
CONservative versus Standard carE for primary spontaneous PneumoThorax (CONSEPT)

# Site Initiation Visit: Training Slides

BRISTOL TRIALS CENTRE

FUNDED BY
NIHR | National Institute for Health and Care Research

NHS
North Bristol
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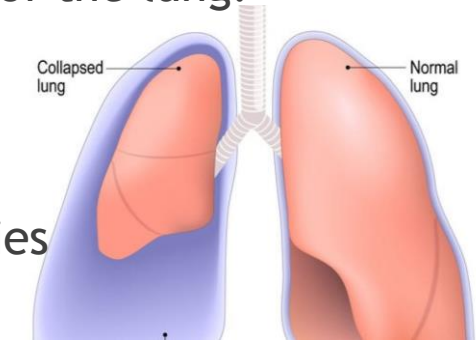
# Study Overview

# Background

- **Primary spontaneous pneumothorax (PSP)** is an abnormal collection of air in the space between the lung and the chest wall, causing collapse of the lung.
- **Primary-** no underlying lung disease
- **Spontaneous-** occurs without injury
- Typically, PSP patients are young with no medical comorbidities




- 3000 patients a year need admission to hospital to treat a PSP
- UK guidance (British Thoracic Society [BTS] 2010) focuses on treating the acute presentation of PSP with short-term drainage (needle aspiration, intercostal drain). These methods often result in longer admissions and increased risk of complications such as infection.
- Patients whose lung has only partially collapsed (small PSP) or who have fewer symptoms can be managed “conservatively”, thus not draining the air and being observed instead.

# Evidence for use of conservative care in PSP

- **Brown SG et al: Conservative versus interventional treatment for spontaneous pneumothorax. New Engl J Med 2020**

- Significant issues-  limited its adoption into routine clinical practice
- Radiographic endpoint vs patient focussed outcome
- Survey to understand current UK practice. Respondents comprised 85 UK physicians and  demonstrated that, despite the recent Brown trial, conservative care has not been widely adopted.
- None of the responders said they would conservatively manage a patient with a large symptomatic PSP

*The CONSEPT trial will investigate whether observation only in patients with a large symptomatic PSP is safe and effective with respect to outcomes that are important to patients, such as the need for invasive treatments and length of hospital stay.*

# Aims and Objectives

**Aim:** To evaluate whether conservative care for large symptomatic PSPs is superior to usual care.

Objectives:

- To test whether conservative care is superior to usual care with respect to subsequent pleural procedures over first 30 days.
- To estimate the difference between groups with respect to a range of patient-reported and clinical secondary outcomes over first 30 days.
- To estimate the difference in recurrence rates between groups over 12 months follow-up
- To estimate the cost-effectiveness of conservative care compared to usual care

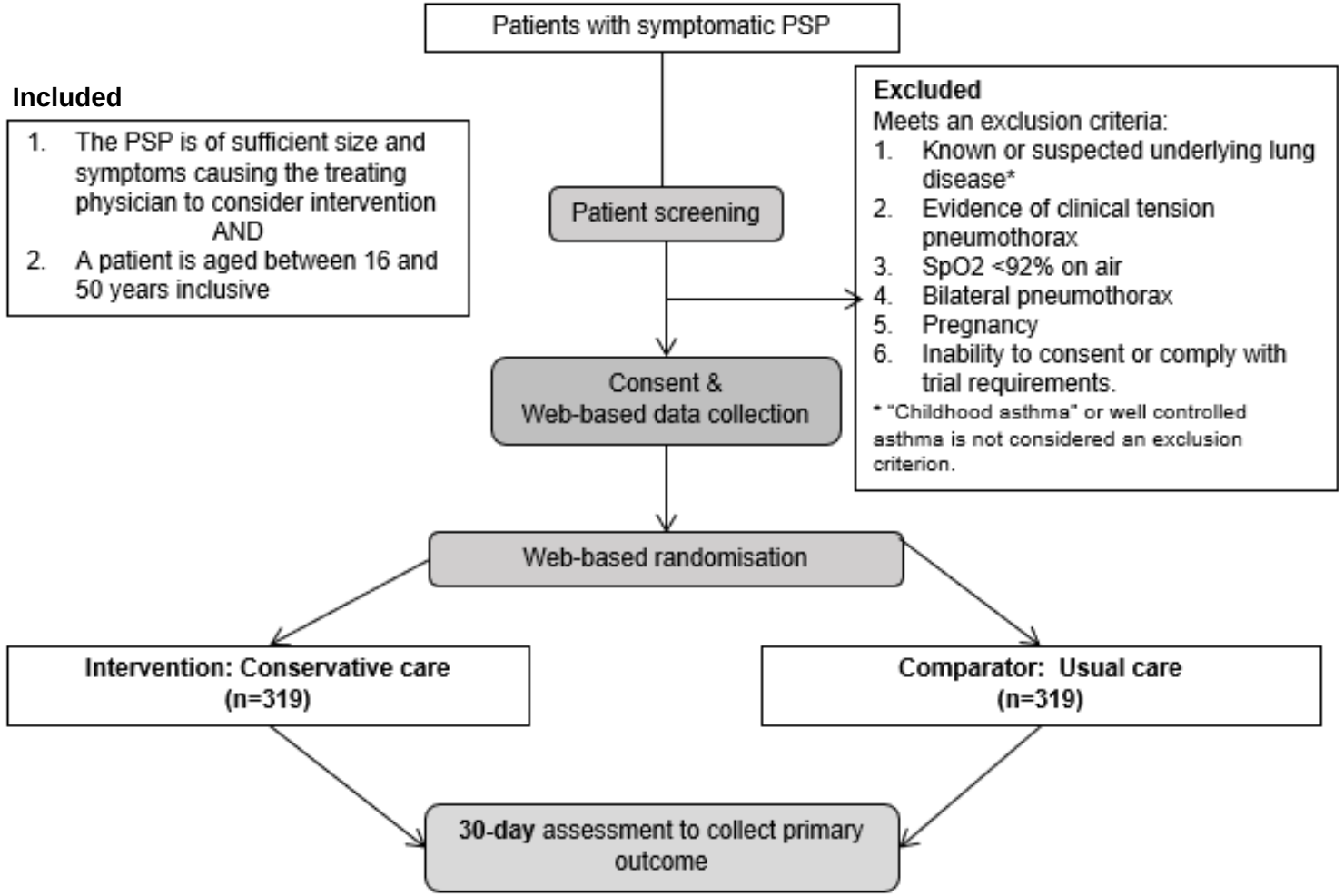

# Trial Overview

- A multicentre, parallel, individually randomised controlled superiority trial in 35 hospitals in England, Scotland and Wales

**Intervention-** *CONSERVATIVE CARE*- patient managed without invasive intervention and enters a period of observation for symptoms only.
**Comparator** – *USUAL CARE*- patient managed using usual invasive care (e.g. needle aspiration/chest drain) Procedure administered at the discretion of treating physician.

- 638 patients, randomised in a 1:1 ratio, recruited from participating UK hospitals over a total recruitment period of 42 months (14-month internal pilot phase)
- Patient follow up at 30 days (research visit) and 12 months (routine data)

# Trial Schema




Recruitment target: 0.7 patients per site per month = Approx 8-10 patients per year

# Outcomes

- **Primary outcome**

Any pleural procedure (including ICD insertion, Needle Aspiration, pleural vent, video-assisted thoracoscopy) administered at any time after randomisation and completion of initial care up to 30 days after randomisation.

In the usual care group, any pleural procedure beyond the initial pleural procedure will count as a primary outcome event (whether Needle Aspiration, ICD or pleural vent).

In the conservative care group, initial care will be complete immediately after randomisation, following which any pleural procedure will count as a primary outcome event.

# Secondary Outcomes

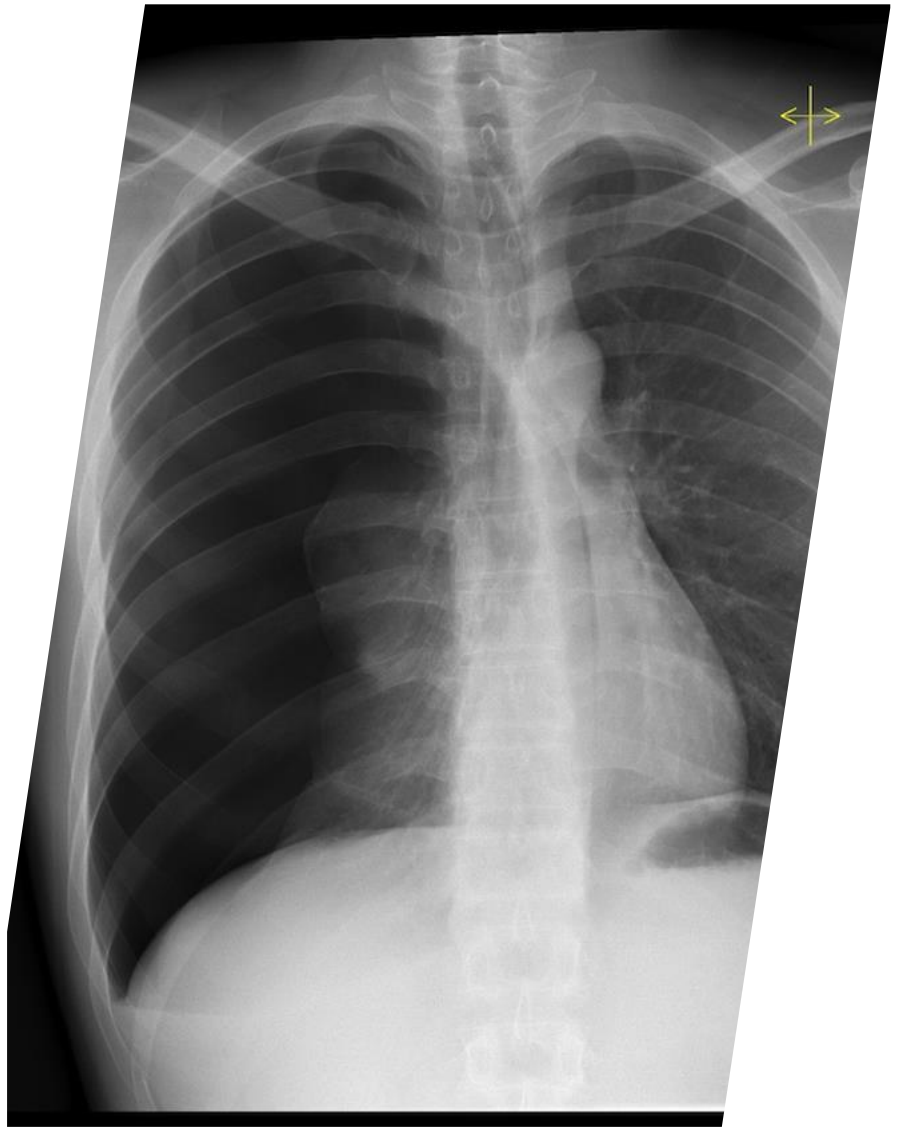
- Number of days in hospital up to 30 days after randomisation, including initial hospital stay and re-admissions.
- Pain and breathlessness visual analogue scale (VAS) scores measured at baseline, 48 hours, 14 and 30 days collected using an online application.
- Participant-reported health status (EQ-5D-5L questionnaire) measured at baseline, 48 hours, 14 and 30 days
- Perceived participant acceptability of the intervention or comparator at 30 days
- Radiographic resolution of PSP at 30 days
- Adverse events up to 30 days
- Total number of subsequent pleural procedures up to 30 days.
- Time to return to work (if employed)
- Hospital resource use up to 12 months, including emergency, admitted, critical and outpatient care
- Time to recurrence of pneumothorax up to 12 months (estimated at 12 months).

# Trial eligibility

- **Inclusion criteria**
  - PSP of sufficient size and symptoms where treating physician is considering intervention.
  - Age between 16 and 50 years old (inclusive)

- **Exclusion criteria**
  - Known or suspected underlying lung disease*
  - Evidence of clinical tension pneumothorax
  - SpO2<92% on air
  - Bilateral pneumothorax
  - Pregnancy
  - Inability to consent or comply with trial requirements

*"Childhood asthma" or well controlled asthma is not considered an exclusion criterion. Patients with a diagnosis of asthma in childhood/young adulthood who do not require the use of a regular "preventer" inhaler (i.e. inhaler containing a steroid or long-acting beta-agonist), and only occasionally use a "reliever" inhaler (short-acting beta-agonist) and have never been hospitalised due to asthma remain eligible for participation in this study.



# Size and Symptoms

- No set size of pneumothorax or degree of symptoms
- Typically, would need >2cm intrapleural distance to safely intervene

# Treatment Groups

## Intervention: CONSERVATIVE CARE

- Patients managed ***without*** invasive intervention

- Patients to be observed (length of observation period prior to discharge is at discretion of treating clinician)

- Symptoms may be managed using analgesia
- After the observation period the participant should be discharged if they meet all of the following criteria:

    - a) Symptoms controlled sufficiently to mobilise comfortably;
    - b) Acceptable vital signs to a senior physician;
    - c) No requirement for supplementary oxygen.

We recommend an early clinical follow up (within 7-10 days post randomisation) for patients managed on the conservative pathway- this is to ensure patient safety.

# Usual Care Following Initial Allocation to Conservative Care

There may be circumstances whereby patients initially allocated to conservative care are required to undergo usual care.

If during the observation period:

a) Patient requests intervention due to significant symptoms
b) Patient develops physiological instability (SpO2 <92% on air, respiratory rate > 25 breaths per minute)
c) Repeat chest radiograph demonstrating an enlarging pneumothorax with clinical concern from a senior clinician (e.g. ST4 or above) with the reason recorded.

If, after the observation period, the patient does not meet the criteria for discharge, they will undergo usual care.

*If a patient allocated to conservative care, goes on to receives a pleural procedure, this will count as a primary outcome event *

!

# Treatment Groups

## Comparator: USUAL CARE

- Patients managed using usual **invasive care**
- Pleural procedure administered is at the discretion of treating clinician. Procedures should be attempted as per BTS guidelines and in accordance with local protocols
  - Needle Aspiration (NA)
  - Intercostal Chest Drain (ICD)
  - Pleural Vent

# Data Collection and Study Documentation

# Recruitment

Patients not eligible

**1.** Patients who present in the Emergency department with a PSP and fit the inclusion criteria are identified and SL1 CRF completed

**2.** Patient is approached by local research team and given an overview of the trial with the **Patient Information Leaflet (PIL).** The accompanying animation may also be shown.

Patients not interested

**3.** Patient gives **written** consent. This is taken by a delegated member of staff and documented in patient notes.

GP Letter sent

**4. Patient randomised** using Sealed Envelope

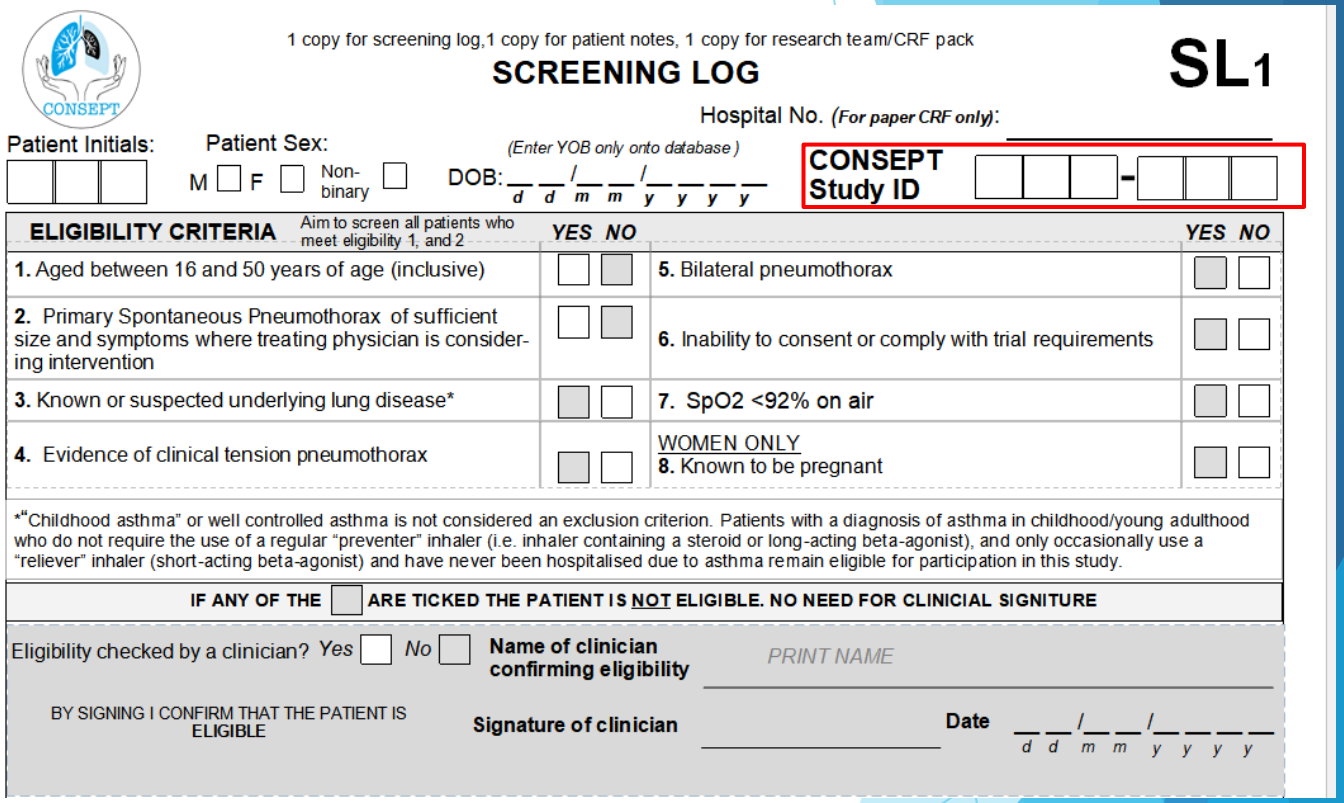
**Treatment group allocated**

Conservative Care

Usual Care

# Screening

- Sites **should aim** to screen all patients who fit the **inclusion** criteria (Points 1 and 2).
- We request a screening log entry for all patients who meet the inclusion criteria, regardless of whether they are eligible or not. This is important for monitoring and will be valuable for the study team to know why patients weren't recruited to the study.
- Screening logs with pre-filled study IDs will be sent to site



1 copy for screening log,1 copy for patient notes, 1 copy for research team/CRF pack

**SCREENING LOG** **SL1**

Hospital No. *(For paper CRF only)*:

Patient Initials:

Patient Sex: M ☐ F ☐ Non-binary ☐

DOB: __ __ / __ __ / __ __ __ __ *(Enter YOB only onto database)*

**CONSEPT Study ID** ☐☐☐-☐☐☐

| **ELIGIBILITY CRITERIA** Aim to screen all patients who meet eligibility 1, and 2 | YES | NO | | YES | NO |
|---|---|---|---|---|---|
| **1.** Aged between 16 and 50 years of age (inclusive) | ☐ | ☐ | **5.** Bilateral pneumothorax | ☐ | ☐ |
| **2.** Primary Spontaneous Pneumothorax of sufficient size and symptoms where treating physician is considering intervention | ☐ | ☐ | **6.** Inability to consent or comply with trial requirements | ☐ | ☐ |
| **3.** Known or suspected underlying lung disease* | ☐ | ☐ | **7.** SpO2 <92% on air | ☐ | ☐ |
| **4.** Evidence of clinical tension pneumothorax | ☐ | ☐ | WOMEN ONLY **8.** Known to be pregnant | ☐ | ☐ |

*"Childhood asthma" or well controlled asthma is not considered an exclusion criterion. Patients with a diagnosis of asthma in childhood/young adulthood who do not require the use of a regular "preventer" inhaler (i.e. inhaler containing a steroid or long-acting beta-agonist), and only occasionally use a "reliever" inhaler (short-acting beta-agonist) and have never been hospitalised due to asthma remain eligible for participation in this study.

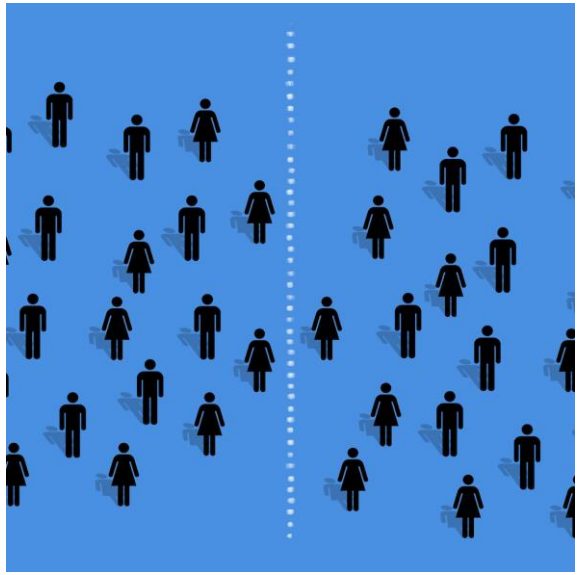
**IF ANY OF THE ☐ ARE TICKED THE PATIENT IS NOT ELIGIBLE. NO NEED FOR CLINICIAL SIGNITURE**

Eligibility checked by a clinician? *Yes* ☐ *No* ☐ **Name of clinician confirming eligibility** *PRINT NAME*

BY SIGNING I CONFIRM THAT THE PATIENT IS ELIGIBLE **Signature of clinician** **Date** __ __ / __ __ / __ __ __ __

# Randomisation

sealed envelope™



- Patient has provided written informed consent
- Member of staff is delegated to perform this task
- Prior to any invention given for treatment of PSP

- Currently, randomisation is performed using the online Sealed Envelope simple randomisation service – we will provide an instruction document with the trial password.
- Please use your personal work email address and the pre-filled Trial ID from the SL CRFs.

- Once developed, randomisation will be performed through a bespoke Sealed Envelope service and linked with the trial database.

# Training Requirements

- Members of the team undertaking trial specific activities will be required to complete trial specific training (attend SIV or review slides), hold a valid GCP certificate and provide a copy of their current CV
- All staff undertaking trial specific activities must be signed off by the local PI on the delegation log

# The Associate PI Scheme

CONSEPT is registered to the **NIHR Associate PI (API) Scheme**, aiming to develop Principal Investigators of the future.

- Six month in-work training/mentorship opportunity
- Provides practical experience for health and care professionals starting their research career
- For people who would not normally have the opportunity to take part in clinical research in their day-to-day role
- The chance to experience what it means to work on, and deliver, an NIHR portfolio study under the mentorship of an enthusiastic Local PI
- Receive formal recognition of engagement in NIHR Portfolio research studies through the certification of Associate PI status, endorsed by the NIHR and Royal Colleges

# Applicant Eligibility Criteria

- Any qualified NHS health and care professional (doctor, nurse, midwife, AHP, pharmacist, etc). This also includes Trainees from FY1 upwards
- Applicants can only be an Associate PI for one study at a time
- The general rule is that the NIHR allow one Associate PI, per study, per site (1 Associate PI to 1 PI)
- Not eligible if your role is specifically funded to work on research or you are funded to deliver the study
- Associate PIs must be able to commit to 6 months of working on a study at their site
- Associate PIs must gain prior approval from their Local PI

# How to get involved

Interested staff are welcome to contact the CONSEPT team for more information. Alternatively for more details and the registration form please follow the links below:

**Go to the NIHR Associate PI Scheme Website:**
www.NIHR.ac.uk/AssociatePIScheme

Complete the Associate PI Scheme Applicant Registration Form


NIHR | National Institute for Health Research

Associate PI Scheme - Applicant Registration Form

This form should be completed by applicants wishing to register for the Associate PI scheme.

If you would like to apply for Covid-19 Urgent Public Health studies, please use the form at the following link:
https://docs.google.com/forms/d/e/1FAIpQLSc-y-Y_qql42hFkznZk_eZLCNkCq7liUYZkiI4I0Kxy0nDykQ/viewform

The scheme has been endorsed by the NIHR Clinical Research Network and the following Royal Colleges:

# Trial Systems – In development

| Site Files | Patient Database | Follow-up Management |
| --- | --- | --- |
| Electronic Investigator Site File held on SharePoint – trial team arrange access to specific email addresses<br><br>Electronic delegation log, CV, GCP & training records held on MANGO database – registration required | Until developed, please complete paper CRFs. We will request scanned copies of SL & consent forms for randomised patients, via trial NHS mailbox | Until developed, the CONSEPT trial team will let you know when the follow up questionnaires are due for your patients |
|  |  |  |

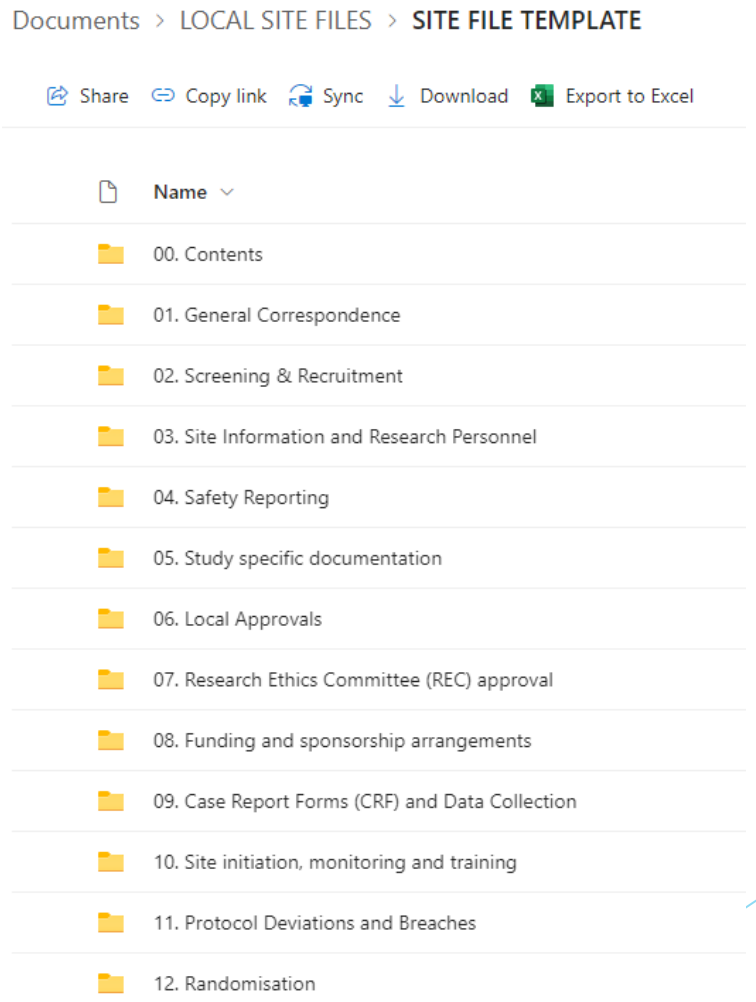
# SharePoint: electronic ISF

CONSEPT uses electronic ISFs, which are accessed via SharePoint. We will provide an instruction document and ask you to let us know email addresses of those who require access.

Some parts of the ISF will be pre-populated with documents - there will also be file notes for you to complete.

You should use the folders as you would a paper ISF, e.g., localised documents, amendments, local approvals.

We will monitor the electronic ISF so please ensure that it is kept up to date.



# MANGO Trial Management System

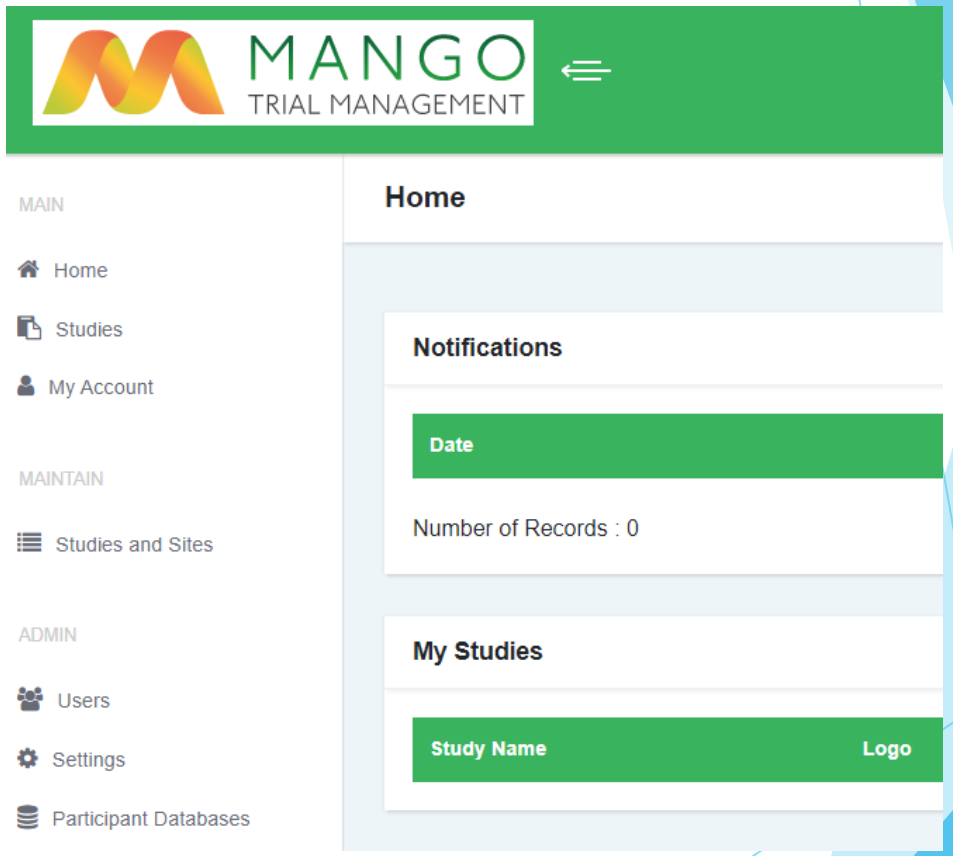
In place of paper documents and numerous emails, this trial will be using the MANGO system for:

- Electronic delegation log
- CV and GCP certificate upload
- Evidence of trial training

Following the SIV, we will send registration instructions and a link to the system.

You will first register to MANGO, and then request access to the CONSEPT area of the system.

You should not carry out any study activities until your CONSEPT registration has been approved by the local PI.



# Delegation log approval

- 1. Study team member registers for the online Trial Management System
- 2. In the case of the PI:
  - The coordinating centre will check and approve the PI's access
- 3. For all other study team members:
  - The coordinating centre checks the registration and documents, and if ok, set the person as 'checked'
  - The PI then needs to log in and approve access for their team

* The coordinating centre can approve access on behalf of the PI if we receive an email stating the name of the person to be approved.

**REGISTER → CHECK → PI APPROVAL → ACCESS**

# Data Collection Timepoints

**Table 2: Data collected from each participant for the trial duration.**

| Data collection | Pre-screening | Enrolment & randomisation | Discharge | Follow-up | | | |
|---|---|---|---|---|---|---|---|
| Time | | 0 | | Online 48 hrs (±24 hrs) | Online 14 days (±72 hrs) | 30 days (+1 week) | Up to 12 months |
| Eligibility assessment | X | X | | | | | |
| Provide PIL | X | | | | | | |
| Consent | | X | | | | | |
| Chest radiograph | X | | | | | X | |
| Clinical assessment | | X | | | | X | |
| Length of hospitalisation | | X | X | | | X | |
| Pleural interventions | | X | X | | | X | |
| Surgical procedures | | | X | | | X | |
| Assessment of pain/ breathlessness (VAS) | | X | | X | X | X | |
| Hospital re-attendance | | | | | | X | X |
| Resolution of PSP | | | | | | X | |
| EQ-5D-5L score | | X | | X | X | X | |
| Acceptability questionnaire | | | | | | X | |
| Routine data | | | | | | | X |
| Pneumothorax recurrence | | | | | | | X |
| Adverse events | | Recorded as and when they occur | | | | | |

# CRF Overview

| | |
|---|---|
| SL | Screening CRF |
| A | Patient Details CRF |
| B | Baseline CRFs |
| C | Procedure Details CRFs |
| E-F | Follow Up |
| P | Change of participation status CRF |
| S0-3 | Safety CRFs |
| AE | Adverse Events and Code List for Expected Events |
| N | Note To File |

# Questionnaires

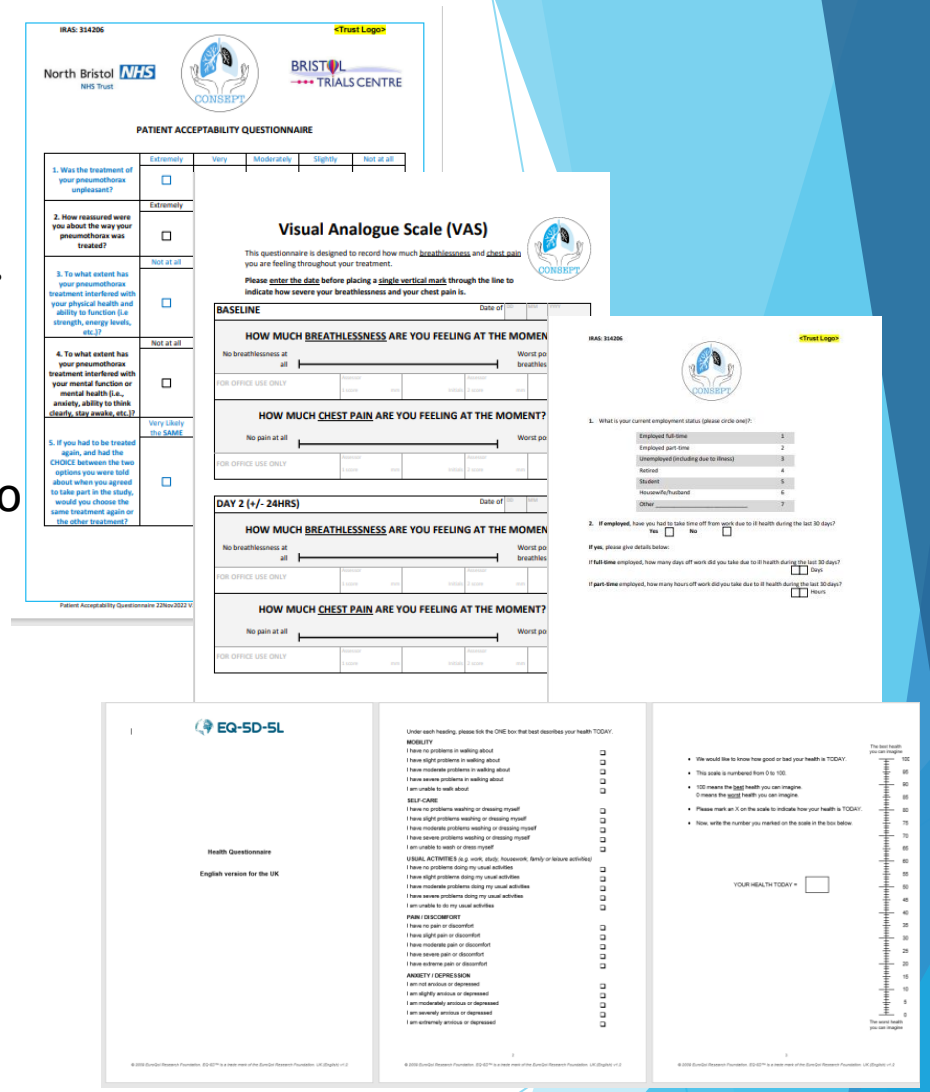
Patient reported outcomes are central to the success of this study.

- **Visual Analogue Scale (VAS)** (Baseline, 48hrs, 14 day and 30 day)
  - Used to record the level of chest pain and breathlessness experienced throughout their trial participation. Patients to mark on linear scale the severity of both.

- **EQ-5D-5L Health Questionnaire** (Baseline, 48hrs, 14 day and 30 day)
  - Used to record generic health related quality of life and data collected will be incorporated in analysis of economic issues.

- **Acceptability questionnaire** (30 day visit)
  - Perceived participant acceptability of the intervention or comparator

- **Employment Questionnaire** (Baseline and 30 day visit)
  - Economic Analysis for impact on return to work



# Follow up

- Patients will be followed up at 48hrs, 14 days and 30 days post-randomisation
- 12 month follow up will be collected via routine data
- Data on pain, breathlessness, adverse events, and quality of life will be collected
- Pending development of the follow up management system, the CONSEPT trial team will inform sites when their participants are due for questionnaires and follow up
- Follow up data collection will be via paper questionnaire or through a link emailed to the participant, depending on their preference
- Reminder emails/phone calls will be managed by sites

# Data Entry and Good Practice

- Paper documents should be stored in a secure location, with suitable archiving arrangements planned for the end of the trial
- Any corrections to paper documents should be made with a line through, leaving the original information visible – each correction should be dated and initialled
- Access to trial systems (e.g., SharePoint, MANGO) should be set up using individual email addresses and passwords should not be shared

# Safety Reporting

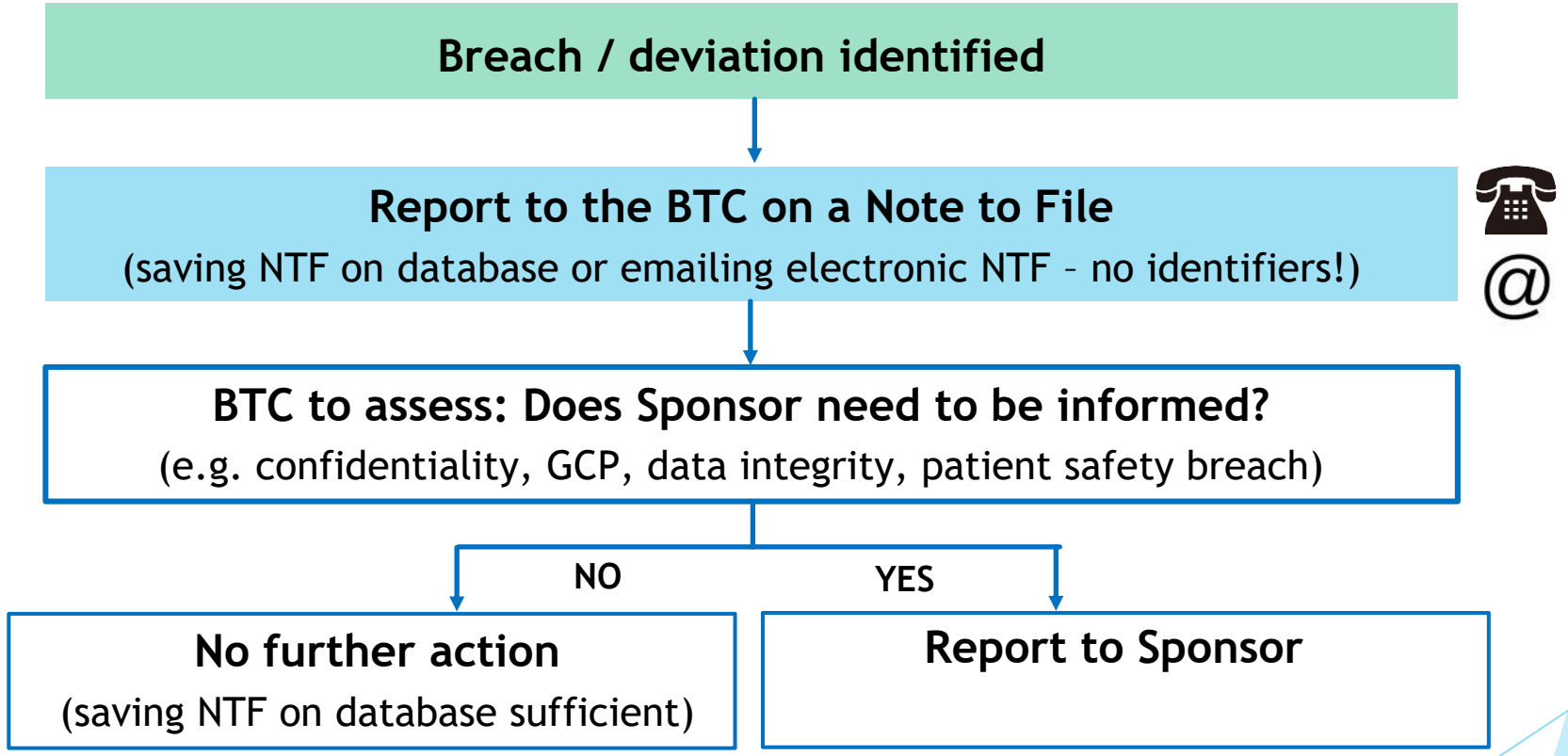
- Adverse events are categorised as expected or unexpected:
  - **Expected events** are listed in the protocol and the CRFs. These do not require an SAE report form to be completed, **except for deaths.**
  - **Unexpected events** are not listed in the protocol or CRFs. These do require reporting on an SAE report form but **only if they fulfil the serious criteria listed below and are related to the trial intervention (SUSAR).**

**Serious criteria:**

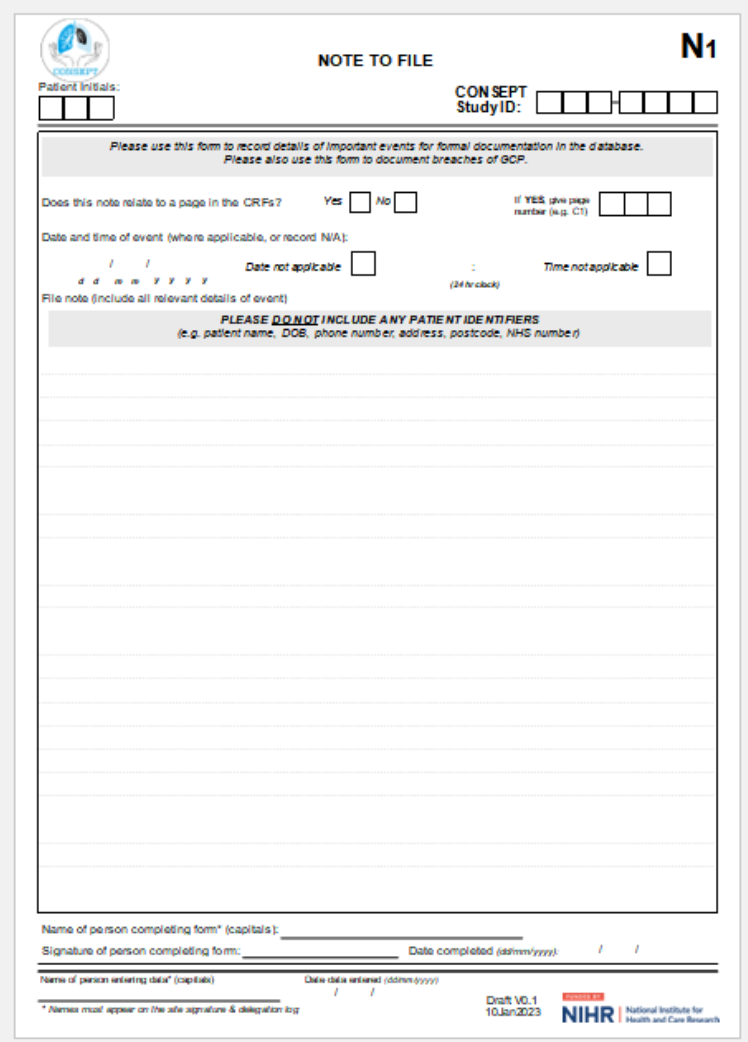
- Resulted in or increased length of hospital admission
- Is/was life threatening
- Resulted in persistent or significant disability/incapacity
- Resulted in death
- Other significant medical event

Details of all 'expected' AEs, including a description of the event and the date it started, will be recorded in the study CRFs, from the time of randomisation and for a 30 day period post randomisation.

# Protocol Deviations & Breaches



# Note to File



NOTE TO FILE

N1

Patient Initials:

CONSEPT StudyID:

*Please use this form to record details of important events for formal documentation in the database.*
*Please also use this form to document breaches of GCP.*

Does this note relate to a page in the CRFs? Yes No If YES, give page number (e.g. C1)

Date and time of event (where applicable, or record N/A):

d d m m y y y y Date not applicable

: (24 hr clock) Time not applicable

File note (include all relevant details of event)

***PLEASE DO NOT INCLUDE ANY PATIENT IDENTIFIERS***
*(e.g. patient name, DOB, phone number, address, postcode, NHS number)*

Name of person completing form* (capitals):

Signature of person completing form: Date completed (dd/mm/yyyy): / /

Name of person entering data* (capitals) Date data entered (dd/mm/yyyy) / /

* Names must appear on the site signature & delegation log

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- Date/time of event
- Finding
- Corrective actions
- Preventative actions

# Site Payments

| | |
|---|---|
| **Per site set-up fee** | **£300** |
| **Per-patient fee (upon completion of baseline, randomisation, 48 hr, 14 day and 30 day visits)** | **£145** |
| **Archiving fee** | **To be agreed** |

- Please note payment will be approved after review of quarterly activity reports and resolved data queries.
- Per participant fees can be invoiced for quarterly; the central trials team will provide sites with a breakdown and an invoice can then be sent to Sponsor

# Next Steps

You will be sent an SIV report, listing the activities still to be completed before we can issue the “green light” for your site to start recruitment. These may include:

- Local trial team have completed and been approved on delegation log
- Patient facing documents localised
- PI protocol signature sheet completed and returned
- Contract (mNCA) fully executed
- Confirmation of local capacity & capability


Any trial staff unable to attend this SIV must complete the trial training before undertaking any trial specific activities

# Contact us

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# Thank you for your time

# Any Questions?