treatment and its implementation in wider practice we will interview clinicians involved in the trial patient pathway. Interviews will explore views of initial conservative management/chest drain, potential hidden benefits of initial conservative management, barriers to and facilitators for introducing conservative management into practice and what influences decision-making concerning traumatic pneumothorax management. (27)

Interview topic guides will be used to ensure similar topics are covered in each interview but applied in a flexible manner to enable issues of importance to the participants to emerge. Topic guides will be informed by study aims and previous literature and developed with PPI input. Interviews may be conducted over the telephone (or alternative method if requested and where it is appropriate and feasible, e.g. Sponsor/NHS-approved video/tele-conference platforms). To ensure inclusivity, equality and diversity an interpreter will be used for interviews with non-English speaking participants (28) (where feasible). Interviews are expected to last 45-60 minutes and will be recorded using an encrypted digital voice recorder. Audio recordings will be transcribed by a member of the study team or a University of Bristol-approved professional transcription service, and anonymised. Interpreters (or translation services) will be required to sign a confidentiality agreement (and align with University of Bristol approval) before engaging with participants.

Maximum variation/purposive sampling will be used to ensure diverse participant characteristics are included (range of sites, patients from both intervention arms (oversampled in the conservative treatment arm), and patient demographics e.g. age, sex and clinician roles). Sampling will be guided by sufficient "information power" relevant to the study aims (27). We anticipate approximately 25 patient interviews at the two timepoints (total 50 interviews) and 15 clinician interviews.

11.2.2 Identifying and consenting participants for qualitative interviews (phase 1&2)

Patients/consultees

Patients being invited to take part in this trial (or their personal consultees) will be informed about the (optional) interviews through the study information sheet. If they are happy to be contacted about an interview, they will indicate this on the study consent/declaration forms. Patients will be interviewed only if they have mental capacity at the time of being invited to join the trial. This includes pre-randomisation invitation for participants with capacity (pathway A) and post-randomisation for those without capacity at the time of randomisation (pathway B, deferred consent). If a patient does not have capacity at the time of being invited, or loses capacity within the study period, their consultee may be invited to be interviewed (where appropriate). If a patient regains capacity within the study period, they will be informed about the option to take part in qualitative interviews in the 'Recovered Capacity letter and supporting Patient Information Sheet'.

Those who agree to be contacted and who are selected to be invited for an interview will be contacted by the qualitative researcher who will provide the qualitative interview PIS (either electronically or via the post), explain more about the interview and answer any questions. If the patient/consultee then agrees to take part in the interview, the researcher will arrange a convenient time and preferred method to conduct the interview. As interviews will be conducted remotely, verbal consent for participation in the interview will be obtained from participants before the interview starts. Verbal consent will be obtained from a Good Clinical Practice (GCP) trained researcher and audio recorded. This will involve the researcher reading out standard consent form statements and, if appropriate, the participant verbally agreeing to them. To reduce burden on the participants, verbal consent for the qualitative interviews will not be followed up with written consent (or e-consent). Verbal consent at the time of the interview also ensures the participant understands what is involved and is happy with taking part in the interview at that

time. The audio recorded excerpts will be retained for auditing purposes in line with trial archiving policies.

Patients can participate in interviews even if they decline consent for the main study or later stop taking part in the study. Patients who decline consent for the main study will be asked whether they would like to take part in a qualitative interview about why they declined. This will help to understand the reasons for not participating and to identify potential misconceptions or misunderstandings. The following data will be requested from decliners who are interested in taking part in the qualitative interview and will be held securely by the study team for contacting potential participants: name, contact information (telephone and email address (if appropriate)) and preferred contact days/times. For participants who take part in interviews the following (optional) data will also be collected for analysis and reporting purposes: date of birth; sex; ethnicity, postcode.

Clinicians

Clinicians will be identified through the site PIs and study team. These may include senior emergency clinicians, anaesthetists, intensive care and emergency surgeons and emergency care nurses. The qualitative researcher will provide clinicians with the healthcare professional interview information sheet. If the clinician is interested in taking part in the interview, the qualitative researcher will explain more about the interview, answer any questions and if they agree to take part, arrange a convenient time and preferred method to conduct the interview (e.g. via telephone or alternative method if requested and where it is appropriate and feasible, such as Sponsor/NHS-approved video/tele-conference platforms). Consent for the interview will be obtained by the qualitative researcher verbally using the same process outlined for patients/consultee (as above).

Members of the qualitative research team will be responsible for obtaining consent and maintaining suitable records.

11.2.3 Qualitative data analysis

Within the pilot phase, audio-recordings of interviews and field notes will be triangulated and analysed alongside data collection using a framework rapid analysis approach (29) to identify key issues as well as what went well.

Within the main trial phase anonymised transcripts will be analysed using reflexive thematic analysis (30). Transcripts will be coded for key categories and concepts, using deductive coding (based on the research aims and Theoretical Framework of Acceptability) (31) and inductive coding (developing new codes based on issues emerging from the data) with the aid of NVivo software. Analysis will be ongoing and iterative with interviews and analysis proceeding concurrently. Relevant data from the pilot phase interviews will be included in the phase 2 (main trial) analysis. Analysis will be led by the qualitative researcher, with a sub-set of the data independently coded by the qualitative lead to enhance trustworthiness of the analysis process and to contribute to theme development. Any discrepancies will be discussed and incorporated

into the final coding framework. Findings will be considered in relation to quantitative results and provide enhanced understanding of conservative management in the emergency context.

11.2.4 Data management, protection and patient confidentiality in relation to the qualitative research data

Interviews will be recorded using an encrypted audio recorder and transferred as soon as possible after the interview to secure UoB storage. The recording will then be deleted from the recorder. If recordings are made through a video conferencing platform, then only the audio-recording file will be transferred securely to the UoB and both the audio and video files will be deleted from the video-conferencing platform. Audio-recordings of interviews will be transcribed by a UoB member of staff or UoB approved transcription service that has signed the necessary confidentiality agreements. Audio-recordings and transcripts will be labelled with an appropriate screening number or appropriate (unique) study I.D number and stored securely, adhering to the University of Bristol's data storage policies.

Transcripts will be edited to ensure anonymity of respondents. Anonymised quotations may be used for training, teaching, research and publication purposes for this and future studies. Anonymised transcripts may be made available by controlled access to other researchers who secure the necessary approvals for purposes not related to this study, subject to individual recorded informed consent from participants. Excerpts of audio-recordings concerning verbal consent will be retained for auditing purposes in line with trial archiving policies. The remaining content will be deleted at the end of the study.

11.2.5 Safeguarding participants during interviews

We will ensure that participants are not subjected to undue distress during the qualitative interviews. To mitigate this, and the possibility that participants may disclose information to provoke concern about risk, the interviewer will be an experienced qualitative researcher who will adhere to the following:

Participants will be informed that the interview is strictly confidential, but should they disclose information to suggest that they or others are at significant risk of harm, the interviewer will discuss this with a clinical advisor and may need to disclose these details to the designated safeguarding authority. The interview will only continue if participants are happy to proceed and engage with the interview topics. If the researcher feels a participant is becoming tired, confused or distressed, they will ask the participant if they wish to have a break or discontinue the interview (with the option to continue later) and will offer support. A safeguarding protocol for researchers and participants will be implemented.

12 HEALTH ECONOMIC RESEARCH

We propose a cost utility analysis with a maximal time horizon of 6 months (corresponding to the period of maximal follow-up for patient-reported pain, dyspnoea and mortality) since this is the time period that clinicians and patient advisors advise us is long enough to capture all relevant effects. It is however possible that, when we have the data we will see convergence of costs and outcomes within 30 days (which corresponds to the primary outcome), and, in order to explore this, we intend to report cost-effectiveness at both 30 days and 6 months.

The Quality-Adjusted Life Year (QALY) will be derived by applying the cross-walk algorithm to the EQ-5D-5L and combining information on survival. Proxy report may replace self-report for the EQ-5D-5L where patients do not have capacity at the time of assessment.

In the internal pilot trial, NHS resource use data will be collected by bespoke trial CRFs (secondary care) and compared with TARN database records. This preliminary inspection of overlapping methods of data capture will allow us to optimise efficient data collection in the full trial without sacrificing completeness. In the pilot trial we additionally plan to collect anonymised 'trauma timelines' (these are timelines routinely recorded by trained trauma scribes in ED, together with anonymised information where subsequent interventions occur in operating theatres e.g anaesthetic charts and "pick" sheets) where available. While it is not our intention to micro-cost every aspect of trauma care, review of these timelines will be carried out to enhance our understanding of the trauma pathway and to inform and validate our costing approach (for instance with regards to procedural times and staff requirements). Any analysis based on these timelines will be exploratory.

Resource use data will be collected on all NHS and personal social services (PSS) care resources for trial participants up to 6 months follow-up. A patient reported resource use questionnaire (note that the patient questionnaire will incorporate ModRUM with the addition of some study specific questions) at 3 and 6 months will provide additional data on primary and community care resource after discharge. Where possible unit costs for valuations will come from national sources (32, 33).

12.1 Analysis

If missingness is identified, we will explore the pattern and potential mechanisms of missing data, including (for example) the contribution of PPI contributors to offer explanations for observed missing data patterns in patient-reported measures. This will be sought to validate the imputation approach.

Selected statistical methods will deal with skew, baseline imbalance (34), missingness (35) and sampling uncertainty as appropriate, and will include the construction of cost-effectiveness acceptability curves (36) using the net-benefit approach to show the probability that conservative management is the optimal choice over a range of possible values of the ceiling ratio.

While our primary analysis will be based on an NHS and PPS perspective, as indicated, we will extend this to explore specific societal aspects that we think are important to patients, e.g. lost work and education, in exploratory analyses.

Methods will be detailed further in a separate Health Economic Analysis Plan (HEAP).

13 SAFETY (ADVERSE EVENT REPORTING)

Serious and other adverse events will be recorded and reported in accordance with the GCP guidelines and the Sponsor's Research Related Adverse Event Reporting Policy. Participant safety will be monitored by the Trial Management Group (TMG), Sponsor and oversight committees (e.g. TSC and DMC) and the trial will be stopped if any indication of harm from using the intervention is found.

13.1 Definitions

Adverse events

Term	Abbreviation	Definition
Adverse Event	**AE**	Any unfavourable and unintended sign or symptom that develops or worsens during trial participation, whether or not it is considered to be related to the trial intervention. In all instances, it will be the decision of the PI of each participating site (or appropriate delegate, e.g. clinician) to determine whether the person's change in health is related to the trial. AEs are not continuous and persistent disease or symptoms, present before the trial, which fail to progress; signs or symptoms of the disease being studied (in this case pulmonary complications or development of frailty syndromes); or treatment failure.
Adverse Reaction	**AR**	The distinguishing feature between an AR and AE is whether there is evidence to suggest there is a causal relationship between the event and the research procedure.
Serious Adverse Event	**SAE**	Any untoward medical occurrence that: • Results in death • Is life threatening[A] • Requires hospitalisation or prolongation of existing hospitalisation[B] • Results in persistent or significant disability or incapacity • Consists of a congenital anomaly or birth defect • Or is considered by the investigator to be an important medical event *[A] The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.* *[B] The definition of hospitalisation is an unplanned overnight stay. Note, however, that the patient must be formally admitted – waiting in outpatients or an Accident & Emergency Department (A&E) would not count as hospitalisation (even though this can sometimes be overnight). Prolongation of an existing hospitalisation qualifies as a SAE. Planned hospital stays would not be counted as SAEs, nor would stays in hospital for "social reasons" (e.g. respite care, the fact that there is no-one at home to care for the patient). Also, if patients had a day-case operation, this would not qualify as hospitalisation. However, if a planned operation was brought forward because of worsening symptoms, this would be*

		considered as an SAE. Hospitalisations for the purpose of the intervention are an exception to SAE reporting unless complications occur.
Serious Adverse Reaction	**SAR**	Any SAE that is classed in nature as serious and there is evidence to suggest there is a causal relationship between the event and the research procedure.
Suspected Unexpected Serious Adverse Reaction	**SUSAR**	Any SAE that is classed in nature as serious and there is evidence to suggest there is a causal relationship between the event and the research procedure, but where that event is unexpected.
Accidents Incidents or near Misses	**AIMS**	The AIMS (DATIX) system is common in many NHS Trusts and implements the NHS Trust's policy on Incident Reporting – including relevant AEs that occur in relation to research and during normal clinical practice.

Severity classifications

Mild event	An event that is easily tolerated by the patient, causing minimal discomfort and not interfering with everyday activities.
Moderate event	An event that is sufficiently discomforting to interfere with normal everyday activities.
Severe event	An event that prevents normal everyday activities.

Relatedness

Not related	Temporal relationship of the onset of the event, relative to administration of the intervention, is not reasonable or another cause can by itself explain the occurrence of the event.
Unlikely to be related	Temporal relationship of the onset of the event, relative to administration of the intervention, is unlikely and it is likely there is another cause which can by itself explain the occurrence of the event.
Possibly related	Temporal relationship of the onset of the event, relative to administration of the intervention, is reasonable but the event could have been due to another, equally likely cause.
Probably related	Temporal relationship of the onset of the event, relative to administration of the intervention, is reasonable and the event is more likely explained by the intervention than any other cause.
Definitely related	Temporal relationship of the onset of the event, relative to administration of the intervention, is reasonable and there is no other cause to explain the event, or a re-challenge (if feasible) is positive.

13.2 Identification of AEs

AEs are likely to occur throughout the course of the trial. AEs may be volunteered by the participant or detected by a member of the research team through questioning or observation, during either the initial hospital attendance or follow-up contact (timepoints). Local research teams are responsible for assessing *all* AEs that they become aware of for their participants during the trial, i.e. those occurring from when they are enrolled (randomised) into the trial until the 6 month follow-up time point.

Recording and reporting details of AEs and SAEs are outlined, below from section 13.3 to section 13.6.

The PI of each participating site (or appropriate delegate, e.g. clinician) is responsible for assessing all AEs and categorising whether they are serious, expected, and related.

13.3 Classification of AEs and SAEs

We do not expect any AEs or SAEs related to conservative management (above those SAE and AEs already expected of the control arm i.e. normal care). If an expected serious adverse event is prolonged or more serious than expected, this will be reported as an unexpected SAE.

A list of events that can be expected during this trial, or within this patient population can be found below; other factors such as participant history should not be taken into account.

The following events can be expected during this trial, or within this patient population:

- Prolonged hospitalisation (due to complications from initial injury, social care needs, or other reason)
- Death due to initial injury or complications from initial injury; it is anticipated that some patients randomised will die from injuries outwith the chest injury/pneumothorax e.g. predominantly brain injury but may include pelvic injury/visceral injury or spinal injury.
- Anaesthetic complications
- Critical Care admission due to complications from initial injuries (if not directly admitted to Critical Care from the ED as part of routine care)
- Wound/pleural/other infection
- Chronic pain
- Bleeding/haemorrhage
- Recurrent or persistent pneumothorax
- Tension pneumothorax
- Delayed haemothorax
- Subcutaneous emphysema
- Subsequent (outside of ED) positive pressure ventilation
- Tracheostomy
- Pneumonia (required treatment with antibiotics for pneumonia during inpatient stay; excluding prophylaxis for traumatic injuries)
- Ventilator Associated Pneumonia
- Amputation
- Surgical intervention due to injury outside the chest
- Delirium

- Events related to analgesic interventions

The following events can be expected during this trial for patients who have a pleural intervention :

  - Puncture of solid organ: liver, spleen, heart, lung, oesophagus
  - Puncture of intercostal vessel (bleeding)
  - Drain failure (dislodgement/kinked/blocked)
  - Re-expansion pulmonary oedema
  - Bronchopleural fistula

13.4 Recording and reporting non-serious adverse events (AEs)

Only expected non-serious AEs (according to protocol section 13.3) or non-serious AEs caused by pleural interventions up to 30 days post-randomisation (as per our secondary outcome measure) will be recorded within the relevant study CRFs. All other non-serious AEs will be recorded in the participant's medical notes, but will not be captured as part of the study documentation.

13.5 Recording and reporting serious adverse events (SAEs)

Following HRA guidance (37) on safety reporting for non-CTIMP (clinical trials of investigational medicinal products), only reports of Serious Adverse Events (SAEs) that are:

- **related** to the study (i.e. they resulted from conservative management or from administration of any research procedures) **and**
- **unexpected** (i.e. not listed in the protocol as an expected occurrence)

will be subject to reporting to the Sponsor and Research Ethics Committee (REC). Further details can be found in section 13.5.2 (recording and reporting of unexpected SAEs).

Local research teams will record **all SAEs** in the study , which will be filed in the ISF. Summary reports of SAEs will be available to the central trial team (study office) from the secure study database for monitoring and reporting purposes. The central trial team will review these events and report SAEs as needed on a regular basis to trial oversight committees/ Sponsor.

The study CRF will capture the following data for expected SAEs (as a minimum):

- SAE title
- Start date/time (where known)
- Assessment of relatedness to the study (e.g. conservative management or research procedure)
- If the event resulted in death and if so, the cause of death where known. During the pilot phase, where cause of death during the 30 day follow up period is not immediately apparent, it will be adjudicated whether this is related to pneumothorax or chest injury, as detailed in section 4.5.2.

SAEs should also be recorded in participants' clinical notes, by the research nurse or other suitable member of the research team. The PI, or delegate, should complete the overall assessment.

SAEs identified in the study CRFs as **related to the study (e.g. conservative management or any research procedure) and unexpected** will be reported to the Sponsor and REC as detailed in section 13.5.2 below. A summary of the SAE reporting requirements are detailed in Figure 4.

13.5.1 Recording and reporting of expected SAEs

Expected SAEs will be recorded (as noted above in section 13.5) and reported to the Sponsor routinely by the central trial team via summary reports.

13.5.2 Recording and reporting of unexpected SAEs

All unexpected SAEs which ARE causally related to the study (i.e. *are* related to conservative management or any research procedure) (SUSARs): will be reported to the Sponsor within 24 hours of the local research team becoming aware of the event. SUSARs will also be reported to the REC immediately (must be within 7 days if the event resulted in the death of the participant or 15 days if the event did not result in death) by the central trial team (UoB). Local reporting of clinical events related to the study (e.g. conservative management or any research procedure) should also be reported through local adverse event reporting systems such as DATIX and managed according to local governance processes.

Unexpected SAEs which are NOT related to the study (i.e. are *not* related to conservative management or any research procedure): will be recorded in the study CRFs, as detailed above in section 13.5 and will be reported to the Sponsor routinely by the central trial team via summary reports.

13.6 Completing and sending SUSAR forms

All SAEs that require reporting to the Sponsor (i.e. unexpected and related SAEs) must be documented on the full SUSAR Initial Report Form, which is provided by the central trial team. An initial report may be provided orally but a written SUSAR Initial Report Form must be completed and sent within 24 hours of the local research team becoming aware of the event.

Reporting process:

- **Sites** should scan and email the form, with high importance, to the (i) Sponsor, (ii) CoMiTED central trial team (Trial Manager), and (iii) cc'd Professor Edward Carlton, Chief Investigator; see **'Key Trial Contacts'** for contact details (pages 2-3).

*(**Please note**: typical University (central trial team) staff working hours are Monday to Friday, 09:00-17:00 (subject to variation). In the event of University closure dates or limited availability, an out of office automatic response will notify the site of alternative contact details/arrangements).*

- The **Sponsor and/or central trial team** will confirm receipt and, if required, forward the completed form to REC within the reporting period (see below).

For each SUSAR reported to the Sponsor, the following information (as a minimum) will be collected:

- Full details in medical terms and case description
- Event duration (start and end dates, if applicable)
- Action taken
- Outcome

- Seriousness criteria
- Causality (i.e. relatedness to research procedures), in the opinion of the PI
- Whether the event would be considered expected or unexpected.

Each SUSAR must be reported to the Sponsor separately and not combined on one SUSAR form. If the PI/delegate is unable to review/sign the SUSAR Initial Report Form, the form should be submitted without this and a copy with PI/delegate signature should then be submitted within 48 hours.

Any change of condition or other follow-up information relating to a previously reported SUSAR should be documented on the separate SUSAR Follow Up Report Form provided by the central trial team.

As above, sites should scan and email the form to the relevant personnel who will confirm receipt, and if required, forward to the REC within the necessary timeframe.

Events will be followed up until the event has resolved or a final outcome has been reached.

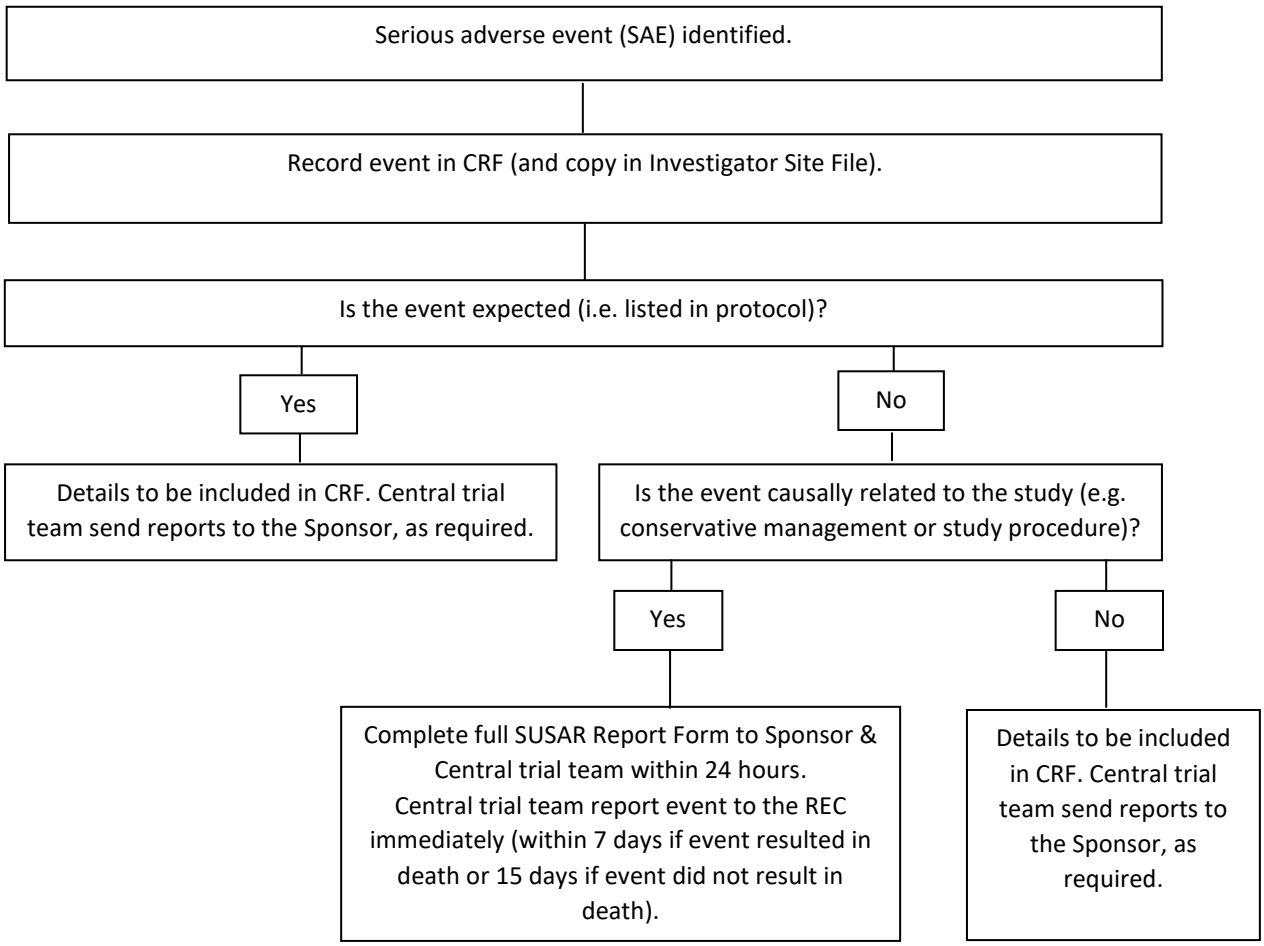


Figure 4 Summary of the SAE safety reporting requirements

13.7 Responsibilities

All adverse events will be documented and reported in accordance with North Bristol NHS Trust's Safety Reporting Standard Operating Procedure (SOP) and as above, agreed by the Sponsor.

Principal Investigator (PI)/research nurse. PIs and research nurses (or suitably trained delegates) at each site will be checking for AEs when participants attend for treatment/follow-up, and at specified data collection points. The appropriate persons will be responsible for:

- Using medical judgement in assessing and assigning seriousness, causality and expectedness.
- Ensuring that all appropriate AEs and SAEs are documented.
- Ensuring that all SAEs are recorded and reported as per the procedures noted above, including the provision of further follow-up information as soon as available.
- Ensuring that SAEs are chased with the Sponsor/central trial team if a record of receipt is not received within 2 working days of initial reporting.
- Investigators should also comply with any internal SAE reporting requirements within their host institution.

Chief Investigator (CI). The CI (or agreed delegate) will be responsible for:

- Clinical oversight of the safety of patients participating in the trial, including an ongoing review of the risk/benefit.
- Using medical judgement in assessing and assigning seriousness, causality and expectedness of SAEs where it has not been possible to obtain local medical assessment.
- Immediate review of SAEs requiring reporting to the Sponsor/REC.
- Ensuring safety reports are prepared in collaboration with appropriate members of the TMG group for the relevant oversight committees and regulatory authorities.
- Reporting of SAEs to the REC within required timelines.
- Notifying PIs of SAEs that occur within the trial (where applicable).
- Central data collection of SAEs.

Trial Manager. The Trial Manager will provide a summary of AEs and SAEs to the relevant oversight committees and Sponsor, as required.

14 STUDY COMPLETION

Individual participants will normally complete the study after the 6 month follow-up has been completed. The study itself will end when the last participant has completed the 6 month follow up, all qualitative interviews have been completed, and all data has been finalised (all data queries have been resolved and the study database has been locked).

14.1 Premature termination of the study

If the TSC or Sponsor recommends early termination of the study for any reason, the CI will notify the Funder and relevant regulatory authorities (e.g. REC). If the trial is prematurely terminated, no new participants will be recruited, and a decision on data collection for active participants will be made in discussion with the TSC and Sponsor. The CI will be responsible for informing participating sites of the premature termination of the study.

15 CHANGES IN PARTICIPATION

Participants will remain in the trial unless they (or their consultee) choose to stop their participation, or they are unable to continue for a clinical reason. In the event that a clinician feels it is unsafe for a participant to continue in the study, agreement should first be sought from the PI. Any changes to a participant's continuation in the study should be recorded on the appropriate study document (e.g. Change of Permissions/Withdrawal Form). Trial specific guidance will be provided to participating sites on recording and reporting procedures.

The trial will retain any research data collected up to the point of stopping participation (or death) for analysis purposes (noting potential exception – see section 15.2). Furthermore, as advised in the trial participant information materials, the trial team will continue to collect relevant data about the patient's health from their electronic medical records unless they explicitly request otherwise.

It is of paramount importance to note that participants who do not (wish to) follow their randomised allocated intervention (treatment) should ***not*** stop their participation in the trial and they should continue to be followed up as per Protocol. Adherence to treatment allocation will be recorded and monitored via study data collection records.

Participants retrospectively confirmed as under 16 years of age. If an (unknown/unidentified) patient who appeared to be 16 years of age or over at the point of initial enrolment is later confirmed to be under the age of 16 years, then their participation in the trial will stop and their data will not be used in the study.

15.1 Participants who lose capacity during the trial period

If a participant loses capacity during their trial involvement and they stop participation in the trial, any data already collected up to the point of when their participation stopped will be retained, as noted in the study information material and consent form.

15.2 If a patient (participant) regains capacity during the trial period

If a patient, who lacked capacity at point of trial enrolment, regains capacity during their trial involvement and does *not* wish to continue participation (i.e. does not provide recovered capacity consent), their participation in the trial will stop. Permission will be sought to retain and analyse any data already collected (up to the confirmed point when their participation stopped); if, however, the patient does not give permission to retain and analyse the data, it will be destroyed. Where appropriate, permission will also be sought to continue collecting follow up data from central medical records.

15.3 If a patient (participant) does not regain capacity and a consultee cannot be found

If a patient, who lacked capacity at point of trial enrolment, does not regain capacity during their trial involvement and neither a Personal nor Nominated Consultee can be found within adequate time, the patient's participation in the trial will stop. Any data already collected up to this point will be retained and used in the analysis.

15.4 Patients who die before consent can be taken

If a patient, who was automatically enrolled in the trial in the ED, dies before consent to continue in the trial (e.g. post randomisation) can be obtained, any data already collected up to, and including, the date of death will be used in the analysis. This includes data regarding any adverse events, and associated reports.

16 STATISTICAL CONSIDERATIONS

16.1 Sample size

Our observational data suggests that 10% of our study population will require emergency pleural intervention following conservative management; our primary outcome.

Our group recently identified a reintervention rate of 10% following initial chest drain insertion in a single UK site (10), which was partly related to the low rate of penetrating trauma cases (5%). We will recruit from sites with a higher proportion of penetrating trauma, e.g. London and Manchester, and therefore anticipate the incidence of the primary outcome in the control group to be at least 10%. A retrospective study of patients with an initial chest drain following trauma showed 21% of patients required subsequent additional pleural intervention, increasing to 28% in patients with penetrating trauma such as knife injuries (14).

Our PPI contributors unanimously support the potential advantages of initial conservative management, such as avoiding an invasive procedure, improved mobilisation after injury, and reduced longer term pain. However, they also recognise the need to balance these benefits against the risk of avoidable harm. When asked, our PPI group felt that an increase of 5-10% in subsequent emergency pleural intervention would be acceptable compared to usual care, given the anticipated reduction in the overall number of chest drains in the intervention group. These views have been used to select a non-inferiority margin of 7.5%. We will conclude that the study population can be safely managed conservatively if the incidence of subsequent emergency pleural intervention is no more than 7.5% higher in the intervention group than in the control group (i.e. no more than 17.5% in the intervention group if the rate in the control group is 10%). If the incidence of the primary outcome is 10% in both study groups, a sample size of 674 (337 in each group) will allow non-inferiority to be concluded with 90% power when comparing a one-sided 97.5% confidence interval, for the absolute difference in primary outcome incidence, to a non-inferiority margin of 7.5%. Allowing 10% loss to follow-up increases the total sample size to 750 (patients confirmed to be aged 16 years and over).

16.2 Estimates of recruitment and retention rates

We have based our recruitment rates on TARN data from the host site (North Bristol), which sees approximately 78 patients per year who meet inclusion criteria (11). We will target the higher-recruiting sites in the internal pilot and the main trial as described earlier, some of which see >100 potential participants per year, so 78 patients is a conservative estimate of the population.

16.3 Data Analysis

A detailed statistical analysis plan (SAP) will be written and made publicly available before the follow-up period concludes. The data will be analysed according to the intention to treat (ITT) principle and reported according to the CONSORT guidelines. The findings for the primary outcome measure (one or more emergency pleural interventions in the 30 days following randomisation), will be presented as an absolute difference in incidence between conservative management and control groups, with the limit of the one-sided 97.5% confidence interval compared to the non-inferiority bound of an absolute difference of a 7.5% higher incidence of the primary outcome in the conservative management group. Patients who are withdrawn from the

study within 30 days of randomisation will not be included in the primary analysis, but the potential impact of this missing data on the study conclusions will be investigated in sensitivity analyses. If non-inferiority is demonstrated, evidence from the risk difference, two-sided 95% confidence interval, and p-value, will be presented to allow inference about the superiority of conservative management compared to usual care. Further sensitivity analyses and any sub-group analyses that assist in the interpretation of the analysis of the primary outcome will be pre-specified in the SAP.

Analysis of secondary outcomes will utilise appropriate regression models, with covariates distinguishing the allocated groups, study centres, whether the participant had a penetrating injury, and whether the participant required ventilation at recruitment.

17 DATA MANAGEMENT

17.1 Source data and documentation

Source data is the first place the data is recorded. Source data for this trial will consist of paper or electronic (where eConsent has been taken) copies of the consent form(s) (plus verbal consent for qualitative interviews), participant completed questionnaires (paper and/or electronic), CRFs designed specifically for the study (paper and/or electronic), and audio-recordings of interviews. Where data is recorded first in the patient's medical records that is, and will remain, the primary source data and any specifically designed CRFs would be considered supplementary source data.

Each potential participant screened will be allocated a unique screening number. Randomised participants will additionally be allocated a unique study I.D. Participants will be identified in all study-related documentation by (at least) their study I.D number (or screening number, if not randomised). A record of trial participants' names and contact details (and, where relevant, their Consultee), hospital numbers and assigned trial numbers will be retained by the research team at each site and stored securely for administrative purposes (in the ISF, for example). Personal data entered directly into the password protected database will be migrated to a secure database accessible only to the central trial team (study office). A SQL Server database system within the University of Bristol may be used to facilitate this process but will not retain the data. Any data stored on laptops will be encrypted. Any information that is analysed or transferred outside the European Economic Area (EEA) will be anonymised.

Participants will be informed via the information materials (and consent form, where appropriate) that personal information such as their name, email address and phone number will be stored on the secure database with the central trial team (study office, University of Bristol). Where a participant or consultee has selected completion of questionnaires electronically, their email address will remain on a password protected but publicly accessible server for this purpose. Furthermore, for the purpose of conducting the trial randomisation only, some essential participant information will be entered into the secure online randomisation system (see section 8). All data that are entered on to the Sealed Envelope™ system is done so via Transport Layer Security (TLS) connections and stored on secure servers located in the UK and Ireland that comply with both UK and EU regulations on data privacy. User-access to the system will be managed by the central trial team (study office), who will in turn generate password-protected user-accounts for authorised site staff, who will in turn generate password-protected user-accounts for authorised site staff.

Data obtained by paper will also be entered onto the password protected database (by trained members of site and/or central trial team staff). Information capable of identifying individuals and the nature of treatment received will be held in the database with passwords restricted to trial staff. Information capable of identifying participants will not be removed from clinical sites apart from when securely transferring data to the central trial team at the University of Bristol. This data will not be made available in any form to those outside the trial, with the exception of inspection purposes by the sponsor and/or other regulatory authorities. Consent forms and clinical letters (and any other documentation) with personal identifiable data will be stored in a locked filing cabinet (or locked equivalent). Participant details will be anonymised in any publications that result from the trial.

For details regarding qualitative interview data, see section 11.

17.2 Data collection

Data collection is detailed in section 10, above (and throughout).

Data will be recorded directly into CRFs and questionnaires (paper and/or online), and where applicable, will either be entered at site by delegated clinical/research site staff into a trial specific database, or transferred securely (electronically or by post) to the central trial team (study office, University of Bristol) for entry into the trial specific database.

At agreed time points, relevant TARN data will be transferred to researchers at the University of Bristol via secure email. Separate study specific guidance, and data management plan, will include further details about this element of the trial.

The eConsent (online) forms and online questionnaires will be completed via the REDCap database system and process (see below for REDCap details), which can be securely accessed via the internet. It is expected that participating sites will be provided with a study-specific tablet device (with a wipeable screen and cover), which would be handed to the participant to support this process, where feasible. In such cases, the tablet device would be password protected and only used by the research team or authorised clinical team for study purposes.

17.3 Database platforms

All administrative and clinical study data will be stored in University of Bristol datacentres using clustered MySQL databases driven by REDCap. REDCap is a secure, web-based electronic data capture system designed for the collection of research data. The system has been developed and supported by Vanderbilt University. Bristol Trials Centre (BTC), at the University of Bristol (UoB), has set up its own infrastructure so that all systems are hosted at and supported by UoB.

A Relational Database Management System may be used to provide integration services between administrative and clinical databases. This data will be temporarily stored in a SQL Server system maintained by UoB, to support the workflow of the study team. This data will not be made available for analysis.

17.3.1 Administrative Data

Administrative data will be kept in a secure REDCap database that is only accessible from within the UoB firewall. All users will require (at least honorary) contracts with UoB to access it.

17.3.2 Clinical Data

The clinical data will be stored on a separate server to the administrative data. Anonymised clinical data is linked by a study I.D. If an email address is collected, the 'Email Address' field is flagged as an identifier and not included in the export for the statistician, so the data set can be considered pseudonymised at export and does not need further processing.

17.4 Data storage

North Bristol NHS Trust and the Bristol Trials Centre (University of Bristol) are joint data controllers for this trial. Data will be held at the University of Bristol and will conform to the University of Bristol Data Security Policy and in Compliance with the General Data Protection Regulation (GDPR) as it applies in the UK, tailored by the Data Protection Act 2018.

17.5 Access to Data

For monitoring purposes, the CI will allow monitors from the Sponsor team (or delegate), persons responsible for the audit, representatives of the REC and other Regulatory Authorities to have direct access to source data/documents.

The BTC IT Development Team will manage access rights to the data set under instruction from the trial manager (on behalf of the CI). Prospective new users must demonstrate compliance with legal, data protection and ethical guidelines before any data are released.

17.6 Archiving and destruction of trial materials

An archiving plan will be developed for all trial materials. Data will be held in compliance with the Sponsor's SOPs (and any associated data sharing agreements, e.g. with TARN). All research data will be retained in a secure location during the conduct of the trial and for at least 5 years after the end of the trial. Medical case notes containing source data or other trial-related information should be identified by a label (or equivalent for electronic notes, where feasible) "Keep until at least dd/mm/yyyy" where the date given is at least five years after the end of the trial. Data will be kept at the University of Bristol (and/or Sites) for this time and, at the end of the archiving period, will be destroyed by confidential means with the exception of a final trial dataset which will be made available for data-sharing purposes (see section 17.7 below). Where electronic records are in use, University of Bristol and/or North Bristol NHS Trust's policy will be followed. The approval of NBT as owner of data and Study Sponsor, as well as the CI, will be sought prior to destruction of the data.

Participating sites will be responsible for ensuring that all study records held at site are archived appropriately when notified by the Sponsor / central trial team (UoB).

17.7 Access to the final trial dataset

Anonymous research data, which may include qualitative audio-recordings and/or associated data such as anonymised transcripts, will be stored securely and kept for future analysis with participant consent. We anticipate that anonymised trial data will be shared with other researchers to enable international prospective meta-analyses. Members of the TMG will develop a data sharing policy consistent with UoB policy. Data will be kept anonymous on the research data storage facility (RDSF). Requests for access to data must be via a written confidentiality and data sharing agreement (DSA) available from the RDSF website which will be confirmed by the CI (or appointed nominee).

The DSA should cover limitations of use, transfer to third parties, data storage and acknowledgements. The person applying for use of the data will be scrutinised for appropriate eligibility by members of the research team.

18 TRIAL MANAGEMENT

The CI will take overall responsibility for managing the various components of the trial, with the support of the BTC trial manager, and will meet with other relevant personnel (as required) for each component. The BTC, a UK Clinical Research Collaboration (UKCRC) registered trials unit, will support the delivery and conduct of the trial.

18.1 Trial Management Group (TMG)

The project will be led by the trial management group (TMG) which will include the CI, the BTC trial manager, trial statistician and other relevant personnel (e.g. clinical colleagues, BTC representatives, Sponsor representative, PPI representatives as required). The TMG will meet regularly throughout the duration of the trial to ensure development of study documentation and approvals, monitor progress (including participant recruitment), resolve day-to-day problems as they arise, review the budget, discuss analysis, results, draft reports and dissemination.

18.2 Trial Steering Committee (TSC)

The TSC will oversee the conduct and safety of the trial, seek to help to ensure that milestones are achieved and that general scientific probity is maintained. The TSC will monitor progress of the trial, adherence to the protocol and consider new information of relevance to the research question. Membership, responsibilities and reporting mechanisms of the TSC will be formalised in a TSC charter (Terms of Reference), which will be agreed in advance.

The membership will consist of an independent chair, independent members, patient contributors and the Chief Investigator. Observers may also attend at the invitation of the Chair.

18.1 Data Monitoring Committee (DMC)

The DMC will oversee the safety, primary outcome data completeness and adverse events data. The DMC will make recommendations to the TSC as to whether there are any (ethical or) safety issues that may necessitate a modification to the protocol or closure of the trial. Membership, responsibilities and reporting mechanisms of the DMC will be formalised in a DMC charter (Terms of Reference), which will be agreed in advance.

18.2 Patient and Public Involvement (PPI)

Aims:

- to enhance the quality and relevance of this research through active and ongoing PPI involvement
- to engage with existing and recruit additional PPI members from the three target populations (young people who have experienced violent/knife crime, older people who have fallen and people who have experienced multiple trauma) as the study progresses - with the support of existing PPI representatives, links, and networks.

- to utilise PPI representatives' knowledge and experience to ensure the trial asks the right questions and is accessible, sensitive, and suitable for all three target populations
    - to feed into study processes and participate in developing patient information materials and a range of dissemination outputs to inform and support practice change
- to ensure that PPI representatives benefit from their involvement by feeling supported, that their voices are heard, their expertise is acknowledged, they can access training and be reimbursed for their costs
- to ensure PPI members are clear about their roles, what they can influence and why the study team value their input

A co-applicant will lead on PPI throughout the trial in collaboration with the wider trial team. In this role they will act as a single point of contact for all public contributors and provide appropriate induction and training, ongoing mentoring, and support, liaise with the research team and report on PPI activities throughout the research. A PPI group made up of existing PPI co-applicants/members and supplemented through networking and outreach work will meet as needed throughout the trial and ensure an iterative and responsive PPI strategy. A PPI group of knife crime and violence reduction professionals will meet separately (approximately 12 monthly) to address this important element of the trial supplemented through ongoing engagement activities with schools, youth clubs and charities. An overarching Patient Advisory Group led by PPI co-applicants will discuss feedback from the PPI groups and report to the TSC where relevant.

18.3 Sponsor

The study Sponsor is North Bristol NHS Trust. Selected sponsorship responsibilities will be formally delegated to the BTC under the terms of an appropriate service level agreement.

18.4 Funding

The trial is funded by the National Institute for Health and Care Research (NIHR) Health Technology Assessment Programme (HTA) (ref: NIHR132889). The views expressed are those of the author(s) and not necessarily those of the NIHR or the Department of Health and Social Care.

19 MONITORING, AUDIT AND INSPECTION

This trial will be monitored in accordance with the Sponsor's (North Bristol NHS Trust) Monitoring SOP, which is consistent with the UK Policy Framework for Health and Social Care Research. All trial related documents will be made available on request for monitoring and audit by North Bristol NHS Trust, the Research Ethics Committee (REC) and available for inspection by other licensed bodies.

A trial monitoring plan will be developed by the Sponsor and agreed by the TMG and CI based on the trial risk assessment which may include on site monitoring.

The Sponsor usually delegates some of the monitoring to the central trial team (UoB). The following checks would be typical:

- That consent is taken by an appropriately authorised person
- That informed consent has been properly documented
- That data collected are consistent with adherence to the trial protocol
- That CRFs are only being completed by authorised persons
- That SAE recording, recording of protocol deviations and reporting procedures are being followed correctly
- That no key data are missing
- That data is valid
- Review of recruitment rates, withdrawals, and losses to follow-up.

19.1 Protocol compliance

There will be no prospective, planned deviations or waivers to the protocol. Accidental protocol deviations can happen at any time, but they must be adequately documented on the relevant forms and reported to the CI and sponsor. In the event of systematic protocol deviations, investigation and remedial action will be taken in liaison with the CI, TMG and the TSC.

A serious protocol breach will be reported to the Sponsor as soon as possible. The sponsor will determine the seriousness of the breach and whether onward reporting to the REC is necessary.

19.2 Notification of serious breaches to GCP and/or the protocol and poor-quality data

A "serious breach" is a breach which is likely to affect to a significant degree:

a) the safety or physical or mental integrity of the subjects of the trial; or
b) the scientific value of the trial.

The Sponsor must be notified immediately of any case where the above definition applies during the trial conduct phase. They will assess the seriousness of any breach as per appropriate Sponsor SOP. Repeated major breaches may be considered serious breaches and notified to the REC and Health Research Authority (HRA).

20 ETHICS AND REGULATORY APPROVALS

20.1 Research Governance

The study will be undertaken at several sites in England and Wales, subject to appropriate REC approval and HRA approval. The trial will be conducted in accordance with the protocol, the conditions and principles of the Declaration of Helsinki and GCP. Any amendments of the protocol will be submitted to the REC for approval. On request, the study investigators and their institutions will permit trial-related monitoring and audits by the Sponsor and relevant REC by providing direct access to source data and other documents (i.e. patients' hospital notes, X-ray reports etc. where relevant).

20.2 Governance and legislation

This trial will be conducted in accordance with:

- Conditions and principles of GCP guidelines
- UK Policy Framework for Health and Social Care Research
- Data Protection Act (DPA) 2018
- General Data Protection Regulation (GDPR)
- Mental Capacity Act (MCA) 2005

Any amendments to the trial documents must be approved by the Sponsor prior to submission to the REC.

Before any site can enrol participants into the trial, the CI or designee will obtain confirmation of capacity and capability for each site in-line with HRA processes along with other documentation required for the sponsor to grant sites with a greenlight letter.

For all amendments the CI or designee will confirm with the Sponsor, the HRA (+/- REC) and sites' R&D departments that permissions are ongoing.

This research trial will be conducted in accordance with conditions and principles of GCP. GCP is the international ethical, scientific, and practical standard to which all clinical research is conducted. Compliance with GCP provides public assurance that the rights, safety, and well-being of people taking part (trial participants) are protected and that research data are reliable.

20.3 Research Ethics Committee (REC) review and reports

Ethics review of the trial protocol and other trial related participant facing documents will be carried out by a UK REC. HRA approval will be sought alongside REC. Any amendments to these documents, after a favourable opinion from the REC/HRA has been given, will be submitted to the REC/HRA for approval prior to implementation.

All correspondence with the REC will be retained in the Trial Master File (TMF)/ISF.

An annual progress report will be submitted to the REC within 30 days of the anniversary date on which the favourable opinion was given, and annually until the trial is declared ended. The CI (or designee) will notify the REC of the end of the study and if the study is ended prematurely (including the reasons for the premature termination). Within one year after the end of the study,

the CI (or designee) will submit a final report with the results, including any publications/abstracts, to the REC.

GCP training will be carried out by certain staff members depending on their delegated responsibilities within the trial, the level of training required will be determined according to the NIHR Delegation and Training Decision Aid. Informed consent to participate in the trial will be sought and obtained according to GCP guidelines.

20.4 Peer Review

The proposal for this trial has been peer-reviewed through the NIHR peer-review process, which includes independent expert and lay reviewers.

20.5 Poor quality data

The quality of the trial data will be monitored throughout the trial and data completeness will be reported to the TSC, and any cause for concern over data quality will be highlighted and an action plan put in place.

20.6 Financial and other competing interests

This applies to the CI, PIs at each site and committee members for the overall trial management. Research team, trial committee members and all PIs must disclose any ownership interests that may be related to products, services, or interventions considered for use in the trial or that may be significantly affected by the trial. Competing interests will be reported in all publications and in the final report.

20.7 Risks and benefits

We believe this study does not pose any specific risks to individual participants, nor does it raise any serious ethical issues.

As with all trials the main benefit of participating is an altruistic one to improve care for subsequent patients who suffer from traumatic pneumothoraces.

The trial information materials will provide clear details of the anticipated risks and benefits of taking part in the study. The risk and benefits of the study will be discussed with the participating sites as part of the process of inviting patients to take part and providing written informed consent.

20.8 Statement of indemnity

This is an NHS-sponsored research study. For NHS sponsored research HSG(96)48 reference no.2 refers. If there is negligent harm during the clinical trial when the NHS body owes a duty of care to the person harmed, NHS indemnity covers NHS staff, medical academic staff with honorary contracts, and those conducting the trial. NHS indemnity does not offer no-fault compensation and is unable to agree in advance to pay compensation for non-negligent harm.

21 DISSEMINATION POLICY

We will endeavour to keep trial participants informed of trial progress at the relevant timepoints via CoMiTED study newsletters which will be co-produced with PPI partners. The CI and TMG will establish a writing committee which will be responsible for preparing scientific reports of the study findings. The aim will be to publish our primary manuscript in a high impact medical journal, and present our findings at multiple conferences. We will communicate our findings to the British Thoracic Society, NICE and NHS England to incorporate our work into relevant national guidelines and develop a film about the project with the help of involved patients and our patient advisors to ensure our findings reach diverse audiences.

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23 DOCUMENT HISTORY

Version Number	Version Date	Summary of Changes
1.0	08APR2022	n/a [first implemented].
2.0	11MAY2022	Correction of minor typographical errors and editing of document names in Figure 3.
3.0	07JUL2022	Clarified eligibility criteria where bilateral pneumothoraces are present. Corrected length of stay outcome. Updated time horizon for health economic analysis. Updated NIHR name and logo. Minor wording changes and clarifications throughout.

24 SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the trial in compliance with the approved protocol and will adhere to the principles outlined in the Medicines for Human Use (Clinical Trials) Regulations 2004 (SI 2004/1031), amended regulations (SI 2006/1928) and any subsequent amendments of the clinical trial regulations, GCP guidelines, the Sponsor's (and any other relevant) SOPs, and other regulatory requirements as amended.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the clinical investigation without the prior written consent of the Sponsor

I also confirm that I will make the findings of the trial publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the trial will be given; and that any discrepancies and serious breaches of GCP from the trial as planned in this protocol will be explained.

For and on behalf of the Trial Sponsor:

Signature: Date:

..../...../.....

Name (please print):

.....

Position:

.....

Chief Investigator:

Signature: Date:

..../...../.....

Name: (please print):

.....

Statistician:

Signature: Date:

..../...../.....

Name: (please print):

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