Short Study Title

RELIEF-HNC

Full Study Title

Is complete decongestive theRapy a fEasibLe and acceptable IntervEntion for patients with lymphoedema Following treatment for Head and Neck Cancer?

Aim: To refine individualised complete decongestive therapy (CDT) through co-production and investigate feasibility/acceptability of integrating the intervention into the head and neck cancer (HNC) care pathway.

This research will work together with people who have treatment for head and neck cancer (HNC), their partners/carers, and health professionals to find out about their experiences and challenges of managing long-term side effects of cancer treatment. The aim is to refine a personalised head and neck lymphoedema (HNL) treatment programme. The agreed solution will then be tested with HNC patients to get their view.

Protocol Version 1.5 01.02.2026

Research Reference Numbers

IRAS Number:	**344718**
Sponsor Reference Number:	**UoL001991.**
Funder Reference Number:	**NIHR305252**

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 publicly 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):

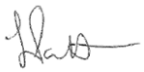
Mrs Karen Jennings-Wilding

Position:

Senior Clinical Research Governance Manager

Chief Investigator:

Date: 11/11/25

Signature: 

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Name: (please print):

PROFESSOR JOANNE PATTERSON

Key Study Contacts

Insert full details of the key study contacts including the following;

Chief Investigator	Joanne Patterson, joanne.patterson@liverpool.ac.uk
Study Co-ordinator	Alison Smith, alison.smith3@uhcw.nhs.uk PhD student
Contact for Clinical Queries	Alison Smith, alison.smith3@uhcw.nhs.uk
Sponsor	The University of Liverpool is the research Sponsor for this Study. It is recognised that as an employee of the University the Chief Investigator has been delegated specific duties, as detailed in the Sponsorship Approval letter. For further information regarding the sponsorship conditions, please contact: Mrs Karen Jennings-Wilding Senior Clinical Research Governance Manager Sponsor@liverpool.ac.uk
Key Protocol Contributors	Alison Smith – PhD Student Study Investigator Alison.smith3@uhcw.nhs.uk Prof Joanne Patterson, +44 (0)151 795 1359 joanne.patterson@liverpool.ac.uk Primary Supervisor Dr Gemma Cherry, Cherry, Gemma gcherry@liverpool.ac.uk- Secondary Supervisor Mr Jason Fleming, Jason.fleming@liverpool.ac.uk Secondary Supervisor Dr Grahame Smith, G.M.Smith@ljmu.ac.uk, 0151 2314115 – Living Labs Collaborator Professor David McWilliams, Coventry University, david.mcwilliams@uhcw.nhs.uk Practice Supervisor

	Professor Cherith Semple, Ulster University, c.semple@ulster.ac.uk Practice Supervisor Professor Heather Starmer, hstarmer@stanford.edu Practice Supervisor Mrs Helen Cassidy, helen.cassidy@communities.gov.uk Patient Co-author Sonia Kandola, sonia.kandola@uhcw.nhs.uk Research Governance and Operations Manager University Hospitals Coventry & Warwickshire NHS Trust
Committees	Patient & Public Involvement Groups

Study Summary

Study Design	WS1: To identify and critically review the content and relevance of the literature on head and neck lymphoedema (HNL) interventions and their impact on dysphagia outcomes, retention and adherence. WS2: Co-Production: Identification of solutions to acceptability, refining a HNL intervention, and materials used with patient and Healthcare Professional (HCP) stakeholder workshops, along with a principal patient co-creator. WS3: To deliver a co-produced individualised complete decongestive therapy (CDT) intervention to head and neck cancer (HNC) patients with HNL and evaluate its acceptability and feasibility.
Study Participants	**Work Stream Two** • HNC patients who have completed curative treatment for HNC • Partners/caregivers of HNC patients • HNC Allied health professions (AHPs) (i.e., dietitians, speech and

	language therapist, lymphoedema nurses) • HNC clinical nurse specialists • Head and neck consultants –oncologist, surgeons, anesthetists. • Members of Head and Neck Clinical Quality Groups (CQG) including cancer alliance or other stakeholders **Work Stream Three** Patients diagnosed with advanced HNC for treatment with curative intent with head and neck lymphoedema following surgery, radical radiotherapy (+/- chemotherapy)
Planned Size of Sample (if applicable)	WS2 Co- Production n= 27 This includes up to 16 lived experience HNC patients/caregivers and up to 10 Healthcare professionals/stakeholders) and 1 patient co-creator WS3 Feasibility study target n= maximum~ 30 to complete the feasibility study. A sample of 50 patients are projected to be screened for eligibility during the available study period. A maximum of 30 patients will be recruited to complete this study. Recruitment will stop after one year or when recruitment target has been met. Qualitative sub study target n= maximum 10
Follow up duration (if applicable)	3 months (baseline assessment – post treatment assessment 3 months post intervention)
Planned Study Period	01.05.2026 – 31.12.2027 WS2 will be undertaken in years 1-2 and WS3 in years 2-3 of the PhD
Research Question/Aim(s)	**Background:** As the incidence of head and neck cancer (HNC) is increasing with the Human Papilloma Virus (HPV), patients are living for longer

	with effects of HNC treatment, including chronic swallowing (dysphagia) impairments and head and neck lymphoedema (HNL). Up to 90% of HNC survivors will develop HNL. We know that HNL can make swallowing difficult, but we don't know how, or if, swallowing function improves following treatment of HNL. Emerging evidence supports the use of complete decongestive therapy (CDT) for treating secondary lymphoedema of the head and neck. However, patient acceptability and feasibility of CDT is limited. Adherence to rehabilitation for HNL is highlighted as a barrier to treatment, despite early research suggesting improvements in swallowing after CDT. Other practicalities such as transport and financial costs associated with hospital appointments, amongst others have been highlighted. It is crucial to understand the patient's experience of CDT to identify potential solutions to these barriers, before more robust testing of the impact of CDT on swallowing outcomes. **Research Question:** Is Complete Decongestive Therapy a feasible and acceptable intervention for patients with lymphoedema following treatment for head and neck cancer? **Aim:** To refine a programme of individualised CDT through co-production and investigate feasibility/acceptability of integrating this intervention into the HNC care pathway. **Objectives** • Perform an up-to-date systematic review on the effectiveness of CDT as an intervention in HNL patients to improve dysphagia outcomes. • Co-production to refine intervention. Address challenges identified in pre-feasibility pilot testing and potential solutions for HNC survivors' eligibility, recruitment, adherence, compliance and retention rates. This will include uptake time point in their HNC pathway, intervention components and fidelity. • Explore the mechanism of action of intervention delivery using programme theory with an embedded behaviour change framework. • Test candidate outcome measures on quality of life (QOL), patient reported swallowing outcomes measures,

	objective swallowing outcome measures, and volumetric analysis of HNL. • Obtain HNC survivors' and professionals' perspectives on acceptability of the intervention, study processes and integration into usual care using a nested qualitative sub-study. • Determine a power calculation for future RCT. • Obtain preliminary estimate of intervention cost.

Funding and Support in Kind

FUNDER(S)	FINANCIAL AND NON-FINANCIAL SUPPORT GIVEN
NIHR - NIHR305252 to complete a NIHR Doctoral Clinical and Practitioner Academic Fellowship	**Total of £ 285,129 over 3 years to support the research and training outlined in the fellowship application**

Roles and Responsibilities of Study Management Committees/Groups & Individuals

Project group – Supervisors and Collaborators

- Monthly virtual/online meetings
- Supervisors will provide guidance on data collection and analysis
- Supervisors will review research conduct and study fidelity
- Supervisors will advise on developing topic guides for co-production workshops and qualitative interviews
- Will check themes and codes from workshops and qualitative interviews to review and exchange interpretation of key issues/themes identified from data analysis
- Supervision meeting notes will be recorded within University of Liverpool supervision logs
- Living Labs specialist will provide coaching for co-production process
- Patient co-author will be involved in all aspects of the research for authorship, review of all research documentation and dissemination

Project management

AS will be responsible for overall study management, with support from applicant supervisory team. AS will meet monthly, reviewing progress, recruitment and expenditure, plan forthcoming work and addressing problems with primary academic team JP, GC, JF. AS will meet quarterly and annually for practice supervision with HS, DM & CS to review progress, support methodological research skills and professional development. Supervision sessions will be in-person or virtual. GS will will provide coaching and guidance throughout the co-production process.

A principal patient co-creator (HC) has been recruited. She is a HNC patient who received individualised CDT so is able to bring her real-world experience/validation to this study, and helped develop this proposal. She has a professional background in qualitative research and is an excellent resource for contributing towards intended feasibility objectives and co-production of the qualitative interviews. We shall act as reciprocal researchers.

The Gantt chart has study milestones which will be reviewed at regular supervisory meetings. AS will be responsible for ethical/governance processes and applications, and undertaking all aspects of study design, conduct and write up; the majority of which will aim to be completed during WS1 in conjunction with the principal patient co-creator who will meet monthly with AS.

Upon DCAF completion AS will complete a report to share with key stakeholders, researchers and the NIHR. AS will seek advice and guidance from UHCW's research department about intellectual property for the prototype at the beginning of the DCAF to ensure the prototype is secured within a contract, compatible with the header agreement with the NIHR.

Committees

This research proposal has been developed and reviewed by two patient and public involvement and engagement (PPIE) groups; Patient and Public Research Advisory Group at UHCW compromised of 14 patients, carers, and members of the public with an interest in using their experiences and perspectives to guide and influence research at UHCW; Liverpool Patient and Public Involvement group formed of 12 HNC patients accessed via the Liverpool Head and Neck Cancer Centre who reviewed the plain English summary. Patients and carers have been involved with informing this research protocol by highlighting the importance of co-production/co-production to establish an acceptable intervention and timing of this within the complex pathway.

Feedback requested:

- Research idea.
- Importance of the research question.
- What outcomes are important for patients to capture.
- The research was meaningful, important and would benefit patients.
- There should be a range of quality-of-life questionnaires provided for participants pre and post treatment.
- The carers' perspective should be included.

- Members appreciated the study aim and how some patients prefer having home therapy programmes.
- 'Non-generalised' CDT routine is more personalised.
- HC and both PPI groups have reviewed the proposal and suggestions have been made relating to:
- Recruitment information needs clearer description of impact of HNL and progressive nature of impairments.
- Plain English Summary and Abstract.
- How this research could be expanded in future to support other HNC patients and their families with a larger trial.

Continued study conduct:

These established PPI groups have both been invited to continue to support with the conduct/co-production and dissemination of this study over the next 3 years and review study conduct. I have also approached other national support groups/charities to support with study dissemination, activities will include

- Reviewing of patient information leaflets and consent forms for both work streams
- Inform themes for discussion within co-production workshops
- Review of outputs from co-production workshop and support with creation of infographics and dissemination plan to public
- Understand any recruitment barrier/ facilitators across both work streams
- Dissemination support

Finance

Financial management will be led jointly with the Trust finance lead. AS has working relationships with the research and development department, the Trust finance manager and DM from undertaking an NIHR Pre-Doctoral Clinical Academic Fellowship. AS will continue to uphold these working relationships throughout the DCAF and beyond.

Protocol Contributors

- PhD Student (and dual trained registered Speech & Language Therapist & Certified Lymphoedema therapist) – Alison Smith – Is responsible for study design, conduct, data analysis and interpretation, manuscript writing, and dissemination of results
- Supervisory team: Prof Joanne Patterson, Dr Gemma Cherry and Mr Jason Fleming– have experience in methodologies to ensure that this study follows a rigorous process. They will provide the student with support in relation to study conduct, analysis and interpretation. They will check any bias throughout the study. The student will have final decision in the output of this study.
- Dr Grahame Smith- Protocol contributor will provide specific guidance and coaching in undertaking and implementing a Living Labs process in conducting work stream two: co-production study. They will support with facilitation of workshops and check any bias in analysis.

- Practice supervisory team: Professor David McWilliams, Coventry University, Clinical Professor Heather Starmer, Stanford University and Professor Cherity Semple, Ulster University. They will provide the student with support in relation to study conduct, dissemination and data analysis.
- The protocol has received peer review from the NIHR funding review panel. The funders have no control or final decision over any final decisions within the project.

Key Words: Rehabilitation, Head and Neck Cancer, head and neck lymphoedema, Co Creation, Feasibility, swallowing.

Study Flow Chart

See Appendix 1 for flow chart: *"Complete Decongestive Therapy for patients with lymphoedema Following Treatment for Head and Neck Cancer – A Flowchart"*

Glossary of Abbreviations

AHP	Allied health professional
BCW	Behaviour change wheel
CDT	Complete decongestive therapy
CNS	Clinical nurse specialist
CRT	Chemo-radio therapy
DCAF	Doctoral clinical academic fellowship
HCP	Healthcare professional
HNC	Head and neck cancer
HNL	Head and neck lymphoedema
HPV	Human papilloma virus
HRA	Health Research Authority
MDADI	MD Anderson Dysphagia Inventory

MLD	Manual lymphatic drainage
MRC	Medical research council (complex interventions framework)
NIHR	National Institute Health & Care Research
PPI	Patient and public involvement
PICs	Patient identification centres
PROMs	Patient reported outcome measures
QOL	Quality of life
RCT	Randomised controlled trial
RDS/RSS	Research design service (now known as research support service)
REC	Research Ethics Committee
SOC	Standard of care
UHCW	University Hospitals Coventry & Warwickshire
UoL	University of Liverpool
VF	Videofluroscopy xrays
WS	Workstream

Contents

1. INTRODUCTION

This protocol describes the study entitled: **RELIEF-HNC - Is Complete Decongestive Therapy a feasible and acceptable intervention for patients with lymphoedema following treatment for head and neck cancer?** and provides information about procedures for entering participants, study procedures, safety reporting and governance requirements. Every care was taken in its drafting, but corrections or amendments may be necessary. These will be circulated to investigators in the study following receipt of required approvals.

Queries relating to this study should be referred, in the first instance, to the Chief Investigator, Professor Joanne Patterson.

This study will adhere to the principles outlined in the UK Policy Framework for Health and Social Care Research. It will be conducted in compliance with the protocol, the Data Protection Act 2018 and the UK GDPR as amended from time to time and any successor legislation in the UK and any other directly applicable regulation relating to data protection and privacy as well as any other regulatory requirements as appropriate.

2. BACKGROUND

What is the Problem?

Globally, head and neck cancer (HNC) is the 6th most common cancer [1]. As the incidence of HNC is increasing with Human Papilloma Virus (HPV) related tumours, and survival rates are improving, patients are living for longer with chronic effects of HNC treatment, one of which is head and neck lymphoedema (HNL). Lymphoedema is a chronic, incurable condition which causes an accumulation of protein-rich fluid, fibrosis and fat in the interstitial tissues as a result of failure of lymphatic drainage [2].

The impact of damage to this complex network of lymphatics in the head and neck is significant compared to the extremities [3]. External HNL refers to visible swelling of the face, neck, shoulders, lips and eyelids, whereas internal HNL encompasses swelling of the tongue, lips, cheeks, palate, oro-pharynx, and larynx [3]. Earlier stages of lymphoedema are reversible; however, if fluid is not drained, it develops over time into fibro-fatty scarring which is irreversible and less susceptible to treatment [3]. Lymphoedema treatment is identified as a priority by the Department of Health and NHS through “Living with and beyond cancer” initiative [4].

The Population

Historically, HNL has been hugely under-reported and under-treated [5]. It is now estimated that 90% of patients treated for HNC with a combination of surgery +/- chemo-radiation will develop HNL within 2-4 months of completing treatment, peaking at 9 months [6]. Patients receiving multi-modality treatments are at higher risk of developing HNL [7]. Around half of HNC patients also present with chronic dysphagia 2–3 years post treatment [8]. Chronic, late dysphagia is thought to be due to progressive fibrosis and neuropathy [9]; however, more recent evidence suggests an association between chronic dysphagia and HNL [6].

Why is it important?

Long-term side effects of HNC treatment can be as devastating as the cancer diagnosis and treatment itself, with many lasting years longer. HNL can impact on a patient’s quality of life (QOL), nutrition, hydration, social isolation, depression and appearance. Increasing severity of HNL correlates with a higher functional burden and lower QOL [8]. HNL can negatively impact on the swallow, with chronic swallowing problems identified as the

most important issue for both patients and their families when asked about QOL following HNC treatment [10,11].

Review of existing evidence

A recent scoping review as part of the 'Developing Intervention' phase of the Medical Research Council (MRC) Complex Interventions Development framework, was published prior to undertaking a full systematic review in WS1 and feasibility testing in WS2 [12]. Results found Complete Decongestive Therapy (CDT) is currently the gold standard treatment for lymphoedema in the limbs and this is well supported in the literature for breast cancer and lower limbs [13]. CDT is based on the pillars of lymphoedema treatment of compression, skincare, exercise and lymphatic drainage [14]. CDT does not easily transfer to the head and neck region due to difficulty creating, and poor tolerance of wearing, compression garments over the face and neck [15]. Whilst there are published and ongoing studies that specifically use CDT to treat HNL, there are currently no studies identified on the impact of CDT on dysphagia [12].

Internal lymphoedema (thickening/stiffness of the oral, pharyngeal and laryngeal structures) can negatively impact upon function of these structures [16]. A recent cohort study examined the relationship between chronic internal and external lymphoedema and dysphagia [17]. HNL in the epiglottis, arytenoids and pyriform sinus was associated with food and drink entering the airway, and more restrictions in the type and texture of food eaten. The authors postulated that the more structures involved, and the more severe the internal HNL, the greater the association with dysphagia. Preliminary data from a small case-series (n=4) suggested external MLD to the head and neck may have beneficial results on mobilising fluid, facilitating drainage of internal structures and improving dysphagia function [18].

There is a lack of consensus and evidence base to support effective dose, frequency and intensity of CDT, or alternative interventions [19]. Although there have been studies purporting MLD or CDT as an effective treatment for HNL [16,20,21], there are no completed RCTs examining this topic. Studies conducted so far have demonstrated methodological inconsistencies including a lack of blinding, variations in selection criteria, and principal investigators performing outcome measures [12]. An ongoing RCT registered in 2019 aims to compare CDT with a control cohort for patient's experiencing post-surgical head and neck lymphedema after surgery [22]. Results are awaited, which may provide robust evidence in support of CDT for HNL, as is hoped this study will contribute to in future.

A UK Survey of Practice undertaken in my Pre-Doctoral Clinical Academic Fellowship found disparity between services across the UK for HNL, with no consistent standard of care in assessment or treatment [23]. The most common interventions appeared to be the four pillars of CDT. Open text responses identified four themes of treatment barriers; clinician skills and knowledge, service capacity restrictions, stage of cancer pathway and patient acceptability. A sub-theme highlighted that patient motivation and compliance were prevalent issues when accessing/engaging with services, along with patient transport restrictions. It is crucial to understand the patient's experience of CDT to identify potential solutions to these barriers [45]. Pilot testing using individualised CDT to improve dysphagia outcomes with 10 patients was conducted at UHCW [24]. Results showed improvements in patient reported dysphagia outcomes following 3-months of treatment, with patients increasing both volume and texture of diet orally. However, only a 60% retention rate was achieved.

Patient transport to travel to appointments impacted on retention, corroborating my UK survey findings and other research [23,25]. Acceptability data collected in pilot testing via a patient feedback questionnaire,

suggested that intensity of CDT impacted on adherence [24]. More qualitative data on acceptability of a co-produced intervention is essential to understand how to integrate CDT into a care pathway, as current research is lacking. Further feasibility testing is proposed here to refine the protocol with flexibility for delivery, specifically to reduce the intensity of the routine to target adherence.

The Proposed Study

We know that HNL can make swallowing difficult, but we don't know how, or if, swallowing function improves following treatment of HNL. Programme Theory currently is: CDT may be an effective intervention to treat external lymphoedema, causing a consequential mobilisation of fluid which facilitates drainage of internal structures, which in turn, may improve dysphagia outcomes. However, patient acceptability and feasibility is limited. A co-produced CDT intervention is proposed here to address the gap in evidence. A preliminary estimate of the cost of intervention would be beneficial when investigating feasibility.

3. RATIONALE FOR CURRENT STUDY

Up to 90% of patients who have HNC treatment can develop HNL. These long-term side effects can be as devastating as the cancer and treatment itself, but last many years longer. Previous work has shown that people with cancer can benefit from a treatment programme known as Complete Decongestive Therapy (CDT). As explained above, CDT is made up of four parts; skincare, exercise, manual lymphatic drainage (MLD) and compression. MLD is a series of hand movements on the skin that direct fluid from an area that doesn't function to a functioning area that allows the fluid to be drained. Investigation of a personalised programme of CDT for HNC patients is suggested here.

This research will work together with people who have treatment for head and neck cancer (HNC), their partners/carers, and health professionals to find out about their experiences and challenges of managing long term side effects of cancer treatment. These side effects are known as 'late effects', one of which is head and neck lymphoedema (HNL). HNL is a backlog of fluid that collects under the skin and causes a negative impact on a person's quality of life (QOL), nutrition, hydration, social isolation, depression & how they look and feel. This research aims to provide an example of how patients receiving treatment for HNL can have an improved quality of life and better chances of swallowing a normal diet without needing to eat softer foods or rely on high calorie alternatives like drinks or liquid food through feeding tubes in the stomach. Ideas of what could be done to improve patient care and help to better manage HNL will be identified and discussed. The aim is to refine a personalised HNL treatment programme. The agreed solution will then be tested with HNC patients to get their view.

4. THEORETICAL FRAMEWORK

This study consists of three work streams designed to follow the Medical Research Council framework and guidance for developing and evaluation complex interventions (27) the **I**de**N**tifying and critiquing different approaches to **D**eveloping compl**EX** interventions (INDEX) guidance for intervention development (27,28) and process evaluation (29).

WS1: Evidence Synthesis

Evidence synthesis methodology will be used to appraise evidence on effectiveness and patient acceptability. The review will be conducted in accordance with internationally recognised standards (e.g. Centre for Reviews ad Dissemination Report 4) [30] and reported in accordance with appropriate review guidelines (e.g. Preferred Reporting Items for Systematic Reviews and Meta-Analyses) [31]. The review protocol will be registered with PROSPERO International Prospective Register of Systematic Reviews by the lead researcher (AS)

WS2: **Intervention development through co-production** – Phase one of development of complex intervention

The NIHR Innovations in Clinical Trial Design and Delivery for the Under-served (INCLUDE) guidelines (41) will be used to support inclusivity throughout the co-production process. This will involve a co-production/co-creation research methodological approach involving patients, caregivers and stakeholders as equal partners to review and refine a personalised HNL intervention. This will follow a Living Labs process which ensures a user centric approach to the development of an innovative solution that will then be sustainable for use within the real-world context/environment. This is an iterative process following four key steps, open design, co-design, co-production and co-customisation (35). Co-production research methodology is chosen as an integrative knowledge translation approach involving patients and stakeholders as equal partners to help answer the research question via stakeholder workshops.

WS3: Feasibility Study including process evaluation

This project sits overlapping between 'Prototype Development' and the 'Feasibility & Piloting' phase of the MRC Complex Interventions Framework and Actions 2,9 & 10 of the INDEX Guidance [27,28]. Programme theory utilising a behaviour change wheel will be applied to create an updated logic model to inform the intervention from the beginning [39].

A single centre randomised feasibility study of the co-produced prototype intervention in WS2 with a control arm of 'usual standard of care' at a local West Midlands community-based service. This will give a greater understanding of how the intervention interacts within this local cancer pathway in practice and answer the key uncertainties below. Acceptability of the study protocol, understanding the mechanism of change and context will be explored through qualitative semi-structured interviews using a reflexive thematic analysis approach [29,47]. A topic guide will be devised influenced on the outcomes of WS1 and WS2, the literature and all stakeholders.

Key Uncertainties

- How many patients are eligible for CDT?
- Can HNC patients be recruited to CDT?
- Do patients continue treatment?
- What are the reasons for drop out?

- Are patients able to adhere to CDT?
- What optimises adherences to CDT?
- Are any groups/patients under-served / underrepresented?
- Are the programme theory and intervention sufficient to upscale to a definitive trial?

Nested Qualitative Sub-Study: Semi-Structured Interviews

Topics will include questions directed towards the research aim, e.g., "*Can you tell me your experience of the therapy you received*," and topics as directed by participants. The guide will be used flexibly so interviewees can discuss issues in an order that is natural to them. Interviews will be selected at different time points (during and after the intervention), covering a range of fully to limited programme compliance. Fidelity will be monitored via a checklist to record and standardise consultations, recording any deviations, and a random selection of recorded consultations (10%).

This study will require ethical approval from health research authority (HRA) through IRAS approval for WS2-3. Ethical considerations will be considered during co-production work.

5. RESEARCH QUESTION/AIM(S)

To refine individualised CDT through co-production and investigate feasibility/acceptability of integrating the intervention into the HNC care pathway by:

WS1: Identify and critically review the content and relevance of the literature on HNL interventions and their impact on dysphagia outcomes, retention and adherence contributing to evolving programme theory in WS2.

WS2: Co-Production: Identification of solutions to acceptability, refining the intervention, and materials used with patient and HNC professionals stakeholder workshops, along with a principal patient co-creator.

WS3: To deliver a co-produced personalised CDT intervention to HNC patients with HNL and evaluate its acceptability and feasibility.

5.1. Objectives

1. Perform an up-to-date systematic review on the effectiveness of CDT as an intervention in HNL patients to improve dysphagia outcomes.

2. Co-production of refined intervention.

3. Address challenges identified in pre-feasibility testing and potential solutions for HNC survivors' eligibility, recruitment, adherence, compliance and retention rates. Includes uptake time point in HNC pathway, intervention components and fidelity.

4. Explore the mechanism of action of intervention delivery using programme theory with an embedded behaviour change framework.

5. Test candidate outcome measures on QOL, patient reported swallowing outcomes measures, objective swallowing outcome measures, and volumetric analysis of HNL.

6. Obtain HNC survivors' and professionals' perspectives on acceptability of the intervention, study processes and integration to usual care using a nested qualitative sub-study.

7. Determine a power calculation for future RCT.

8. Preliminary estimate of intervention cost by using a bottom-up calculation for clinical items (sessions × rates) and analogous/parametric calculations for larger items (devices, staffing).

5.2. Outcome

1. Report patient acceptability, recruitment, adherence, value, compliance and fidelity (HNL/dysphagia).
2. Co-production of intervention development
3. Updated Logic model of the programme theory using the behaviour change wheel.
4. Preliminary estimate of intervention cost.

Outputs/Dissemination:

Outputs will include: tailored CDT support materials; tools to support CDT compliance and adherence; a detailed individualised CDT intervention/study protocol (using TIDiEr checklist); information for HNC professionals; a full understanding of barriers to accessing HNL treatment; a roadmap of integration of a CDT programme to the HNC care pathway; a power calculation and estimate of sample size needed for effectiveness testing; a preliminary estimate of intervention cost, and an informed decision on feasibility for a future study with a detailed logic model.

5. A comprehensive peer-reviewed journal paper and conference presentations for key stakeholders are anticipated to report study evaluation, feasibility and acceptability (patient conference, multi-disciplinary national meeting; professional groups). Briefing notes will be prepared for Clinical Commissioning Group newsletters and HNC charities. Regular updates will be disseminated through social media. Study information will be published on key stakeholder/organisation websites including the Liverpool Head and Neck Cancer website. Podcasts/Infographics designed videos and Key Fact Sheets will be used for HNC professional training and patient dissemination.

Impact:

6. (1-3 years): Dissemination of the co-produced intervention solutions including logic model and results of feasibility testing will provide other HNC teams with an example of implementation or adaptation of the developed intervention to consider within their own services. This would benefit HNC patients by raising awareness and highlighting potential avenues for improvements in treatment experience, QOL, and improved functional outcomes.
7. Beyond DCAF: Post-doctoral fellowship funding will be sought for a definitive RCT to test the prototype across multiple settings and contexts. The definitive trial would explore the impact of the intervention on efficacy, patient experiences, outcomes, and cost-effectiveness.

6. STUDY DESIGN AND METHODS OF DATA COLLECTION

WS1: Evidence Synthesis

Aim: Locate, appraise and synthesise the evidence around effectiveness of HNL interventions on dysphagia outcomes and acceptability of these interventions. Findings will be used to generate key messages about the impacts of CDT as an acceptable intervention for HNL. Findings will be validated in WS2 through qualitative enquiry with the co-production stakeholder group and used to contribute to decision-making in the development/revision of the methodological design phase.

WS2: Co-Production

Sample:

Previous co-produced HNC studies have invited 14-32 patients and professionals [37]. A stakeholder group will be recruited to co-produce and refine the intervention and research processes following a 'Living Lab' approach/process [35,26]. This will target a maximum of 16 recruited HNC patients/care givers split into two groups, 1 patient co-creator and a maximum of 10 health care professionals/stakeholders involved with HNC. Participants will be identified through routine outpatients clinics and departments at the assigned patient identification site, University Hospitals Coventry & Warwickshire. This will either be done by the co-investigator (AS) or other professionals involved with their care.

- A principal patient co-creator.
- HNC patients who have completed curative treatment for HNC with primary or adjunctive CRT or
- surgery.
- HNC patients treated with CDT in previous pilot study.
- Partners/Carers of HNC patients.
- HNC Health Care Professions (HCP), eg. Dietitians, SLTs, Radiographers, Physiotherapists, Clinical Nurse Specialists, Consultant Oncologists, Consultant Surgeons.

- Established patient support/Patient & Public Involvement groups.

Method:

The NIHR INCLUDE guidelines [38] will be used to support inclusivity throughout the co-production process. National recruitment will ensure that potential contextual issues, problems and solutions are explored nationally to make sure that the research is applicable to multiple UK geographical areas in future. Group discussions will be summarised, and action points agreed at each meeting. Demographics will be collected to inform the experience/background/education of the sample.

If English is an additional language, an interpreter will be offered prior, during and post intervention for both WS2 and WS3. This will ensure that information is in an accessible/understandable format to gain informed consent. Time will be allowed for interpreter training in specialist terminology and an opportunity given for the participants to meet the interpreter prior to interview should they wish. The group will be facilitated by AS and an experienced member of the John Moore University Liverpool Living Labs team.

Following a similar structure to experienced based co-design, refining through co-production Living Labs will follow 3 phased workshops with patient, family and HCPs, 2-3 hours in duration. Consideration will be given to HNC patients with emotional, energy and communication difficulties. For example, planning frequent breaks or smaller sized groups to maintain comfort, engagement and so all voices are heard.

The study is inclusive of participants who have undergone laryngectomy. Appropriate arrangements will be made to support communication and ensure equitable participation. Where participants are unable to communicate verbally, alternative methods of communication will be offered, including written communication, according to participant preference and ability. Participants will have individually colour coded post it notes and writing pads so it is clear for data collection and analysis purposes who has contributed in this way.

Data will be recorded using the same structured approach as for verbal interviews to ensure consistency and completeness of data capture. Reasonable adjustments will be made as required to support participant communication needs. These arrangements will be discussed with participants in advance and documented as part of the consent and data collection process.

Workshop 1 (Co-Design = Develop):

An introduction activity 'Listening Pairs' will address power imbalances and build relationships among participants to foster a collaborative and inclusive environment. Ground rules will be discussed and agreed using sticky notes. AS will present pilot intervention protocol/feasibility issues (adherence, intensity, frequency and retention). Activities will focus on reflection to identify areas of positive practice and areas which require development, including choice of outcome measures needed to answer the research question [27]. Research

Logic Model [39] activities will focus on describing potential barriers and facilitators to uptake of CDT (e.g., stage in pathway of HNC treatment, how/where the intervention is delivered and intensity of CDT) and potential solutions.

Workshop 2 (Co-Production = Refine):

AS will provide feedback and customised developments from Workshop 1. Revised materials and changes to the intervention protocol will be discussed and explored. Strengths and weakness will be sought from the group and further feasibility revisions will be recommended. An implementation strategy will be devised which will consider how the prototype will work in practice and sent to the group for final input and consensus prior to workshop 3.

Workshop 3 (Co-Customisation = Deliver):

AS will provide an overview of workshop 1 and 2 outcomes. It is anticipated that workshop 3 will focus on key topics to include in the revised protocol and implementation issues. The co-production participants will develop solutions e.g., a printed or digital training resource, or both in order to provide patient centred innovations which meet the diverse needs of the HNC population. Suggestions need to be realistic and include solutions that can be developed within the dedicated scheduled period for this phase (6-12 months), alongside study set up and the ethical approval process. At the end of the workshops, the prototype will be finalised by AS and a consensus reached. An implementation research logic model will be utilised to help frame the implementation phase for the feasibility testing in WS3.

Public co-production participants will be reimbursed for their expenses and time in line with NIHR good practice payment for public contributors. Professional co-production participants will also be offered reimbursement for their time and for any additional travel expenses outside of their usual work. Refreshments/catering will be provided for all workshops.

WS3: Recruitment and delivery of intervention of personalised CDT

The feasibility pilot study aims to assess the acceptability and feasibility of delivering an individualised Complete Decongestive Therapy (CDT) protocol for the management of head and neck lymphoedema (HNL) following treatment for head and neck cancer. The control group will receive the standard of care, which comprises a similar lymphoedema intervention delivered by a specialist lymphoedema nurses at a West Midlands community-based service. This control arm has been selected to reflect current clinical practice, ensure ethical integrity, and support key feasibility objectives needed to inform the design of a future full-scale randomised controlled trial (RCT).

Pragmatic and Clinically Relevant Comparison:

The ultimate goal of this research programme is to evaluate whether an individualised CDT protocol improves

swallowing outcomes in patients with HNL after head and neck cancer treatment. In clinical practice, CDT—or elements of it—are variably delivered by different provider groups, often without protocol standardisation or a focus on swallowing specifically. Comparing delivery of our current service model in Coventry & Warwickshire with a custom/tailored approach allows for a pragmatic assessment of feasibility and provides real-world relevance to future implementation.

This comparator has been selected to reflect real-world practice and assess the feasibility of conducting a future RCT. It ensures ethical provision of care while enabling evaluation of whether an individualised CDT protocol, delivered by a designated provider (lymphoedema trained SLT), is feasible, acceptable, and potentially beneficial in improving swallowing outcomes. Key aspects such as recruitment, retention, adherence, fidelity, and outcome data completeness will be assessed across both arms.

Ethical Considerations:

Given that current standard care may include elements of CDT (e.g., manual lymphatic drainage, compression, skin care, exercise), it would be unethical to allocate participants to a "no treatment" control. The chosen control condition ensures that all participants have access to a recognised level of therapeutic support, consistent with existing clinical guidelines and practices. This design meets ethical standards for equipoise while avoiding withholding of care.

Intervention: Structured Complete Decongestive Therapy (CDT)

Participants allocated to the intervention arm will receive a structured, but individualised protocol of Complete Decongestive Therapy (CDT) for head and neck lymphoedema. CDT is a complex, multimodal intervention comprising four core components:

1. Manual Lymphatic Drainage (MLD) – series of hand movements to encourage lymph flow
2. Compression Therapy – use of bandages or garments (where appropriate)
3. Skin Care – education and management to reduce risk of infection
4. Therapeutic Exercises – specific movements in the head and neck to support lymphatic drainage including swallowing exercises

This protocol has been adapted for patients with HNL following head and neck cancer treatment, in consultation with lymphoedema specialists and speech and language therapists.

Intervention sessions will be delivered by a trained speech and language therapist who is also a certified lymphoedema therapist over a 3-month period. This will be a combination of in-person and home-based components. Intervention fidelity will be monitored using structured treatment logs, and fidelity checklists completed after each session.

In addition to CDT delivery, participants will receive written self-management resources (or formatted

solutions created in co-production) and routine clinical follow-up at 3 months.

Control: Standard Care for Head and Neck Lymphoedema

The control group will receive standard care for head and neck lymphoedema (HNL), consisting of lymphoedema management as currently delivered in routine practice, typically by specialist lymphoedema nurses at a West Midlands based community-based service (which is a separate clinical team to ensure there is no risk of contamination between groups). This will include some elements of Complete Decongestive Therapy (CDT) such as manual lymphatic drainage or compression, but without a standardised protocol and may involve other interventions such as kinesiotape or garments. Kinesiotape is a latex free hypoallergenic cotton fiber tape that is used to move lymph fluids by microscopically lifting the skin, change muscle tone, improve posture, and correct movement patterns.

To minimise contamination, intervention procedures will be delivered separately for each group at different locations. Fidelity checks will be implemented using treatment logs. A template fidelity log will be provided for the West Midlands based community-based service to complete.

Sample

Inclusion Criteria:

- Patients with a HNC diagnosis.
- Patients presenting with Stage 1a oedema or above [5]. Surgical patients at least 8 weeks post treatment.
- Oncology patients at least 8 weeks post chemo-radiation. 50 Gy or higher dose of radiation to bilateral neck and primary tumour site in 30 or more fractions.
- Aged 18 years or older.

Exclusion Criteria:

- Medical contraindications (listed in Adverse Events section).
- Patients with active/recurrent HNC disease.
- Patient who are unable to provide informed consent.
- Patients with head and neck lymphedema from non-cancer aetiologies

Recruitment and Sample Size

The annual referral rate of newly diagnosed HNC patients at UHCW is approximately 245. HNC patients will be screened for eligibility at the HNC Consultant surveillance clinics and recorded in a screening log. AS will introduce the study, provide a study information sheet to take away and consider, prior to consent.

Consecutive referrals will be identified via surveillance clinics, at a maximum capacity of 4 new patients per month, as AS is the only lymphoedema trained clinician. Recruitment will be documented, quantifying the rate and timing of uptake. If a patient refuses to participate, reason for refusal will be sought, while respecting their right to refuse without giving a reason. Participants from WS2 co-production workshops will not be recruited into WS3 feasibility testing.

Sample size was determined pragmatically using feasibility study conduct guidance recommending that 24- 35 participants are sufficient to estimate key parameters in a single arm feasibility [40,41]. Rates of attrition in HNC dysphagia rehabilitation studies are reported to be between 25-35% [42]. A sample of 50 patients are projected to be screened for eligibility during the available study period. A maximum of 30 patients will be targeted to be recruited to complete this study. Recruitment will stop after one year or when recruitment target has been met. Attrition is expected, however a maximum of 30 will aim to be recruited within the time limits of the study period.

Data Collection

Equality Diversity and Inclusion (EDI) characteristics will be collected to monitor the sample to ensure that they are representative of the population and explore any different experiences/intervention adaptations that may be required to ensure inclusivity following NIHR INCLUDE guidance [38,43]. Traditional HNC cohorts present at an older age, have considerable co-morbidities due to significant smoking and alcohol consumption, and low socioeconomic status associated with poor health literacy, making them hard to reach for rehabilitation engagement [44,55]. Demographic data (eg age, gender, education level and ethnicity) will inform sample diversity and used in data analysis.

The NIHR toolkit for EDI [43] has been utilised to inform data collection and make this research accessible/inclusive. Intervention Prototype (mechanisms and resources to support behaviour change developed from WS2 will be integrated below); Appointments will be at the participants preferred time e.g., around work/school times where possible.

The study is inclusive of participants who have undergone laryngectomy. Appropriate arrangements will be made to support communication and ensure equitable participation. Where participants are unable to communicate verbally, alternative methods of communication will be offered, including written communication or written interviews, according to participant preference and ability.

Data will be recorded using the same structured approach as for verbal interviews to ensure consistency and completeness of data capture. Reasonable adjustments will be made as required to support participant communication needs. These arrangements will be discussed with participants in advance and documented as part of the consent and data collection process.

The following intervention is based on a 3-month CDT programme which was piloted with 10 post-treatment HNC survivors previously [24]:

- 1-hour assessment as soon as possible prior to CDT to perform a Videofluroscopy (VF): X-ray sequence used to grade swallowing - **further protocol for VF found below****
- Flexible nasendoscopy (FNE) to grade internal lymphoedema. This involves a small, flexible camera inserted trans-nasally to view internal structures in throat which is performed as a routine clinical test that is performed by appropriately trained clinicians for the purpose of cancer surveillance. This will be performed by the Consultant as part of their surveillance clinic and a video taken at the time, rather than a separate procedure to reduce the patient burden – **further protocol for FNE found below*****
- Second 2-hour baseline assessment will collect all baseline outcome measures, stage/grade lymphoedema and create/teach individualised CDT routine.
- Patients will receive personalised tailor-made compression garments, Self Lymphatic Drainage (SLD) routine, skincare & exercises.
- Manual lymphatic drainage will be demonstrated intra-orally in cheek, floor of mouth and tongue areas, and externally to the neck and face. A home-programme will be tailored and taught to patients to continue daily treatment at home. All manual lymphatic drainage routines will be personalised according to their HNL profile to avoid a general routine which may add to the treatment intensity. Compression to be worn at least 3x per week, daily if tolerated.
- Garments will be commercially available chinstraps for neck and lower face from Thuasne. A flat pad and chip pad will be tailor made to cover areas of pitting and non-pitting oedema to fit into the compression garment using Thuasne foam and Mobiderm. Kinesiotape may be used as an alternative if compression is not tolerated.
- Patients will be given a written information handout regarding lymphoedema, skincare and exercise, along with a tailored instruction sheet for the direction and technique of MLD with visual pictures. Accommodations for health literacy and cognitive abilities will be considered & alternatives solutions from co-production can be provided.
- 30-minute patient fidelity review one week later to review technique & resolve any queries. This can be done virtually if patient chooses to reduce burden.
- Final 2-3 hour review will be booked at 3-months to repeat all outcome measures, VF and FNE to assess response to treatment. The intervention will be recorded using the TiDiEr template [53].

The quantitative outcome measures were chosen to explore their potential measure of effect, in preparation for their use as a primary or secondary outcome in a future, larger trial. I will test whether these outcomes are acceptable to participants and the level of data completeness. Although preliminary, this data will be used to estimate standard deviations, responsiveness, floor/ceiling effects. This will help to inform a future sample size calculation.

Qualitative interviews will include probes relating to participants' perspectives on these outcome measures, their acceptability and appropriateness to the intervention.

Qualitative outcome measures: Baseline and 3/12:

- PROM Quality of Life - The Comprehensive Assessment of Lymhoedema Impact in the Head and Neck (CALI-HaN) [45]
- PROMS swallowing: MD Anderson Dysphagia Inventory, Performance Status Scale-Head and Neck

Quantitative outcome measures: Baseline and 3/12:

- 100-ml Water Swallow (bedside timed swallow test)
- MD Anderson Cance Centre HNL Rating Scale (palpation)
- Instrumental Videofluroscopic swallow study using Dynamic Imaging Grade of Swallowing Toxicity (DIGEST) rating scale
- Grading of internal lymphoedema using FNE and Patterson Oedema Rating Scale [46]
- Tissue Dialectric Constant: Lymphscanner (a handheld device that is placed against the skin to measure fluid collection under the skin)
- Superficial Induration: Skin Fibrometer (a handheld device that is placed against the skin to check how stiff or firm the skin is)
- Digital photographs with images taken from the front, sides and neck up and down positions

All pre-post intervention data collection will be digitally recorded, detailing frequency, intensity and duration. Patient outcome measures will be taken using a research assistant to reduce bias.

Professor Heather Starmer (HS), practice supervisor, will be second reviewer to grade the VF swallow ratings, severity of internal lymphoedema with FNE videos and review of treatment plans. All imaging data will be anonymised prior to storage, analysis, and any sharing within the research team. Identifiable patient information embedded within VFSS imaging files (e.g. name, date of birth, hospital identifiers) will be removed using validated software functionality prior to export and analysis. Once anonymised, imaging data will be assigned a unique study identification number and stored securely on password-protected systems in accordance with University and NHS data governance policies.

Access to these videos will be restricted to authorised research team members only (HS), and all data will be handled in accordance with GDPR and Trust information governance policies. An Honorary Research Contract (HRC) will be applied for using a Research Passport for HS to access anonymised videos via a VPN with a Letter of Access.

****Videofluoroscopy (VF) Protocol**

The VF will be conducted by a speech and language therapist with the required level of competency as set out

by the Royal College of SLT guidelines and a radiographer or radiologist. The VF will be recorded onto Picture Archiving and Communication System (PACS) in the Trust. Recordings will be pseudonymised with a unique identifier assigned to participants prior to secure data transfer to the second rater for assessment. Timepoint will be recorded; baseline or post intervention after 12 weeks.

VFs may also be transmitted digitally via (PACS) using the image storage and transfer format DICOM (Digital Imaging and Communication in Medicine).

Examinations should be continuous pulsed fluoroscopy, set at no less than 15 pulses per second, the optimal being 30 pulses per second. For routine VF, patient radiation dose is estimated to be between 0.2-0.85 mSv, exposure times ranging from 150 sec to 1080 secs. This research protocol is not expected to exceed this dose. The participating centre (UHCW) will use the standardised water soluble contrast agent, IOHEXOL Omnipaque 350.

Equipment

Plastic cups, 60mL syringe, weighing scales, plastic spoons, penny, adhesive tape, water, IOHEXOL (Omnipaque 350), Ambrosia Devon Custard, small digestive biscuit.

Consistencies

Omnipaque is a ready-to-use, water-soluble iodinated contrast — you don't add a powder to make contrast with it; instead you dilute or mix the liquid Omnipaque into water or food to achieve the desired appearance and viscosity for VF. Omnipaque is commonly used for VF studies and may be mixed with water / juice / yoghurt / custard / biscuits as needed.

Thin liquid recipe

Deliver 5 ml, 10 ml and 20 ml from a cup

Custard recipe

Goal: maintain custard texture while making it radiopaque. Because custard already provides texture, you add **Omnipaque liquid** (small volume) and stir. Start conservative and increase if fluoroscopy image is too faint.

Pudding/custard bolus (5 mL)

Target: ~85 mg I/mL final

- Measure **5 mL of room-temperature custard** (e.g., Ambrosia Devon).
- Add **1.3 mL Omnipaque 350**.
- Mix thoroughly for ≥1 minute until smooth.
- Serve immediately.

If fluoroscopic contrast is judged too faint, increase Omnipaque to **15–20 mL** (e.g., 15 mL Omnipaque in 53 mL custard ≈ ~83 mg I/mL final; 20 mL → ~100+ mg I/mL), but document the amount, check patient iodine limits and get radiologist approval before higher concentrations.

Biscuit bolus (digestive) coated with contrast (3 mL)

Target paste concentrate: ~100 mg I/mL

- Add 0.86 mL Omnipaque 350 and coat evenly over the **1/4 biscuit** just before presenting to patient.

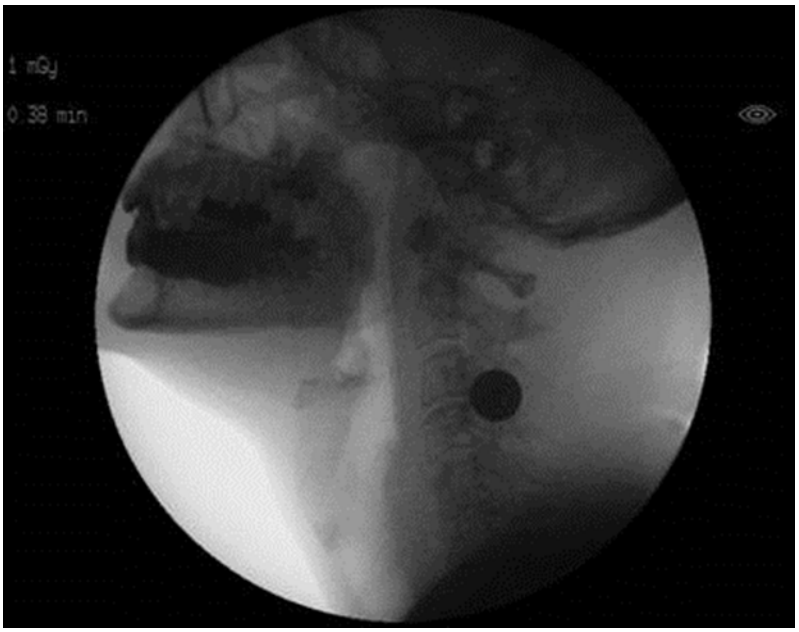
Pre-examination

Prior to the study the following will be adhered to:

- check local departmental protocols (PGD 02 Iohexol V5 final 2025) and get radiology / pharmacy / SLT sign-off via SLT Non-Medical Referrer guidance, confirm patient allergies (iodine/contrast) and renal status via a safety questionnaire
- prepare dilutions immediately before use and discard unused portions
- ensure suction is available on the fluoroscopy trolley in case of aspiration.

A penny must be taped to the subject's neck just below the earlobe during the swallowing study, see picture

below. (NOTE: The circular shape of the penny minimizes the impact of head rotation and the known diameter of the coin allows for calibration of pixels per cm and thus calculation of areas and displacement on videofluoroscopy). Patients will be seated or standing throughout the examination. The field of visualisation for the lateral view includes the lips anteriorly, nasal cavity superiorly, cervical spinal column posteriorly and the pharyngo-oesophageal segment. The larynx should be in full view. Shoulders should not obstruct the view of the larynx and pharynx. The patient should keep their head in a neutral position throughout the test procedure. Compensatory swallowing manoeuvres or postures should not be performed during the research examination. Please instruct the patient to remove any items of jewelry or clothing that might obstruct this view. If the patient has a nasogastric tube, please ensure the external portion of the tube does not obstruct the view.



Examination

Liquids must be administered first to avoid confounding the results from remaining residue in the pharynx after solid consistencies. Please label each bolus on the x-ray according to the labels below (lateral, A-P for anterior-posterior). Wherever possible flaring of the fluoroscope should be kept to a minimum. Expected duration of the assessment is approximately 15 minutes. Self-administration of test boluses is optimal, but clinician administration is acceptable.

The full swallowing sequence needs to be captured. The fluoroscope should be activated by the radiologist or radiographer a few seconds before the administration of the test boluses. The fluoroscope should be deactivated shortly after the bolus tail has exited the pharyngo-oesophageal segment.

Bolus trials should be presented in the precise order listed below:

Lateral / mid-saggital view

A) 5mL thin (2 trials) from a teaspoon or measured cup

Instruction to the patient: *please hold this in your mouth until asked to swallow*.

B) 10mL thin (1 trial) from a measured cup

C) 20mL thin (1 trial) from a measured cup

Instruction to the patient: *please try to take the whole amount and hold it in your mouth until I ask you to swallow*

D) 5mL pudding (custard) (1 trial teaspoon).

Instruction: *swallow when you are ready*.

E) 1/4 biscuit (digestive) - coated with (1 trial)

Instruction to the patient: *chew this up and swallow when you feel comfortable and ready to swallow.*

Anterior-posterior (coronal) view

Please include an oesophageal sweep at the end of the examination, using a single bolus as described below, for the assessment of oesophageal clearance. No further imaging of the oesophagus is required:

F) 10mL thin (1 trial).

Instruction to the patient: *Look forward and slightly raise your chin, hold this in your mouth until asked to swallow*

The stopping criterion for safety purposes will be at the discretion of the clinician conducting the VF, taking into account patients' risk factors. Specific bolus trials may be terminated, or the procedure aborted altogether, if they deem a significant risk to proceeding with the VF assessment. In the event of significant aspiration, local guidelines for management will be followed. The VF should be stopped if the patient has more than 50% aspiration on a large bolus (≥10mLs) or at least 3 swallows with silent aspiration, in more than trace amounts. If a VF for clinical purposes is required, SALTs may conduct any additional trials or try compensations/manoeuvres they deem necessary after completing the bolus trials on the intervention protocol.

The on-site SALT conducting the VF will review, interpret, document, and implement any necessary follow-up as is standard with VF procedures at their site. Quantitative VF analysis for the research study will be conducted per central review by the investigative team.

Volume of Omnipaque used, final concentration, and lot number will be documented in the patient record.

Quantitative analysis of VF studies will be conducted per central review at UHCW by the investigative team (AS). Each VF will be secondary-rated using the outcome measures below on the basis of bolus trials in the above protocol. Additional bolus trials that are administered outside of the protocol or bolus trials in which a swallow strategy/posture was tested will be excluded from the analysis. Published guidelines will be followed for all analyses. Three outcome measures will be summarized from the VF (these scores cannot be calculated in the absence of an VF study):

1. Penetration-Aspiration Scale (PAS)
2. Modified Barium Swallow Impairment Profile (MBSImp)
3. Dynamic Imaging Grade of Swallowing Toxicity Scale (DIGEST):

Penetration-Aspiration Scale (PAS):

The PAS is an 8-point, ordinal rating psychometrically validated as a measure of airway protection from the VF. Intraclass correlation coefficients for inter- and intrarater reliability on the Penetration-Aspiration Scale (PAS) were 0.96 and 0.95-0.97, respectively (Rosenbek, Robbins et al. 1996). PAS scores will be tallied for each bolus trial on the VF. The primary outcome from PAS will be the maximum PAS score across thin liquid bolus trials; maximum PAS for pudding, solids, and all trials will also be recorded. Scoring guidelines and ordinal cutpoints for aspiration are defined in Table 1.

Table 1. Scoring Summary for Penetration Aspiration Scale TVF (true vocal fold) Scores 1-5 = no aspiration (0) scores 6-8 = aspiration (1)

Score	***Penetration-Aspiration Scale***
1	Material does not enter the airway
2	Material enters the airway, remains above TVF, ejected from airway
3	Material enters airway, remains above TVF, not ejected
4	Material enters airway, contacts TVF, ejected from airway
5	Material enters airway, contacts TVF, not ejected
6	Material enters airway, below TVF, ejected
7	Material enters airway, below TVF, not ejected despite effort

8	Material enters airway, below TVF, not effort to eject

The MBSImpairment Profile (MBSImp):

The MBSImp is a validated 16-item standardized measure of the oropharyngeal swallow. MBSImp provides a summary measure of swallow physiology and allows researchers to ascertain the pathophysiology of dysphagia by delineating impairment in discrete events within the swallow. Each component is rated using a 3- to 5-point ordinal scale in which 0 indicates no impairment. Two summary scores can be obtained from the MBSImp: Oral Phase and Pharyngeal Phase scores. The overall oral impairment MBSImp score will be calculated as the sum of the 6 component oral measures, providing a continuous score (range, 0-22) for which higher ratings indicate greater physiologic impairment. The overall pharyngeal impairment MBSImp score will be calculated as the sum of the 10 component measures, providing a continuous score (range, 0-29). Inter- and intrarater concordance with reference standards reportedly exceeds 80% by blinded raters. MBSImp provides a summary measure of swallow physiology, but does not integrate laryngeal penetration or aspiration into the summary score, and must be reported with the PAS for a global assessment of the oropharyngeal swallow (Martin-Harris, Brodsky et al. 2008).

Dynamic Imaging Grade of Swallowing Toxicity Scale (DIGEST):

The DIGEST is a validated, 5-grade, ordinal rating system that summarises global swallowing safety and efficiency from videofluoroscopic (VF) imaging. It was developed for the assessment of swallowing function in head and neck cancer populations, but can be applied in other contexts. The scale combines two primary domains — Safety Grade (S0–S3) and Efficiency Grade (E0–E3) — into a composite DIGEST Grade 0–4, with higher scores indicating greater functional impairment. Psychometric testing has shown strong interrater agreement and test–retest reliability.

DIGEST ratings will be assigned for each participant based on the overall swallowing performance observed across the VF examination, considering all bolus consistencies tested. For each patient, the primary outcome will be the composite DIGEST Grade at baseline and follow-up. Safety and efficiency subgrades will also be reported separately.

Scoring is based on pre-defined ordinal cutpoints (Table 1) for safety (degree and frequency of penetration/aspiration) and efficiency (residue severity and bolus clearance). The final DIGEST Grade is determined from the worst observed safety or efficiency domain performance, following published scoring rules.

Table 1. Scoring Summary for DIGEST

DIGEST Grade	Safety Subgrade (S) – Worst airway invasion pattern	Efficiency Subgrade (E) – Worst residue/clearance pattern	Functional Interpretation
0	S0 = Safe (no airway invasion or penetration only, PAS 1–2)	E0 = Efficient (≤ mild residue, complete clearance)	No functional impairment
1	S1 = Penetration without aspiration (infrequent, PAS ≤3)	E1 = Mild inefficiency (residue ≤10% in one or more regions)	Mild impairment
2	S2 = Occasional aspiration (PAS 6–7, not on all boluses)	E2 = Moderate inefficiency (residue 10–50% in one or more regions)	Moderate impairment
3	S3 = Frequent aspiration or silent aspiration (PAS 8 or recurrent PAS ≥6)	E3 = Severe inefficiency (>50% residue in ≥1 region)	Severe impairment
4	(Composite grade) Safety or efficiency at grade 3 *and* the other domain ≥2	—	Profound impairment

Key scoring notes:

- Safety domain is anchored to PAS categories but incorporates frequency of occurrence across bolus trials.
- Efficiency domain is anchored to validated bolus clearance/residue severity ratings (percent of bolus retained).
- Composite DIGEST Grade is the higher of the two domain grades, with a possible upward adjustment if both domains are impaired.
- Scores reflect *functional* swallowing impairment, not just structural observations

***** Flexible Nasendoscopy (FNE)**

Flexible nasendoscopy (FNE) will be performed by an appropriately trained clinician (Ear Nose & Throat surgeon/ Consultant Oncologist / SLT with competency or research clinician credentialed in endoscopy) using a single-use or reprocessed flexible nasendoscope according to institutional policy. Local topical anaesthetic and decongestant (e.g., lidocaine 2% spray and phenylephrine 0.5% or equivalent) may be applied to reduce discomfort and promote nasal patency. The procedure will visualise the nasal cavity, nasopharynx, oropharynx and larynx and will be video-recorded for later grading of internal lymphedema.

Expected patient burden:

- Time: The entire visit including consent and prep is expected to add approximately 10 minutes; the scope pass itself is typically 2–5 minutes.
- Discomfort: Participants may experience nasal irritation, throat tickle, coughing or sneezing during the procedure. Swallowing or voice may feel different for a short period after the test.
- Recovery: No specific recovery period is required; participants may resume normal activities immediately unless they feel unwell. We will advise avoiding hot drinks for 30 minutes if topical anaesthetic is used.

Risks (frequency categories and mitigation):

- Very common / expected (≥1 in 10): mild nasal discomfort, sneezing, watery eyes, mild throat irritation. Mitigation: topical local anaesthetic or decongestant where clinically indicated; use of smallest practical scope; experienced operator.
- Common (1 in 10 to 1 in 100): gagging, cough, retching, mild bleeding at sampling site (if mucosa grazed). Mitigation: gentle technique, stop and allow haemostasis; apply topical vasoconstrictor if needed.
- Uncommon (1 in 100 to 1 in 1000): clinically significant epistaxis (nosebleed) requiring local measures; vasovagal reaction (light-headedness/brief syncope); transient laryngospasm or bronchospasm in reactive airways. Mitigation: pre-procedure risk assessment (coagulopathy, anticoagulants, severe nasal septal deviation, severe asthma), monitoring, immediate availability of suction, oxygen and emergency medications.
- Rare (<1 in 1000): significant bleeding requiring ENT intervention; severe allergic reaction (anaphylaxis) to topical agents; aspiration requiring intervention. Mitigation: screening for allergies, staff trained in anaphylaxis management, resuscitation equipment in the clinic, and escalation protocols.

Any clinically significant findings (for example marked airway compromise, unexpected lesions, or severe laryngeal oedema) will be communicated to the participant and their treating clinician and acted upon as per local clinical pathways. This may include urgent ENT referral and additional clinical testing.

Absolute exclusions to FNE:

- Participant declines nasendoscopy or withdraws consent.
- Known allergy to topical anaesthetics or decongestants planned for use.
- Uncontrolled coagulopathy (INR > institution-specified threshold) or platelet count below local safety

threshold without prior haematology review.

- Severe nasal/septal obstruction precluding transnasal passage.
- Acute severe respiratory infection, unstable cardiac or respiratory status.

Relative exclusions / precautions to FNE:

- Recent (<4 weeks) nasal or sinus surgery — discuss with treating ENT.
- Severe gag reflex/anxiety — consider topical only, distraction, or decline if intolerable; do not sedate within this protocol unless specified.
- Children and cognitively impaired adults — include only with appropriate additional safeguards and local policy for distress management.

Stopping rules during procedure:

- Oxygen desaturation below local safety threshold (e.g., SpO_2 < 92% or >4% drop from baseline) that does not self-correct.
- Uncontrolled bleeding from nasal mucosa.
- Subject requests immediate cessation because of distress.
- New onset severe coughing, laryngospasm, or sustained arrhythmia.

Positions/manoeuvers recommended for endoscopic evaluation to improve visualisation of structures to rate internal lymphoedema [46]

Structure	Posture/manoeuver
Epiglottis	Tongue out to assess pharyngeal thickness, sustained "e" to assess thickness of laryngeal surface
Vallecula	Tongue out
Pharyngoepiglottic folds	Tongue out and/or sustained "e"
Aryepiglottic folds	Sustained "e"
Arytenoids	Sustained "e" and/or sniff
False vocal folds	Sustained "e" and/or slow sniff in
True vocal folds	Sustained "e" and/or slow sniff in
Pyriform sinuses	Sustained "e" and/or cheek puffing

Nested Qualitative Sub-Study: Semi-Structured Interviews

Methods:

Acceptability of the study protocol, understanding the mechanism of change and the context will be explored through qualitative semi-structured interviews using a reflexive thematic analysis approach [29,47]. A topic guide will be devised influenced on the outcomes of WS1 and WS2, the literature and all stakeholders. Topics will include questions directed towards the research aim, e.g., "*Can you tell me your experience of the therapy you received*", and topics as directed by participants. The guide will be used flexibly so interviewees can discuss issues in an order that is natural to them. Interviews will be selected at different time points (during and after the intervention), covering a range of fully to limited programme compliance.

Fidelity will be monitored via a checklist to record and standardise consultations, recording any deviations, and a random selection of recorded consultations (10%) will be evaluated by HS. Transfer of this electronic data will be via dedicated SharePoint folder with password protected documents. OR Transfer of data from NHS sites to lead researcher will be via REDCap. All transferred Data will be anonymised (using participant identifier number) before being transferred. The Caldicott Guardian is advising on which systems are in place at UHCW that are suitable form transfer of data from an NHS research site to an external international hospital.

Data Collection:

Participants will be offered the option of virtual or in-person interview, at UHCW at their preferred times around work/school times where possible. Written consent will be taken. Interviews will be:

- 45-60 minutes.
- Digital recording with field notes.
- Verbatim transcription stored securely in password-protected folder.
- All participants will have opportunity to de-brief and be sign-posted to support if they become distressed (via interpreter if needed).

Participants Following Laryngectomy

The study is inclusive of participants who have undergone laryngectomy. Appropriate arrangements will be made to support communication and ensure equitable participation, most likely in the form of face to face interviews. Where participants are unable to communicate verbally, alternative methods of communication will be offered, including written communication or written interviews, according to participant preference and ability.

Data will be recorded using the same structured approach as for verbal interviews to ensure consistency and completeness of data capture. Reasonable adjustments will be made as required to support participant communication needs. These arrangements will be discussed with participants in advance and documented as part of the consent and data collection process.

Mixed-methods analysis:

Braun & Clarke's [47] reflexive approach to thematic analysis will be used for in-depth data analysis of qualitative interviews. Transcripts will be read multiple times by AS to generate initial conceptual codes, then grouped to develop themes. Themes will be discussed with the research supervisory team, patient co-author and Patient & Public Involvement groups, then re-reviewed alongside the transcripts to explore any missing detail and ensure rigor, reliability and validity. Wider contextual factors such as age, socio-economic status, gender and ethnicity will be considered. Final themes will be established, defined and named. Written analysis will be sent to participants for feedback on data interpretation to ensure the final results are reflective of the qualitative interview data.

Statistical data analysis will be used to evaluate quantitative outcomes using trend analysis of interval nominal scales [54]. Pre and post treatment outcome data will be determined in SPSS by applying one way analysis of variance (ANOVA) to determine score change. This will ensure unbiased treatment effect estimates [48]. The coproduction group will be invited to review and evaluate the results of this study. Qualitative and quantitative results will be triangulated during process evaluation guided by the MRC guidance framework [27,29]. The Capability, Opportunity, Motivation-Behaviour (COM-B) theoretical framework [49] will be used to analyse acceptability, and understand the mechanism of change using behaviour change to support the process evaluation and inform and update the logic model [39].

Primary feasibility endpoints:

- Number of patients screened
- Number of eligible/ineligible patients and reasons for ineligibility
- Number of patients agreed to participate and time point
- Reasons for refusal (where provided).
- Number of patients retained
- Reasons for and timepoint of withdrawal from study
- Adverse events
- Fidelity to the created checklist of actions for the intervention
- Progression criteria for moving to a future randomised controlled trial (RCT); potential funding source NIHR HTA have been developed in accordance with the traffic light system (56).
- Green (progression to RCT with minimal changes to protocol): Proposed sample size is achieved and retained, intervention is considered acceptable and feasible by healthcare professionals and HNC survivors, with only minor changes required. Study procedures are considered acceptable and feasible, >85% of outcome data is collected and an appropriate primary outcome measure is selected, ≥33% of those identified as eligible and approached are recruited.
- Amber (progression to RCT but with minor changes to protocol): Minimum 20 HNC survivors recruited and retained at follow-up, moderate changes to the protocol and/or intervention required, >60% of outcome data is collected.

- Red (progression to RCT inadvisable, major changes required): <20 HNC survivors recruited
- and retained at follow-up, significant changes to the protocol and/or intervention are required, and <60% of outcome data is collected.

7. STUDY SETTING

The ultimate goal of this research programme is to evaluate whether an individualised CDT protocol improves swallowing outcomes in patients with HNL after head and neck cancer treatment. In clinical practice, CDT—or elements of it—are variably delivered by different provider groups, often without protocol standardisation or a focus on swallowing specifically. Comparing delivery of our current service model in Coventry & Warwickshire with a custom/tailored approach allows for a pragmatic assessment of feasibility and provides real-world relevance to future implementation. UHCW is a centralised HNC service with a referral rate of approximately 245 newly diagnosed HNC patients per year. The control arm will be delivered by specialist lymphoedema nurses at a local West Midlands based community service provider which is the current standard of care pathway. The Midlands will be representative of implementing the intervention within an underserved population due to higher levels of deprivation. Understanding any implementation challenges and facilitators within this centre will inform future successful national implementation strategies.

8. SAMPLE AND RECRUITMENT PARTICIPANT ENTRY

8.1 Eligibility Criteria

Sample size was determined pragmatically using feasibility study conduct guidance recommending that 24- 35 participants are sufficient to estimate key parameters in a single arm feasibility [40,41]. Rates of attrition in HNC dysphagia rehabilitation studies are reported to be between 25-35% [42]. A sample of 50 patients are projected to be screened for eligibility during the available study period. A maximum of 30 patients will be targeted to be recruited to complete this study. Recruitment will stop after one year or when recruitment target has been met. Attrition is expected, however a maximum of 30 will aim to be recruited within the time limits of the study period. Recruitment will stop after one year or when recruitment target has been met.

Exclusion Criteria:

8.1.1 Inclusion Criteria

- Patients with a HNC diagnosis.
- Patients presenting with Stage 1a oedema or above [5]. Surgical patients at least 8 weeks post treatment.
- Oncology patients at least 8 weeks post chemo-radiation. 50 Gy or higher dose of radiation to bilateral neck and primary tumour site in 30 or more fractions.
- Aged 18 years or older.
- All genders

8.1.2 Exclusion Criteria

- Medical contraindications.
- Patients with active/recurrent HNC disease.
- Patient who are unable to provide informed consent.
- Patients with head and neck lymphedema from non-cancer aetiologies

8.2 Recruitment

8.2.1 Sample identification

WS3: Consecutive referrals will be identified via surveillance clinics at a PIC (UHCW) by AS, or any of the existing clinical MDT team members who are already involved in the patients' care. This will be at a maximum capacity of 4 new patients per month for the intervention arm, as AS is the only lymphoedema trained clinician. Recruitment will be documented, quantifying the rate and timing of uptake.

A participant/patient information leaflet and consent forms will be used for each of the studies, co-production, feasibility and qualitative sub study. The opportunity for the patient to ask any questions and discuss the study in more detail will be offered with a follow-up phone call provided within 24-48 hours if participant wishes. With their permission, patients who decline to take part in the study will be asked if they can be approached to discuss their reasons for not taking part at a later stage to understand reasons for non-recruitment as part of the qualitative sub study.

Randomisation will be completed after consent. Randomisation will be done at the time of enrolment using a one by one recruitment implementation using a telephone-generated random sequence. Allocation concealment is not possible as a referral will need to be made to the local community-based service provider if randomised to the standard arm of care. The patient information sheet and consent forms will both clearly explain the process of onward referral to the control arm of standard of care at the local West-Midlands based community service if they are randomised into this group. The overall recruitment time is expected to take place over an 18-month period to fit within the scheduled PhD fellowship timeline.

	Screening	Enrollment & Randomisation	Baseline Measures Taken	Intervention Arm	Control Arm	Follow-Up & Outcomes
Timepoint	Weeks 8+ for post-operative for surgical patients Weeks 12+ for post oncology radiation (+/-) chemotherapy	Enrollment & consent within 2 weeks of screening	Completed within 2 weeks of consent May overlap with weeks 1-2 of intervention	Week 1 to 12	Week 1 to 12	Week 12 post intervention outcomes
Activities	- Eligibility screening - Informed consent - Baseline assessments N=30	- Random allocation (1:1) N=15 in each	VF X-Ray PROMS Photographs Nasendoscopy for internal lymphoedema rating	- Intervention individualised CDT	- Usual care	- Outcome assessments - Adherence & acceptability - Adverse events - Retention & recruitment - Fidelity

8.2.2 Informed Consent

Patients must have capacity to consent the study. The process of assessing mental capacity will be undertaken by the trained consultant clinicians and/or PhD Student investigator (a registered Speech & Language Therapist with The Health and Care Professions Council), by following the four key questions outline in the mental capacity act 2005. Can they:

- understand the information relevant to the decision.
- retain that information for long enough to make the decision.
- use or weigh up that information as part of the process of making the decision.
- communicate their decision in any way.

The person must be free to make a choice and if at any stage the PhD Student investigator or any part of the research team feels that a person is being coerced then they will be withdrawn from the study.

Once eligibility has been confirmed as above, full written informed consent will be obtained by signing and dating either a paper or digital consent form (developed with the patient advisory group). Signed informed consent will be obtained by the PhD Student investigator. Any original signed consent forms completed at the recruitment site will be retained in the Investigator Site File (ISF), with a copy filed in the clinical notes and a copy provided to the patient. They will be advised that they can withdraw consent and withdraw from the study at any point again without any impact on their usual treatment of care.

Participants will be advised that they can withdraw from the study at any time up to or at any point during the co-production workshops. It will not however be possible to remove any ideas or experiences shared that inform the co-production work as no individual data is obtained. All potential participants will be given the opportunity to ask questions relating to the study to the research teams at the PICs and the study co-ordinator.

During the study consent discussion, patients will be asked if they are willing to be contacted about a semi-structured interview (30-45mins) for the qualitative sub-study regardless of which arm they have been randomised into. This is an option available to patients who consent, including those who withdraw or drop out early, as well as those who complete. A purposeful sample of up to 10-15 patients who have consented will be contacted by the PhD Student investigator, this will reflect those that have within drawn, dropped out, completed, and declined and include diversity of demographics where possible.

9. ADVERSE EVENTS

9.1 Definitions

Adverse Event (AE): any untoward medical occurrence in a patient or clinical study subject, including unfavourable and unintended signs, including abnormal laboratory results, symptoms or a disease associated with treatment.

Serious Adverse Event (SAE): any untoward and unexpected medical occurrence or effect that:

- **Results in death**
- **Is life-threatening** – refers to an event in which the subject 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
- **Requires hospitalisation, or prolongation of existing inpatients' hospitalisation**
- **Results in persistent or significant disability or incapacity**
- **Is a congenital anomaly or birth defect**

Medical judgement should be exercised in deciding whether an AE is serious in other situations. Important AEs that are not immediately life-threatening or do not result in death or hospitalisation but may jeopardise the subject or may require intervention to prevent one of the other outcomes listed in the definition above, should also be considered serious.

9.2 REPORTING PROCEDURES

During the course of the study, incidental clinical findings may be identified that are not directly related to the study objectives. Any such findings will be managed in accordance with the research governance procedures of University of Liverpool and UHCW. Where an incidental clinical finding is identified, the researcher will discuss this with the appropriate clinical team. Relevant information will be communicated through appropriate clinical pathways, such as referral to the participant's usual care team or General Practitioner. All actions will be documented and handled in line with local governance, safeguarding, and data protection policies.

Contra-indications to MLD or negative clinical outcomes related to the procedure are taken extremely seriously. Where a breach of protocol is identified a clinical incident will be raised and a warning letter will be sent. Where a second breach is identified a clinical incident will be raised and a review of the service will be undertaken. This has been agreed with the Clinical Nurse Specialist lead of the local lymphoedema service.

9.2.1 Non-serious Adverse Events (AEs)

All adverse events should be reported. Depending on the nature of the event the reporting procedures below will be followed. Any questions concerning adverse event reporting should be directed to the Chief Investigator in the first instance.

Adverse Events are any emotional distress related to sharing of experiences in co-production activities.

All information collected during the study will be kept confidential and handled in accordance with data protection regulations. However, there may be rare circumstances where confidentiality cannot be maintained. If information is disclosed that indicates a risk of serious harm to you or to others, or raises a safeguarding or legal concern, the research team may need to share this information with appropriate professionals or authorities. Wherever possible, this would be discussed with the participant first and all local safeguarding procedures will be followed.
Adverse Events (AEs) are any contra-indications and cautions that occur when delivering the **intervention but will be risk assessed prior to intervention and patients will be excluded if they have a history of contra-indications**. These include open wounds or breaks in skin, recent or current infection (risk of spread), congestive heart failure (CHF) (inability to pump fluid throughout system and hypofiltration), cellulitis (risk of spread of infection), cardiac oedema (lack of venus return), renal failure (difficulty excreting waste), acute DVT (can mobilise clots), fistula (can delay healing), uncontrolled HTN (hyperfiltration increased arterial flow/pressure), carotid sensitivity (vasovagal), dermal mets (discomfort & infection), presence of tracheostomy (fluid drained to airway) and certain thyroid medications (can increase hyperthyroidism when working on neck). (Best Practice for Management of Lymphoedema – British Lymphology Society).

The stopping criterion for a Videofluroscopy examination for safety purposes will be at the discretion of the competent clinician conducting the VF, taking into account patients' risk factors. Specific bolus trials may be terminated, or the procedure aborted altogether, if they deem a significant risk to proceeding with the VF assessment. In the event of significant aspiration, local guidelines for management will be followed. The VF should be stopped if the patient has more than 50% aspiration on a large bolus (≥10mLs) or at least 3 swallows

with silent aspiration, in more than trace amounts. If a VF for clinical purposes is required, SALTs may conduct any additional trials or try compensations/manoeuvres they deem necessary after completing the bolus trials on the intervention protocol.

During flexible nasendscopy, any clinically significant findings (for example marked airway compromise, unexpected lesions, or severe laryngeal swelling) will be communicated to the participant and their treating clinician and acted upon as per local clinical pathways. This may include urgent ENT referral and additional clinical testing. However, it is expected to be the treating Consultant that will be passing the scope and performing this procedure.

Stopping rules during FNE procedure:

- Oxygen desaturation below local safety threshold (e.g., SpO_2 < 92% or >4% drop from baseline) that does not self-correct.
- Uncontrolled bleeding from nasal mucosa.
- Subject requests immediate cessation because of distress.
- New onset severe coughing, laryngospasm, or sustained arrhythmia.

All such events, whether expected or not, will be recorded on a Case Report Form and in the electronic patient record.

9.2.2 Serious Adverse Events (SAEs)

Upon identification of an SAE the Principle Investigator should complete a study specific SAE form and sent to the Chief Investigator/Study Team within 24 hours. Relapse and death due to unrelated health events or hospitalisations for elective treatment of a pre-existing condition do not need reporting as SAEs.

Contact details for reporting SAEs

Please send SAE forms to: Joanne.Patterson@liverpool.ac.uk

Tel: +44 (0)151 795 1359 (Mon to Fri 09.00 – 17.00)

All SAEs should be reported to the REC where in the opinion of the Chief Investigator, the event was:

- **'related'**, i.e. resulted from the administration of any of the research procedures; and
- **'unexpected'**, i.e. an event that is not listed in the protocol as an expected occurrence

Reports of related and unexpected SAEs should be submitted within 15 days of the Chief Investigator becoming aware of the event, using the HRA Non-CTIMP safety report to REC form. The Chief Investigator

must also notify the Sponsor of all SAEs.

For NHS REC approved studies please refer to https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/safety-reporting/ - (Scroll to Safety reporting for non-CTIMP studies)

For University of Liverpool Ethics Committee approved studies please refer to https://www.liverpool.ac.uk/intranet/media/livacuk/researchethics/reviewprocedures/Safety,reporting,and,adverse,events,procedure.pdf (Section - Studies which require approval from the University's Sponsorship Committee)

10. STATISTICS AND DATA ANALYSIS

10.1 Sampling

10.1.1 Sample Size

The annual referral rate of newly diagnosed HNC patients at UHCW is approximately 245. HNC patients will be screened for eligibility at the HNC Consultant surveillance clinics, alerted to AS and recorded in a screening log for both WS2 and WS3.

WS2: stakeholder group will be recruited to co-produce and refine feasibility testing following the 'living lab' approach/process [35,26]. Previous co-produced HNC studies have invited 14-32 patients and professionals [37]. The initial open design workshops with HNC patient and caregivers will target a sample of up to 12 co-production HNC patients and caregivers based on size of a small project, approximately 10-15 patients (47). This has been discussed and agreed with supervisory team to practically manage the workshops, ensuring that time and consideration is given to those that are living with a previous diagnosis of HNC who may experience communication difficulties and fatigue, and to ensure that all voices are heard.

For the co-design phase a further sample of up to 12 health professionals and stakeholders will join the co-production patient and caregivers to co-design to agreed intervention. If there are a larger number of interested co-production participants an open innovation platform for consultation of the outputs from the co-production workshops will be considered

WS3: Sample size was determined pragmatically using feasibility study conduct guidance recommending that 24- 35 participants are sufficient to estimate key parameters in a single arm feasibility [40,41]. Rates of attrition in HNC dysphagia rehabilitation studies are reported to be between 25-35% [42]. A projection of 50 eligible patients are identified with a conservative retention rate of 60%, allowing 30 patients to complete this study. Recruitment will stop after one year or when recruitment target has been met.

Nested qualitative sub-study interviews: n= 10-15 (will be those already identified or recruitment for feasibility) was determined due to the size of data analysis required for every intervention WS3 participants.

10.1.2 Sampling Technique

WS2: Consecutive referrals will be identified via surveillance clinics at a PIC (UHCW) by AS and include patients and family/carers who have experience of lymphoedema symptoms or treatment. Stakeholders will be

recruited from local lymphoedema services, PIC (UHCW) snowball sampling through Clinical Excellence Networks and HCPC networks. The NIHR INCLUDE guidelines (56) will be used. The participant identification centre, UHCW was chosen as the co-production workshops will be held within Coventry**.** This will provide access to the inherently underserved populations of patient and caregivers within this Midlands area.

The participants will be purposively sampled to ensure maximum variation based on gender, age, socio demographics, type of cancer treatment and where possible also include those that declined to participate and those that drop out of the study. Where possible they will be selected at the end of treatment, or at later surveillance clinics, as this is more likely when the lymphoedema symptoms will present and span post treatment.

WS3: Consecutive referrals will be identified via surveillance clinics at a PIC (UHCW) by any of the existing clinical MDT team members who are already involved in the patients' care, at a maximum capacity of 4 new patients per month, as AS is the only lymphoedema trained clinician.

Equality Diversity and Inclusion (EDI) characteristics will be collected to monitor the sample to ensure that they are representative of the population and explore any different experiences/intervention adaptations that may be required to ensure inclusivity following NIHR INCLUDE guidance [38,43]. Traditional HNC cohorts present at an older age, have considerable co-morbidities due to significant smoking and alcohol consumption, and low socioeconomic status associated with poor health literacy, making them hard to reach for rehabilitation engagement [44,55]. Demographic data (eg age, gender, education level and ethnicity) will inform sample diversity and used in data analysis. The NIHR toolkit for EDI [43] has been utilised to inform data collection and make this research accessible/inclusive.

Qualitative sub-study: Patients will be purposively sampled from intervention patients already be identified or recruitment for feasibility at the point of consent.

Contamination and Fidelity Monitoring

As both groups may involve delivery of similar components, steps will be taken to reduce contamination:

- Sessions and documentation will be clearly separated.
- Where feasible, providers will be allocated to a single arm and participant crossover will be minimised.
- Fidelity will be assessed in the intervention arm; in the control group, brief treatment logs (fidelity checklist) will be reviewed to understand care variability and potential overlap.

10.2 Data Analysis

WS2: Co-production

Using the Living Labs approach the data analysis will be an iterative process of understanding the priorities, barriers and facilitators and developing a solution based on the needs and views of the co-production group. The workshops will be recorded with an encrypted Dictaphone on each table and transcribed. Field notes will

be taken by the PhD Student investigator, and two facilitators present to support during the workshops. The transcriptions will be transcribed using a professional transcription agency with a secure upload facility. Once returned the transcription will be checked for accuracy and edited to remove any participant identifiable information. Recordings will be deleted once transcriptions have been reviewed. Transcriptions and notes will be managed using NVivo and analysed using a thematic analysis to identify agreed themes and priorities. Paper field notes taken will be retained in the Investigator Site File (ISF) stored in a locked cabinet in a locked keypad locked office in the research suite. these will be checked by the co-production participants to ensure that it reflects their understanding of discussions. This will be an iterative process following each focus group to reach an agreement on the priorities and the development of a quality solution that is acceptable and meets the priorities of the co-production group. This will ensure that this research is flexible and bespoke to the needs of the co-production group.A reflexivity diary will be kept by the PhD Student investigator to be aware of any internal bias and discussed with supervisory team. All field notes and transcription will be kept and stored by the PhD Student investigator within a password secured university computer. They will not contain any personal identifiable information, and pseudonyms will be used in transcriptions.

WS3**:** Feasibility study

Process evaluation analysis involving both quantitative and qualitative data will be undertaken to understand the feasibility and mechanism of the intervention.

Braun & Clarke's [47] reflexive approach to thematic analysis will be used for in-depth data analysis of qualitative interviews. Transcripts will be read multiple times by AS to generate initial conceptual codes, then grouped to develop themes. Data will be analysed using thematic analysis which will involving familiarisation with the data, generating codes, constructing themes, reviewing potential themes, defining and naming themes and producing a report reflecting the Normalisation Process Theory. Themes will be discussed with the research supervisory team, patient co-creator and PATIENT AND PUBLIC INVOLVEMENT groups, then re-reviewed alongside the transcripts to explore any missing detail and ensure rigor, reliability and validity. Wider contextual factors such as age, socio-economic status, gender and ethnicity will be considered. Final themes will be established, defined and named. Written analysis will be sent to participants for feedback on data interpretation to ensure the final results are reflective of the qualitative interview data.

Statistical data analysis will be used to evaluate quantitative outcomes using trend analysis of interval nominal scales [54]. Pre and post treatment outcome data will be determined in SPSS by applying one way analysis of variance (ANOVA) to determine score change. This will ensure unbiased treatment effect estimates [48]. The coproduction group will be invited to review and evaluate the results of this study.

Qualitative and quantitative results will be triangulated during process evaluation guided by the Medical Research Council guidance framework [27,29]. The Capability, Opportunity, Motivation-Behaviour (COM-B) theoretical framework [49] will be used to analyse acceptability, and understand the mechanism of change using behaviour change to support the process evaluation and inform and update the logic model [39].

Data storage:

Quantitative data: All patients will be assigned a unique study identifier number. A record linking the patient's name to the unique study identifier number will be held only in a locked room at the PIC and is the responsibility of the PI and research matron. This unique study identifier number will be used with any data assessment tools. All data will be reported and analysed using descriptive statistics using Microsoft Excel.

Qualitative data: Patient participant interviews will be recorded with a Dictaphone if face to face or within Microsoft Teams if virtually which will also generate a transcription of the recording. Audio transcriptions will be transcribed using a professional transcription agency with a secure upload facility. Once transcripts have been received (including those from video recordings), they will be checked for accuracy and edited to remove any identifiable information to ensure anonymity. Transcribed data will be managed using NVivo software. Once transcribed and reviewed the recordings will be destroyed.

The University of Liverpool has an approved method of transferring confidential data from outside sources called Datanywhere. A Datanywhere link with instructions for uploading information securely will be shared with the PI and either AS or Research Nurse at the PICs to transfer any data relating to the study such as consent forms and data collection forms.

Data will be processed and stored in accordance with the University of Liverpool's Research Data Management Policy, the European Union General Data Protection Regulation (2016), and the Data Protection Act (2018). Computers used to collate data are password protected, and use encrypted digital files. Data collected online will be stored on the University of Liverpool's secure network server (M: drive). Data collected in paper format will be stored in a locked filing cabinet at the University of Liverpool. Data collected via Microsoft Forms will be exported into an EXCEL sheet. Microsoft Forms is encrypted both at rest and in transit. Microsoft forms are compliant with privacy standards HIPAA and BAA (https://support.microsoft.com/en-gb/office/security-and-privacy-in-microsoft-forms-7e57f9ba-4aeb-4b1b-9e21-b75318532cd9). In accordance with the University of Liverpool's Research Data Management Policy, any participant information held at the University of Liverpool will be confidentially destroyed 10 years after the study end date.

11.REGULATORY ISSUES

11.1 Ethics Approval

Before the start of the study, a favourable opinion will be sought from the UK Health Departments Research Ethics Service NHS REC for the study protocol, informed consent forms and other relevant documents e.g. advertisements. Health Research Authority (HRA) approval will be obtained via IRAS. The study will be submitted to each proposed research site for Confirmation of Capacity and Capability (UHCW and West-Midlands based community service-based provider) following IRAS approval. The study will be conducted in accordance with the recommendations for physicians involved in research on human subjects adopted by the 18th World Medical Assembly, Helsinki 1964 and later revisions.

11.2 Confidentiality

The Chief Investigator will preserve the confidentiality of participants taking part in the study and will abide by the

Data Protection Act 2018 and the UK GDPR as amended from time to time and any successor legislation in the UK and any other directly applicable regulation relating to data protection and privacy.

The PhD Student investigator will preserve the confidentiality of participants taking part in the study and will abide by the Data Protection Act 2018 and the UK GDPR as amended from time to time and any successor legislation in the UK and any other directly applicable regulation relating to data protection and privacy.

- All co-production participants will be advised of the importance of confidentially if patients wish to share personal experiences within the co-production workshops.
- Personal contact details (addresses and postcodes) will be kept confidential.
- Manual files will be kept in a locked cabinet in a locked room at the participating sites.
- Identifiable information for the purposes of participant contact will be stored separately to all other data.
- Any collected personal information will be kept secured as discussed above and will be anonymised
- All recruited patients will be assigned a unique patient identifier number
- All NHS staff at PICs will be following NHS confidentiality requirements
- Only the PhD Student investigator, PI and research matrons at the PICS will have access to data
- There will be no personal identifiable information used when writing up the research findings.
- Data may also be looked at by individuals from the University of Liverpool, from regulatory authorities or from the PICs NHS trust, for monitoring and auditing purposes, and this may include access to your personal information. This made clear in the participant information sheet.
- Data will be retained by the University of Liverpool for 10 years before being destroyed
- All information collected during the study will be kept confidential and handled in accordance with data protection regulations. However, there may be rare circumstances where confidentiality cannot be maintained. If information is disclosed that indicates a risk of serious harm to participants or others, or raises a safeguarding or legal concern, the research team may need to share this information with appropriate professionals or authorities. Wherever possible, this would be discussed with the participant first and all internal UHCW safeguarding processes will be followed.

Confidentiality and Anonymity of Treatment Photographs

Treatment-related photographs will be collected as part of the study procedures where applicable. These photographs may include identifiable features. All photographs will be handled confidentially and stored securely in accordance with data protection regulations. Access will be restricted to authorised members of the research team.

Where possible, photographs will be anonymised or pseudonymised for analysis and reporting. If full anonymisation is not possible due to the nature of the image, this will be clearly acknowledged, and the images will not be used in a way that could identify individual participants. Photographs will not be used for publication or presentation outside the study without explicit additional consent.

11.3 Indemnity

The University of Liverpool holds Indemnity and insurance cover with Newline Insurance Company, which apply to this study.

11.4 Audits

The study may be subject to inspection and audit by the University of Liverpool under their remit as sponsor and other regulatory bodies to ensure adherence to GCP and the UK Policy Framework for Health and Social Care Research (v3.2 10th October 2017).

12.END OF STUDY

End of study will be considered 4 weeks after the last patient last contact to allow to the return and collation of any assessments tool and to complete the qualitative interviews. No further data will be collected at this point and all data will go through data analysis and report writing only.

13.DISSEMINIATION POLICY

13.1 Dissemination policy

- This study will be published as a thesis as per the requirements of the University of Liverpool in fulfilment for the degree of Doctor in Philosophy
- Funding body the NIHR will be acknowledged in research outputs.
- Acknowledgement will also be given to University Hospitals Coventry & Warwickshire, University of Liverpool and Liverpool John Moore University.
- A contract for the ownership of data exists between University Hospitals Coventry & Warwickshire and University of Liverpool.
- A collaboration agreement exists with Liverpool John Moore University and University Hospitals Coventry & Warwickshire.
- The results of this study will be published in both academic and public spaces.
- Academic dissemination will be through the publication within peer reviewed journals and presentation at national and international conferences

- The results will be disseminated to charities, support groups and stakeholders through easy to read/understand infographics designed with the patient advisory group and members of the co-production groups.
- The patient advisory group and members of the co-production groups will be involved with the dissemination of all outputs.

13.2 Authorship eligibility guidelines and any intended use of professional writers

The PhD thesis authorship will be by the PhD Student investigator. Any authors named within manuscript publications in academic and peer reviewed journals will fulfil the criteria of authorship outlined by The Internal Committee of Medical Journal Editors for manuscripts submitted for publication.

14. ARCHIVING

Data and all appropriate documentation will be stored for a minimum of 10 years after the completion of the study, including the follow-up period.

15. REFERENCES

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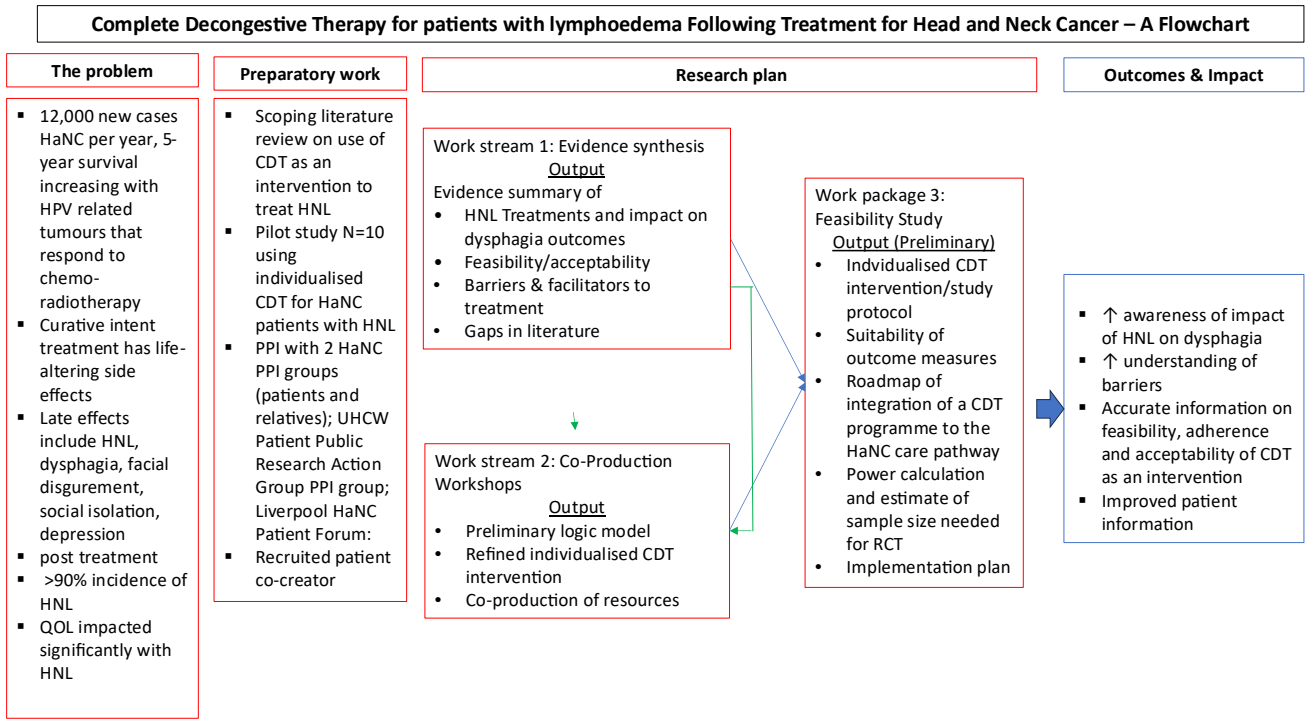
16. APPENDICES

16.1 Appendices 1- Required documentation (will submit after collected, under PPI review)

- Participant information sheet (WS2)
- Participant consent forms (WS2)
- Study advert flyer
- Patient information leaflet: feasibility study (WS3)
- Patient consent forms feasibility study (WS3)
- Patient information leaflet: qualitative sub study WS3)
- Patient consent forms (WS3)

16.2 Appendix 2 – CDT for Patients with Lymphoedema, Study Flow Chart

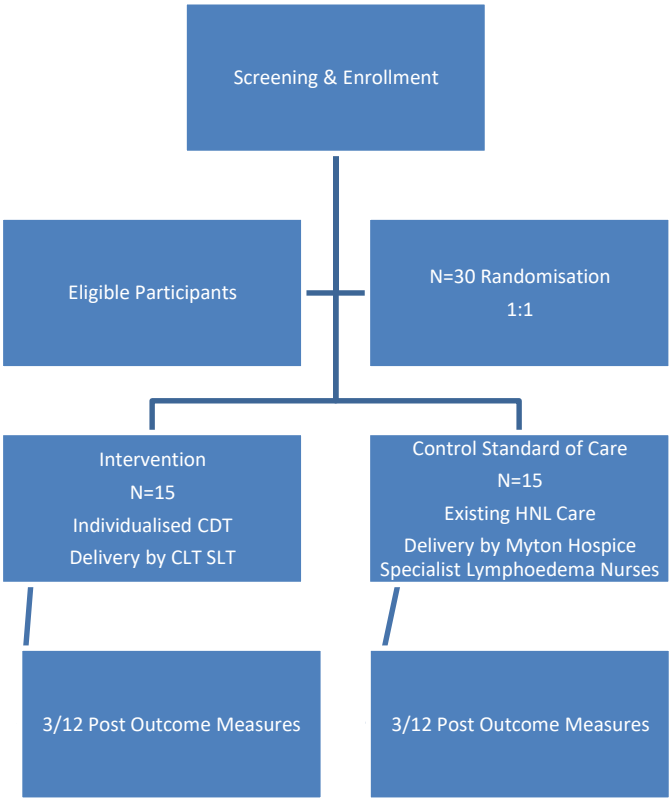


16.4 Appendix 3 – Feasibility Study Design Schema

Proposed Study Design: CDT Feasibility Trial

	Screening	Enrollment & Randomisation	Baseline Measures Taken	Intervention Arm	Control Arm	Follow-Up & Outcomes
Timepoint	Weeks 8+ for post-operative for surgical patients Weeks 12+ for post oncology radiation (+/-) chemotherapy	Enrollment & consent within 2 weeks of screening	Completed within 2 weeks of consent May overlap with weeks 1-2 of intervention	Week 1 to 12	Week 1 to 12	Week 12 post intervention outcomes
Activities	- Eligibility screening - Informed consent - Baseline assessments N=30	- Random allocation (1:1) N=15 in each	VF X-Ray PROMS Photographs Nasendoscopy for internal lymphoedema rating	- Intervention individualised CDT	- Usual care	- Outcome assessments - Adherence & acceptability - Adverse events - Retention & recruitment - Fidelity

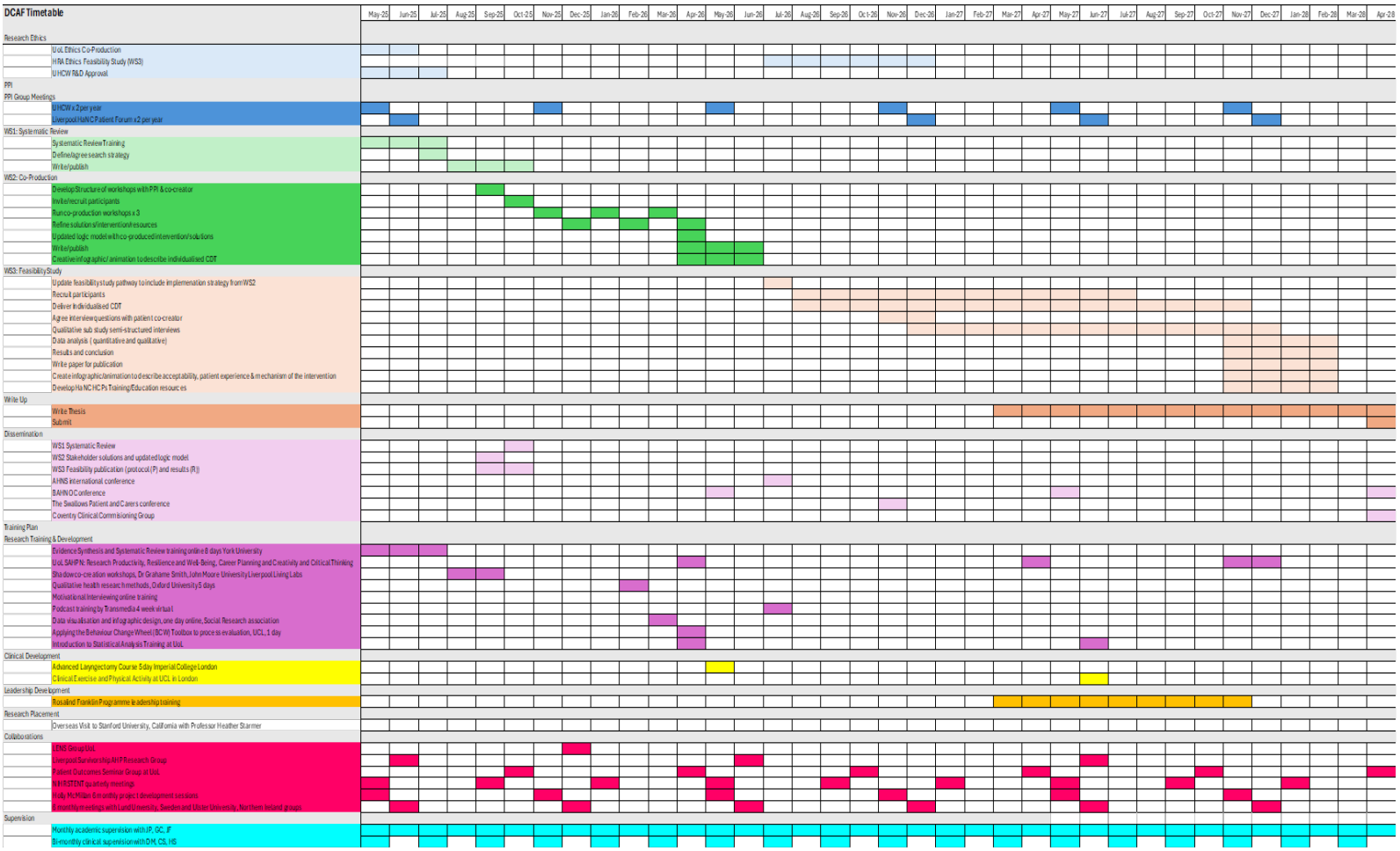
Schematic Overview



Additional Notes

Parameter	Description
Sample Size	30 participants (15 per arm)
Primary Feasibility Outcomes	Recruitment rate, retention, adherence, acceptability

16.4 Appendix 4 – Gaant Chart



16.5 Appendix 5 – Amendment History

Amendment No.	Protocol version no.	Date issued	Author(s) of changes	Details of changes made
1	1.1	15.08.2025	AS	Order of sections, inclusion of X-ray protocol and scope protocol, inclusion of data transfer for second reviewer of data videos

2	1.2	15.09.2025	AS	Track changes accepted & template deleted
3	1.3	17.09.2025	AS	Short title acronym added
4	1.4	07.10.2025	AS	Addition of Caldicott Guardian data transfer process for video images to international research team. Implemented feedback from JRO committee questions. Study logo added.
5	1.5	01.02.2026	AS	REC committee changes