ILO-i

Inducible Laryngeal Obstruction in adults: developing a standardised non-pharmacological intervention.

STUDY PROTOCOL

SPONSOR: **The University of Manchester**

PROTOCOL VERSION NUMBER AND DATE: **Version 1.3, 19.01.2024**

This protocol has regard for the HRA guidance. This project will be conducted in accordance with the study protocol and the ethical principles outlined by Good Clinical Practice (GCP) and the Declaration of Helsinki in its most current version.

AMENDMENT HISTORY

Amendment No.	Protocol Version and date	Details of Changes Made
1	1.0, 23.09.23	Edits based on study steering group review
2	1.1, 06.10.23	Edits based on Sponsor review: • Students/supervisors marked on contacts page • Inclusion of End of Study process (section 9) • Inclusion of overall sample size (section 7) • Inclusion of monitoring and quality assurance (section 9) • Change participating organisations to PIC sites not research sites in line with Sponsor guidance (section 6) • Additional information of risk and mitigation of risk (section 9.1) • Updated information on sample identification (section 7.3)

		• Updated information on consent • (section 7.3.2)
3	1.2, 27.11.2023	• Updated selection technique (section 7.2.2) following Provisional Opinion actions from Research Ethics Committee

RESEARCH REFERENCE NUMBERS

IRAS Number:	335820
SPONSORS Number:	NHS002135
FUNDERS Number:	NIHR Manchester Biomedical Research Centre (NIHR203308). The study is also supported by a project grant from the North West Lung Centre Charity.

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, the Sponsor's SOPs, and other regulatory requirement.

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 investigation without the prior written consent of the Sponsor

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

For and on behalf of the Study Sponsor:

Signature:
.....

Date:
...../...../.....

Name (please print):
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Position:
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Chief Investigator:

Signature:
.....

Date:
...../...../.....

Name: (please print):
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KEY STUDY CONTACTS

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Study Co-ordinator	Jemma Haines, University of Manchester, 2nd Floor, Education and Research Centre, Southmoor Road, Wythenshawe, Manchester, M23 9LT, Tel: 0161 2915879, Email:jemma.haines@manchester.ac.uk
Sponsor	The University of Manchester, Ms Lynne Macrae, Faculty Research Practice Governance Co-ordinator,Faculty of Biology, Medicine and Health, 5.012 Carys Bannister Building, The University of Manchester, M13 9PL, Tel: 0161 275 5436, Email: FBMHethics@manchester.ac.uk
Joint-sponsor(s)/co-sponsor(s)	Not applicable
Funder(s)	The study will be supported by a project grant from the North West Lung Centre Charity.
Key Protocol Contributors	Jemma Haines (Student): Jemma.Haines@manchester.ac.uk Janelle Yorke (Supervisor): janelle.yorke@manchester.ac.uk Stephen Fowler(Supervisor): Stephen.Fowler@manchester.ac.uk Jacky Smith (Supervisor): Jacky.Smith@manchester.ac.uk
Committees	Not applicable

STUDY SUMMARY

Study Title	Inducible laryngeal obstruction in adults: developing a standardised non-pharmacological intervention
Internal ref. no. (or short title)	ILO-i
Study Design	This is a three phase non-interventional qualitative study to develop a standardised non-pharmacological intervention for adults with ILO
Study Participants	• Healthcare professionals who diagnose and treat adults with ILO • Patients (>18 years old) with endoscopically diagnosed ILO
Planned Size of Sample (if applicable)	Stage 1: 5-7 participants (healthcare professionals) Stage 2: 20-27 participants (treatment naïve patients, n=5-7; post treatment patients, n=15-20) Stage 3: 20-27 participants from Stage 1 & 2 (health care professionals, n=5-7; patients, n=15-20)

Follow up duration (if applicable)	N/A
Planned Study Period	Stage 1:February 2024 – March 2024 Stage 2: March 2024 – September 2024 Stage 3: September 2024 – November 2024
Research Question/Aim(s)	To develop and describe a non-pharmacological standardised intervention for adults with ILO, in line with the TIDieR framework

FUNDING AND SUPPORT IN KIND

FUNDER(S)	FINANCIAL AND NON FINANCIALSUPPORT GIVEN
NIHR Manchester Biomedical Research Centre Contact: Zoe Talks Zoe.Talks@mft.nhs.uk	The Chief Investigator is a PhD Fellow, supported by NIHR Manchester Biomedical Research Centre (NIHR203308).
North West Lung Centre Charity Contact: Claire Murray Clare.Murray@manchester.ac.uk	The Chief Investigator is a recipient of a project grant from the North West Lung Centre Charity to support time and project delivery.

ROLE OF STUDY SPONSOR AND FUNDER

The University of Manchester is acting as sponsor for this study and is assuming overall responsibility for the initiation and management of the study. The University of Manchester will provide permission to conduct the research and monitor the progress of that research. The research team all hold substantive or honorary contracts with the University of Manchester and therefore the sponsor has influence over all aspects of the study design, conduct, data analysis and interpretation, manuscript writing, and dissemination of results, which are the responsibility of the research team.

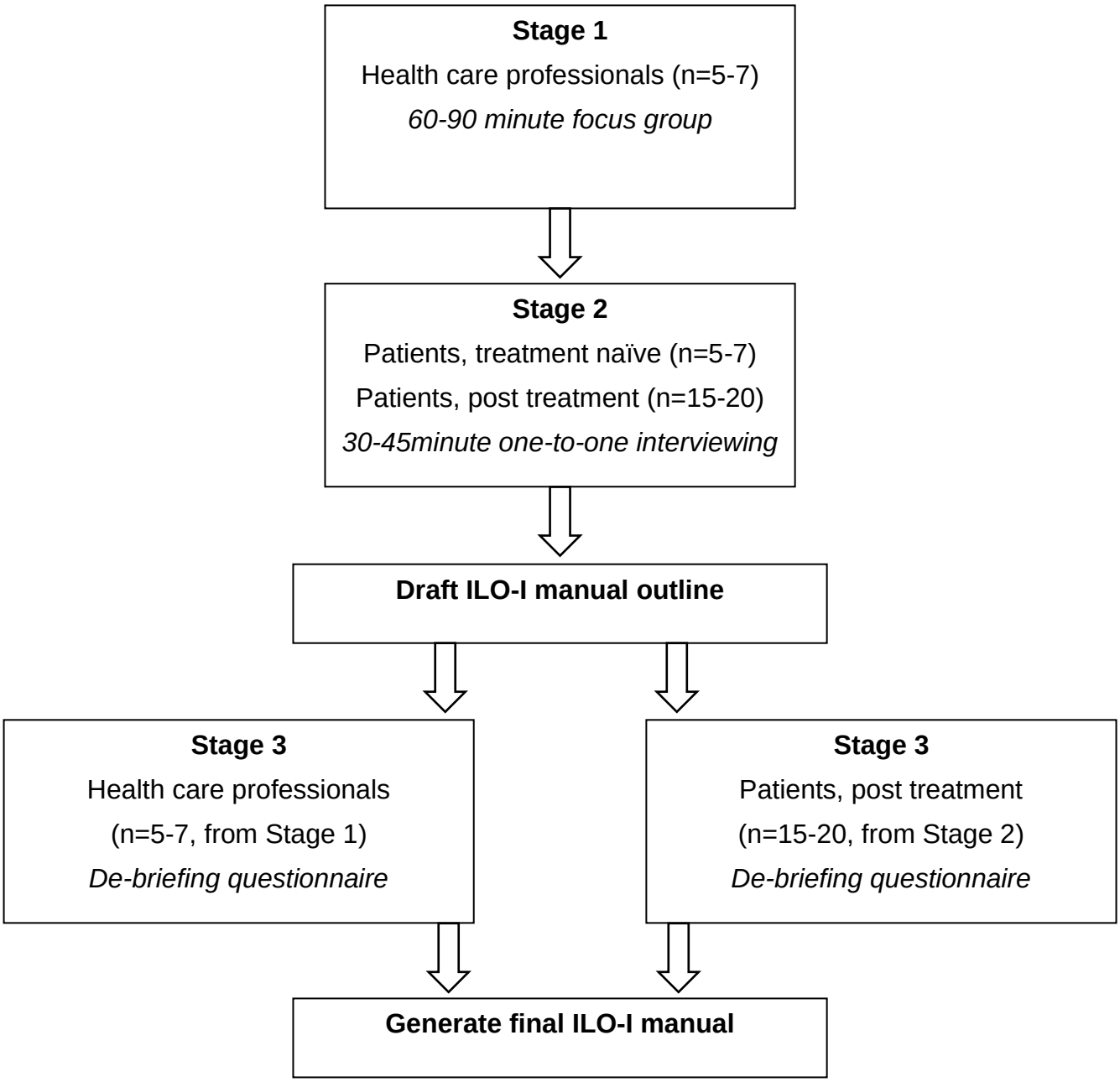
ROLES AND RESPONSIBILITIES OF STUDY MANAGEMENT COMMITEES/GROUPS & INDIVIDUALS

Study Steering Group

Professor Stephen Fowler, Professor Jacky Smith and Professor Janelle Yorke, as part of the Chief Investigator's PhD supervisory team, will offer advice and guidance regarding the study management and conduct.

KEY WORDS: Inducible laryngeal obstruction, complex interventions, non-pharmacological, intervention development

STUDY FLOW CHART



STUDY PROTOCOL

1 BACKGROUND

Inducible laryngeal obstruction (ILO) describes inappropriate laryngeal closure during respiration, with airflow obstruction occurring at the glottic and/or supraglottic level, leading to breathlessness (1). Patients typically present with sudden onset breathlessness and present across various healthcare settings with differing levels of morbidity. Despite a clearly distinct pathophysiology, the symptoms of ILO are akin to asthma and therefore many individuals are mismanaged as such (2). The average time for misdiagnosis is lengthy (5.4 years) (3) meaning escalating pharmacological burden (4) with high healthcare utilisation is prominent, which in turn leads to significant levels of patient morbidity (5).

Research relating to ILO is in the embryonic state which may account for why many individuals are often misdiagnosed as asthma and suffer inappropriate pharmacological burden, such as escalating corticosteroids dosing. The mechanistic drivers for ILO are poorly understood but suggestion of a laryngeal sensitisation and a consequential laryngeal hyper-responsiveness (6) provides a plausible hypothesis; robust testing of this theory is warranted to facilitate further insight.

Even when an ILO diagnosis is objectively confirmed, to date, there is no recognised standardised treatment. Therapy-based management approaches are regularly mentioned in the literature and are often employed in the clinical context; speech and language therapy (SLT) is commonly referred to as the beneficial gold standard (7). Despite non-pharmacological behavioural therapy being the commonly cited treatment efficacy is largely unknown; the potential effective components of intervention, mode of delivery and acceptability is poorly understood.

A recent systematic review (8) synthesised current evidence based on the effectiveness of existing non-pharmacological interventions used to treat adults with ILO. The review concluded the literature is dominated by low-level evidence and high bias publications and no randomised control trials exist, resulting in a lack of robust data to truly inform on the effectiveness of existing interventions. However, positive signals in the synthesis performed support non-pharmacological approaches and indicate further development is justified.

2 RATIONALE

Adults with ILO suffer significant morbidity and place demand on healthcare resource. Sufferers and health care professionals commonly report frustration with the lack of understanding on optimal treatment methods. Therefore, investigation and study to understand the most efficacious approach is justified.

In a clinical context, non-pharmacological interventions used to treat adults with ILO typically involve delivery of multi-modal interacting components in an attempt to effect change. As such, the treatment qualifies as a complex intervention and consideration of the Medical Research Council (MRC) framework for developing and evaluating complex interventions (9) should be applied to support a robust research approach.

In a recent randomised controlled trial of speech pathology intervention in ILO (10), study investigators terminated the study prior to completion. Although early termination of the trial was mainly attributed to complications with placebo delivery, acknowledgment was also given that greater preparation and training of the target intervention may have helped. Therefore, this gives further rationale to ensure any developed standardised interventions are done so robustly, with focus on exploring all aspects of treatment with varied stakeholders.

To date, there are many key uncertainties in the delivery of non-pharmacological interventions used to treat adults with ILO. Specifically the components of intervention, underlying processes to support them, acceptability and mode of delivery are yet to be explored. Further, how any intervention may interact with the context it is delivered is unknown.

Rationale for study is therefore, to develop an intervention for adults with ILO that considers context, develops programme theory, engages key stakeholders, identifies key uncertainties and then is refined to finalise a standardised intervention for future feasibility testing.

3 THEORETICAL FRAMEWORK

The new MRC framework for developing and evaluating complex interventions aims to deliver interventions that are implementable, cost effective, transferrable and scalable to real world practice (11). The framework divides complex intervention research into four phases: development or identification of the intervention, feasibility, evaluation and implementation. As identified, there are no existing, robustly developed, reported standardised interventions to treat adults with ILO. Therefore it is justified to apply the aforementioned MRC framework and to initiate the research programme (i.e. the current study) at the development phase.

It is important in any intervention development that there is completeness of reporting to ultimately improve replicability. It has been reported, in a systematic review, that only 29% of non-pharmacological interventions were described adequately (12). Any developed intervention will therefore be described using the TIDieR (Template for intervention description and replication checklist and guide) framework (13). Template items include: brief name; why; what (materials & procedures); who provided; how; where; when and how much; tailoring; modifications. Detail will be

needed for each component of the intervention and application of the framework will facilitate description in enough detail to support replication.

4 RESEARCH QUESTION/AIM(S)

- To develop and describe a non-pharmacological standardised intervention for adults with ILO, in line with the TIDieR framework

4.1 Objectives

- To establish, from a healthcare professionals focus group, the most important considerations when delivering a non-pharmacological intervention to adults with ILO
- To gather information from adult patients diagnosed with ILO, through patient interviews, what they think should be included in non-pharmacological ILO intervention and how this should be delivered
- To gain constructive feedback on a proposed standardised non-pharmacological intervention for adults with ILO, from both health care professionals and patients

4.2 Outcome

- To produce a treatment manual, ready for future feasibility testing, for a standardised non-pharmacological intervention to treat adults with ILO.

5 STUDY DESIGN and METHODS of DATA COLLECTION AND DATA ANALYIS

The proposed methodology will consist of three stages:

Stage 1:

A focus group with health care professionals will build on previous work from the chief investigator (8,14) and explore attitudes and beliefs on the timing of intervention, dosing, delivery mode and components of non-pharmacological interventions used to treat adults with ILO. The focus group is expected to last approximately 60-90 minutes and will be held virtually and recorded on Microsoft Teams and then transcribed. The transcription will be coded and analysed using thematic analysis and help inform Stage 2 themes for exploration.

Stage 2:

One-to-one interviews will explore adult patients' views and attitudes toward non-pharmacological interventions for ILO. An interview guide will be developed based on triangulation of:

1. a systematic review on the effectiveness of non-pharmacological interventions used to treat adults with ILO (8)
2. the key components of non-pharmacological interventions identified by expert health care professionals during a nominal group technique exercise (14)
3. the key behaviour change techniques identified in use within existing current practice to treat adults with ILO (15)
4. themes identified during Stage 1 healthcare professionals focus group

Specifically, the semi-structured interviews will explore how patients perceive the effectiveness, acceptability and importance of interventions, and if there are any preferences for delivery methods. Interviews will be conducted with treatment naïve and post treatment patients to ensure data capture across the treatment pathway and to support understanding of any variance. Recruitment will be multi-centre to reduce the risk of any bias in treatment approaches skewing patient experience and opinion.

The one-to-once interviews are expected to last approximately 30-45 minutes and will be held virtually and recorded on Microsoft Teams and then transcribed. The transcription will be coded and analysed using thematic analysis. Following this analysis, the first draft of a standardised non-pharmacological intervention for adults with ILO will be complete and enable progression to Stage 3.

Stage 3:

The draft manual for standardised non-pharmacological treatment intervention for adults with ILO, completed in Stage 2, will be shown to both patients and healthcare professionals, together with a bespoke designed debriefing questionnaire. The questionnaire will review the proposed intervention and check clarity of content, acceptability and any additional aspects requiring further stakeholder input following Stages 1 and 2.

The questionnaires will be analysed and any modifications to the draft manual made, based on healthcare professional and patient feedback. A final manual will then be produced for a standardised non-pharmacological intervention to treat adults with ILO.

6 STUDY SETTING

This is a single centre study, hosted by Manchester University NHS Foundation Trust. It will

recruit patient participants from the following Participant Identification Centres (PICs):

- Manchester University NHS Foundation Trust
- Lancashire Teaching Hospitals NHS Foundation Trust
- University Hospitals Birmingham NHS Foundation Trust
- Sheffield Teaching Hospitals NHS Foundation Trust

Health care professionals will be recruited from national professional networks, multi-disciplinary and national meetings.

Stage 1 focus group and Stage 2 one-to-one interviews will be held virtually and recorded on Microsoft Teams. Stage 3 will be completed electronically via an NHS net email account with participants recruited from Stage 1 and 2.

7 SAMPLE AND RECRUITMENT

7.1 Eligibility Criteria

7.1.1 Inclusion criteria

Healthcare professionals:

- Experienced (defined as holding a regular ILO caseload for >3 years) in assessing, diagnosing and delivering non-pharmacological treatment to adults with ILO

Treatment naïve patients:

- An established diagnosis of ILO based on i) clinical evaluation AND ii) endoscopic visualisation of laryngeal obstruction during a symptomatic episode
- > 18 years old
- Have not received and completed non-pharmacological / behavioural therapy intervention for ILO

Post treatment patients:

- An established diagnosis of ILO based on i) clinical evaluation ii) endoscopic visualisation of laryngeal obstruction during a symptomatic episode
- > 18 years old
- Have received and completed a non-pharmacological behavioural therapy intervention for ILO

7.1.2 Exclusion criteria

Healthcare professionals:

- Healthcare professionals who have no specialist experience of assessing, diagnosing and delivering non-pharmacological treatment to adults with ILO

Treatment naïve patients:

- Have received *any* previous therapy intervention for ILO, refractory chronic cough or upper airways symptoms (e.g. muscle tension dysphonia, globus pharyngeaous)
- Have uncontrolled asthma airway inflammation or obstruction (defined as fractional exhaled nitric oxide >50ppb, FEV1/FVC <70%)

Post treatment patients:

- Have completed a non-pharmacological behavioural therapy intervention for ILO greater than 4 months prior to study
- Have uncontrolled airway inflammation or obstruction (defined as fractional exhaled nitric oxide >50ppb, FEV1/FVC <70%)

7.2 Sampling

Sample size will aim to achieve data adequacy; data saturation parameters in previous similar methodological studies (16) have guided sample size justification. The overall sample size will be 25-34 participants.

7.2.1 Size of sample

Stage 1:

- 5-7 healthcare professionals

Stage 2:

- 5-7 treatment naïve patients
- 15-20 post treatment patients

Stage 3:

- 5-7 previously recruited healthcare professionals from Stage 1
- 15-20 previously recruited post treatment patients from Stage 2

7.2.2 Sampling technique

Patient and healthcare professionals who meet inclusion and exclusion criteria will be given an opportunity to participate in the study. Selecting participants based on the inclusion/exclusion criteria set will ensure a representative sample of the target audience. Consecutive recruitment will be employed to achieve the target sample, i.e., every consecutive participant who meets the criteria of inclusion and is willing to consent to the study will be selected. Rationale for using consecutive sampling is to control sampling bias as it will include all available subjects.

7.3 Recruitment

The recruitment sites are all secondary or tertiary referral centres for the assessment, diagnosis and treatment of ILO. All patients referred to each of the clinical sites with suspected ILO will receive a full multi-disciplinary review, endoscopic evaluation and differential diagnosis as part of standard care. Each centre has a minimum of 80 endoscopically confirmed diagnosed ILO patients per annum; Manchester University NHS Foundation trust makes over 180.

Healthcare professionals with experience in assessing, diagnosing and delivering non-pharmacological treatment for ILO will be recruited through the Royal College of Speech and Language Therapists Clinical Excellence Network for Upper Airways Disorders.

7.3.1 Sample identification

Patients:

The clinical team at each site will identify potential participants, during clinical consultations/clinic list review and once an ILO diagnosis is endoscopically confirmed. Clinical staff will ask any potential participants whether they are interested in participating in the study or not. They will provide written information about the study, in the form of a Participant Information Sheet (PIS). The clinical care team will complete a Consent to Contact form with the potential participant. This will seek permission to share their personal data with the research team so they can contact to discuss further.

The clinical team will then inform the chief investigator (Jemma Haines) of any potential participants in receipt of a PIS, who will then contact the patient to discuss in more detail after 24 hours. The patient will be allowed to consider the information for a week, and have the opportunity to question the chief investigator or the existing clinical team before deciding if they wish to participate in the study. If the patient does wish to consider participation in the study or to gain any further information, they should contact the chief investigator by email or phone (details provided on the PIS).

They will provide written information about the study, in the form of a Participant Information Sheet (PIS), and seek permission for the chief investigator (Jemma Haines) to telephone to discuss further. The clinical team will inform the chief investigator (Jemma Haines) of any potential participants in receipt of a PIS, who will then telephone the patient to discuss in more detail after 24 hours.

The patient will be allowed to consider the information for a week, and have the opportunity to question the chief investigator or the existing clinical team before deciding if they wish to participate in the study. If the patient does wish to consider participation in the study or to gain any further information, they should contact the chief investigator by email or phone (details provided on the PIS).

Healthcare professionals:

Potential participants will be recruited through a national professional network, the Royal College of Speech and Language Therapists Clinical Excellence Network for Upper Airways Disorders, which comprises over 200 Speech and Language Therapists working with ILO. The group will be emailed (emails are publicly available to the membership and the CI is a member) and invited to participate and a Participant Information Sheet will be sent.

7.3.2 Consent

Informed consent will be obtained by online consent via a University of Manchester approved survey system, during Microsoft Teams call (recording will not be in progress). The person obtaining consent must be suitably qualified and experienced with up-to-date Good Clinical Practice (GCP) training.

The PIS will appear before the consent form in full together with the data protection statement. Each non-optional point of consent will be able to be agreed by participants with a yes or no box. If a participant does not agree to a non-optional point of consent then they will be taken to a page thanking them for their response but informing them that they are unable to participate. Participants will be able to save a copy of their consent form as a downloadable file. Consent forms will be saved as a file with the pseudonymised participant ID number. Files, only accessible to the research team, will be stored in the University secure servers specifically the Research Data Storage which is a university-approved system for data storage for research projects. In line with University of Manchester information Governance Office Records Retention Schedule, retention of consent forms will be kept 7 years after the end of study.

If a participant who has given consent loses capacity to consent during the study they would be withdrawn from the study. Identifiable data collected with consent would be retained and used in the study. No further data would be collected, or any other research procedures carried out on or in relation to the participant.

8 STATISTICS AND QUALITATIVE ANALYSIS

Demographic and clinical data will be summarised using descriptive statistics. Stage 1 focus group and Stage 2 one-to-one interviews will be recorded on Microsoft Teams and transcribed using a professional transcription, approved by the Study sponsor, namely 1st Class Secretarial. Transcripts will be coded and analysed using thematic analysis (17) to identify emerging patterns and themes from the data and inform the aspects of intervention most likely to effect change. During analysis, a widely accepted six-phase framework will be applied, namely 1) familiarisation of data, 2) generation of initial codes, 3) searching of themes, 4) reviewing of themes, 5) defining themes, 6) write-up. Codes and themes will be stored electronically using NVivo software.

9 ETHICAL AND REGULATORY CONSIDERATIONS

9.1 Assessment and management of risk

We do not anticipate any ethical issues with this study. All data will be stored securely with only relevant team members having access. Data will be pseudonymised with a study number being used in place of the participant name. Personal identifiable information will be stored securely in paper form in the research office until it is archived according to university policy and eventually destroyed.

All participants will provide fully informed consent prior to taking part in the study and will be made aware of how data will be processed via the participant information sheet and during the informed consent discussion. All study staff are suitably trained to carry out the procedures described in the protocol and this DMP under the direction of the lead researcher, with support from the supervisory team.

Participants may feel worried about being honest about their experiences during the study. The researchers will fully inform study participants that what they say in their interviews and focus group and how they answer their questionnaires will be kept confidential and their anonymity will be protected, including from their clinical team. Discussing the lack of standardised ILO treatment may be upsetting for patient participants. However, the aims of the study will not explore lived experience of living with ILO and so it is not expected to cause significant distress. To mitigate any potential stress patients will receive a debrief sheet. This will provide clarity, support and guidance to patient participants who maybe distressed as a result of taking part in the study.

In any one-to-one interviews there could be disclosures of risk of harm to participants/others or identification of bad practice. Should this occur the researchers will escalate as appropriate, following University and NHS policy and procedures. Information regarding breaking confidentiality in these circumstances will be included in PIS and CF.

9.2 Research Ethics Committee (REC) and other Regulatory review & reports

Before the start of the study, a favourable opinion will be sought from an NHS Research Ethics Committee (REC) for the study and all the supporting documents including the protocol, information sheets, informed consent forms and other relevant documents. The study team will be responsible for the maintenance of a study site file or TMF, in which all current and superseded study documents will be retained. Also contained in the site file/TMF will be the approval documentation including

correspondence with relevant authorities such as the HRA and REC. The study team are responsible for producing progress reports throughout the study, including annual reporting (APR) to REC as required. The Chief Investigator will notify the REC of the end of the study, and will submit a final report with the results, including any publications/abstracts, to the REC within 12 months of the end of the study. If the study is ended prematurely, the Chief Investigator will notify the REC, including the reasons for the premature termination. No participants will be enrolled into this research study prior to the study being reviewed by the relevant regulatory authorities and receiving HRA and REC approvals, as well as approval from the R&D office at The University of Manchester.

Regulatory Review & Compliance

Before any site can enrol patients into the study, the Chief Investigator/Principal Investigator or designee will ensure that appropriate approvals from participating organisations are in place.

For any amendment to the study, the Chief Investigator or designee, in agreement with the sponsor will submit information to the appropriate body in order for them to issue approval for the amendment. The Chief Investigator or designee will work with sites (R&D departments at NHS sites as well as the study delivery team) so they can put the necessary arrangements in place to implement the amendment to confirm their support for the study as amended.

Amendments

Any amendments to the study shall be reviewed by the Sponsorship Team prior to submission. Any non-substantial amendments shall be notified to the HRA and any substantial amendments, along with amended documentation, shall be approved by the REC, and HRA, prior to implementation as per nationally agreed guidelines. The Chief Investigator or designee will work with the R&I department to put the necessary arrangements in place to implement the amendment and to confirm their support for the study as amended.

End of study process

In line with UoM/HRAOC/SOP006 (Version 1.0, 23/03/2023), the end of the study will relate to the point at which all data have been collected for the study and contact with participants completed. The predicted end date for this is 30 November 2024.

9.3 Peer review

The study protocol has been peer reviewed by two independent, expert healthcare professionals working with ILO.

9.4 Patient & Public Involvement

Study design and rationale is in response to repetitive feedback during clinical consultations from patients, with confirmed ILO, about the lack of understanding of ILO treatment. During development of the study design, the Chief Investigator discussed with patients attending the Manchester Airways NHS clinical service the aims and objectives of the work and potential impact it would have on ILO suffers quality of life and wellbeing. Following study completion, a general newsletter will be sent to all participants.

9.5 Protocol compliance

- The research team will be vigilant in protocol deviations and will record them on a study specific deviation log which will be regularly assessed by the chief investigator.
- Deviations that may affect the safety, physical or mental integrity of participants or scientific value of the study will be reported to the study sponsor via FBMHethics@manchester.ac.uk by the research team.
- Deviations from the protocol which are found to frequently recur are not acceptable, will require immediate action and could potentially be classified as a serious breach and should also be reported to the sponsor without delay.

9.6 Data protection and patient confidentiality

All participants enrolled in this study will be allocated a unique pseudonymised identifying code to be used throughout the study on all documentation/audio and video recordings. Participant interview recordings/transcriptions, focus group recordings/transcriptions and debriefing questionnaires will be in electronic format and saved onto a University of Manchester secure servers. The data will be transcribed by a University of Manchester approved provider. The transcripts and debriefing questionnaires will only contain a study ID assigned to the participant and no personal data. Any email correspondence regarding individual patients will occur using NHS password protected email approved by NHS confidentially arrangements.

Paper based data (screening log, enrolment log, participant ID log with pseudonymisation key, , case report forms, copies of GP letters) will be stored in a locked office in the basement of the North West Lung Research Centre, Manchester University NHS Foundation Trust, Wythenshawe Hospital. The building is only accessible by swipe card or using a coded door. The office itself has a door code and

is only accessible by staff in the research team. Electronic data (pseudonymised study data collected during study visits and entered in to databases for analysis) will be stored on a secure University of Manchester server, only accessible by relevant team members, comprising of both University of Manchester and NHS staff. Data will be stored under the pseudonymised participant ID number. A backup copy of data is made automatically to a second server.

9.7 Indemnity

The University has insurance available in respect of research involving human subjects that provides cover for legal liabilities arising from its actions or those of its staff or supervised students. The University also has insurance available that provides compensation for non-negligent harm to research subjects occasioned in circumstances that are under the control of the University.

9.8 Access to the final study dataset

The final data set will be accessed by the Chief Investigator (Jemma Haines), the study's steering group (Professor Stephen Fowler, Professor Jacky Smith and Professor Janelle Yorke) and University of Manchester statisticians. The final dataset will be stored using study codes, so considered pseudonymised and stored on an excel spreadsheet/database on a University of Manchester password protected computer. A record of participant's names and their unique subject identifier will be stored in participant ID log with pseudonymisation key, and stored in a locked office in the basement of the North West Lung Research Centre, Manchester University NHS Foundation Trust, Wythenshawe Hospital. The study statistician will not have access to patient identification records or any identifiable patient data and will only receive a full anonymised dataset for analysis. Data generated from the study will be stored for five years and then destroyed in line with University of Manchester policy and procedures.

9.8 Monitoring and quality assurance

The study will be subject to the audit and monitoring regime of the study sponsor, The University of Manchester, in line with applicable standing operating procedures and policy.

10 DISSEMINIATION POLICY

10.1 Dissemination policy

The study results will be shared through conference abstracts, conference presentations and peer-reviewed scientific journals. The study forms part of doctoral studies and anonymized data will be included in thesis submission. The participants will be provided with a general newsletter at the end of the study and provided with a copy of any publications.

10.2 Authorship eligibility guidelines and any intended use of professional writers

The investigators will be involved in writing manuscripts, abstracts and other publications arising from the study. Authors will acknowledge the funders. Authors will be determined in accordance with the International Committee of Medical Journal Editors (ICMJE) guidelines and other contributors will be acknowledged.

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