FULL TITLE OF THE TRIAL

Chin tuck against resistance with feedback: swallowing rehabilitation in frail older people admitted to hospital with pneumonia. A Feasibility Randomised controlled study of two types of rehabilitation exercise using chin tuck against resistance to improve swallowing, eating and drinking.

Trial Acronym	CTAR-SwiFt
Sponsor	Lewisham and Greenwich NHS Trust
Sponsor R&D number	123324
Funder	NIHR RfPB
IRAS Project ID	273240
ISRCTN	
Chief Investigator	Dr David G Smithard
Protocol Version	v1, 19th Aug 2019

SIGNATURE PAGE

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

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

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

For and on behalf of the Trial Sponsor:

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

Name (please print):

.....

Position:
.....

Chief Investigator:

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

Name: (please print):

.....

KEY TRIAL CONTACTS

Insert full details of the key trial contacts including the following

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Committees	Full contact details including phone, email and fax numbers

List of Abbreviations

AE	Adverse Event
AEM	Adverse Events Monitoring
BP	Blood Pressure
CAP	Community Acquired Pneumonia
CI	Chief Investigator
CNORIS	Clinical Negligence and Other Risks Indemnity Scheme
CRF	Case Report Form
CTAR	Chin Tuck Against Resistance
CTAR-SwiFt training	The intervention under investigation in this study
EAT-10	Eating Assessment Tool
EMG	Electromyography
EQ-5D	EuroQuol health-related quality of life questionnaire
FEES	Fibreoptic Endoscopic Evaluation of Swallowing
FOIS	Functional Oral Intake Scale
GCP	Good Clinical Practice
ICF	Informed Consent Form
IF	Incidental Findings
ISF	Investigator Site File
KCL	King's College London
KCTU	King's Clinical Trials Unit
MEWS	Modified Early Warning Score

MOCA	Montreal Cognitive Assessment
NHS	National Health Service
PI	Principal Investigator
QoL	Quality of Life
REC	Research Ethics Committee
SAE	Serious Adverse Event
SOP	Standard Operating Procedures
SWAL-QoL	Swallowing Quality of Life questionnaire
TMF/SMF	Trial Master File/Study Master File
TMSG	Trial Management and Steering Group
TUAG	Timed Up and Go
TWST	Timed Water Swallow Test
UES	Upper Esophageal Sphincter
VF	Videofluoroscopy

LIST of CONTENTS

TRIAL SUMMARY

Trial Title	Chin tuck against resistance with feedback: swallowing rehabilitation in frail older people admitted to hospital with pneumonia. A feasibility randomised controlled study of two types of rehabilitation exercise using chin tuck against resistance to improve swallowing, eating and drinking.	
Internal ref. no. (or short title)	CTAR-SwiFt	
Clinical Phase	Feasibility (Phase II)	
Trial Design	Randomised controlled study (3 arms)	
Trial Participants	Frail older people admitted to hospital with a diagnosis of pneumonia	
Planned Sample Size	20 in each arm (60 in total)	
Treatment duration	12 weeks	
Follow up duration	3 months	
Planned Trial Period	24 months	
	Objectives	Outcome Measures
Primary	Establish whether it is feasible to recruit enough patients in a timely manner (in a subsequent larger-scale randomised controlled trial) to assess the effectiveness of this intervention in reducing dysphagia, community acquired pneumonia and improve the amount eaten orally.. Assess willingness to participate in, and complete the intervention. Establish the measurement variability of the tools for assessing outcome e.g. FOIS, QoL, Swallow Speed. Assess the ease of use and acceptability of the intervention (including the ExerPhager investigational device). Identify the optimum dose of CTAR training (frequency-daily vs twice-a-day).	70% recruitment of total eligible candidates Rate of recruitment Attrition <30% 85% Compliance with the exercise programme 32% Increase in FOIS and 30% decrease in Timed Water Swallow Test
Secondary	Physiological changes seen on VF. Assess changes in bolus flow	

	rates. Measure the % changes in laryngeal elevation. Measure the % change in base-of-tongue retraction during swallowing. Establish whether there is a reduction in the pharyngeal residue after the intervention. Observe the timing of UES opening, before and after intervention.	
Investigational Device	ExerPhager: A prototype device for swallowing rehabilitation using chin tuck against resistance with direct biofeedback.	

FUNDING AND SUPPORT IN KIND

FUNDER(S)	FINANCIAL AND NON FINANCIALSUPPORT GIVEN
National Institute for Health Research (Research for Patient Benefit)	Financial

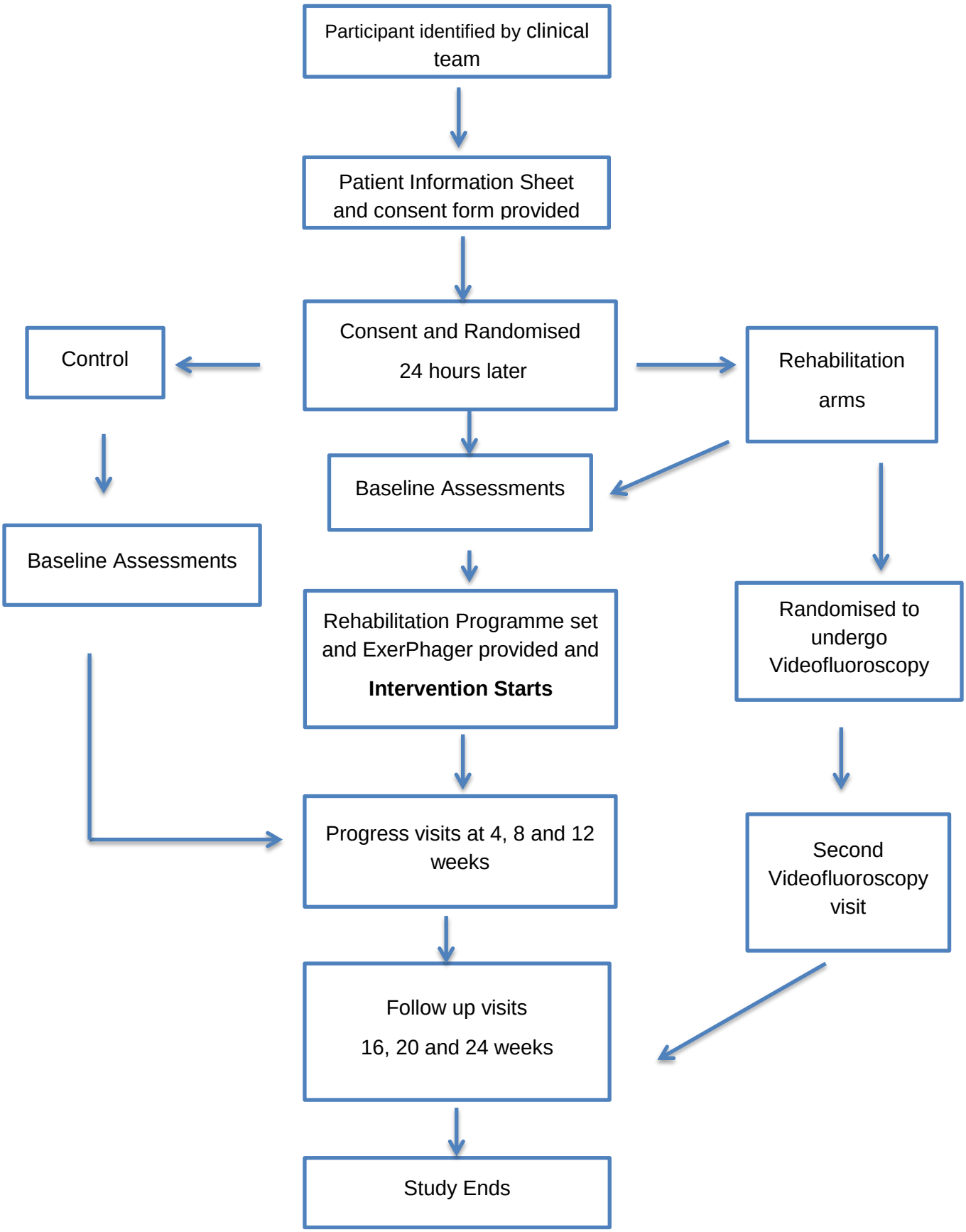
ROLES AND RESPONSIBILITIES OF TRIAL MANAGEMENT and STEERING GROUPS

Trial Management Steering Committees

The Trial Management and Steering Group (TMSG) shall consist of the CI, Dr David Smithard, PI (both Bristol and Woolwich), Prof Swaine, Dr Kulnik, Mrs D Hansjee, Statistician and 2 Patient and Public Involvement (PPI) representatives. The TMSG will meet weekly for the first month then alternate weeks until week 12. At week 20, meetings will revert to weekly; to ensure all practical details of the trial are progressing well and working well and everyone within the trial understands them. The TMSG shall be responsible for Process Mapping during the study to inform the next phase of the research.

The TMSG shall monitor trial recruitment and retention and any adverse events occurring during the study.

KEY WORDS: Dysphagia, Swallowing, Frailty, Old, Rehabilitation, Chin tuck against Resistance


Participant identified by clinical team
Patient Information Sheet and consent form provided
Consent and Randomised
24 hours later
Control
Rehabilitation arms
Baseline Assessments
Baseline Assessments
Rehabilitation Programme set and ExerPhager provided and
Intervention Starts
Randomised to undergo Videofluoroscopy
Progress visits at 4, 8 and 12 weeks
Second Videofluoroscopy visit
Follow up visits
16, 20 and 24 weeks
Study Ends

1. BACKGROUND

1.1 What is the problem being addressed?

The population is getting older, and frequently frailer. Swallowing problems are more common in the frail population, with studies suggesting a prevalence of approximately 30% (higher in those who have other comorbidities or who are acutely unwell). The problem that is being addressed is that of malnutrition, loss of independence, infection and death that are frequent consequences of swallowing problems (dysphagia) in the frail older population. Many frail older people admitted to hospital with community acquired pneumonia (CAP) will have aspirated saliva or food (90%). If the swallow can be improved by a simple exercise thereby improving nutrition and reducing aspiration, it may be possible CAP, loss of independence, infection and death and hence reduce health care costs will be reduced.

1.2 Why is this research important in terms of improving the health and/or well-being of the public and/or to patients and healthcare services?

Between 220,000 and 484,000 people in England have Community-Acquired Pneumonia (CAP) and about 10% of these cases are thought to be due to aspiration pneumonia, which is largely caused by difficulty in swallowing (dysphagia). It is estimated that 22–42% of all people who have CAP are admitted to hospital (approximately 175,000 people in 2013/14). The mortality rate in hospital lies between 5% and 14% and between 1.2% and 10% of adults admitted to hospital with CAP are managed in an intensive care unit. The risk of dying in this group of patients is more than 30%.

Of those with dysphagia, 50% report a significant impairment in their quality of life. By improving the ability to swallow, the oral intake of the patient will improve and reduce the need for supplemental feeding, occurrence of chest infection and admission to hospital. Eating a normal diet improves quality of life by increasing socialisation and satisfaction. Admission to hospital is expensive, recent studies in Denmark and the USA have reported increased healthcare costs. These will be reduced if the swallow is improved.

We have worked with a group of patients who have experienced dysphagia and they have expressed the need for better rehabilitation of swallowing after dysphagia has been diagnosed. With the help of the patients, we have developed a swallowing exercise rehabilitation idea, by taking a previously-established form of the exercise (the Shaker Exercise) and making it safer and easier to do, by instead doing the exercises with a simple 'feedback-enabled exercise ball' that can be squeezed under the chin. After suggestions by patients, the research team has developed a swallowing exercise intervention, to combat dysphagia with the idea to eventually have a significant impact on community-acquired pneumonia, thereby benefiting the health and well-being of thousands of patients and potentially, in the future, reducing the number who die from community-acquired pneumonia.

1.3 How does the existing literature support this proposal?

It is known from the literature that many older frail people admitted to hospital (55%) will have difficulties with swallowing (dysphagia; Cabre et al., 2010). In those admitted with a diagnosis of community-acquired pneumonia, up to 90% may have aspirated saliva or food. The literature suggests that Dysphagia is quite common in those residing in the community, being present in up to 30% of older people living at home (Kertscher et al., 2014). Up to 28% of older people are known to aspirate on instrumentation (Butler et al., 2010; Almirall, 2013). With age, there is an increased risk of aspiration due to changes in motor function, which is often subtly compensated for (Omari et al., 2013). There is a possibility that dysphagia is more common than the published data suggest, because many older people do not report problems (Omari et al., 2013) or have learnt to live with them (Chen et al., 2009).

Swallowing is a complex process that involves elements/phases working in sequence to ensure the safe transfer of food or liquid from the mouth to the stomach. During swallowing, the suprahyoid muscles contract, pulling the larynx in an upward and anterior motion (Curtis et al., 2018). The larynx comes towards the base of the tongue (Shaw and Martino, 2013) and there is a downward movement of the epiglottis (Curtis et al., 2018). This ensures that food does not pass into the airway.

As the bolus passes through the pharynx it is subject to multiple pressures which are dependent on the function of the pharynx and tongue as well as viscosity of the bolus. With age, there is increased residue remaining after the swallow (Omari et al., 2013) secondary to reduced opening and higher resting pressures with increased dwell time of the bolus in the pharynx; these changes correlate well with the known reduction in laryngeal elevation with age and the reduction in UES opening (Curtis et al., 2018).

Instrumental assessment of swallowing is undertaken using either fibre optic endoscopic evaluation of swallowing (FEES) or videofluoroscopy (VF). These two evaluations are complimentary and on occasions are used in tandem. VF has the advantage of being able to demonstrate physiology and function at the same time, in both the AP and lateral projections if required. Studies of pharyngeal function for swallowing manoeuvres such as chin-tuck have used VF.

Despite the frequency of dysphagia, swallowing problems/dysphagia in frail older people is poorly managed in hospital. Weakness in the supra-hyoid muscles (such as that induced by sarcopenia), weakness of the laryngeal elevation and anterior motion, reduced epiglottis depression and opening of the superior oesophageal sphincter.(Curtis et al., 2015; Sze, 2016) and result in dysphagia.

Swallowing is not routinely assessed when frail people are admitted to hospital as stroke patients are (SSNAP, Melgaard et al 2018) and dysphagia is not identified. As a consequence, rehabilitation of the swallow is not provided. Momasaki et al (2014) using a large Japanese database, demonstrated that those patients with dysphagia who were offered appropriate rehabilitation, were more likely to have a total oral intake compared to those not offered oral-pharyngeal rehabilitation (OR 1.2 P<0.001).

It would seem logical that an approach to swallow rehabilitation would be to improve the strength of the suprahyoid muscles. Skeletal (arm and leg) muscle weakness, as treated

with resistance exercise, has been investigated and shown to have a positive effect on muscle strength and bulk (Phu et al., 2016). Resistance exercises may prevent loss or improve muscle bulk and strength (Otusaka et al., 2018; Komi et al., 1978; Anwer and Alghadir, 2014). Changes in crico-pharngeal distensibility or traction, generated by suprahyoid muscle contraction will present with dysphagia (Sze 2016). Yet, the standard hospital rehabilitation frequently consists of postural manoeuvres (including Chin-Tuck) to enable a safe swallow rather than an improved swallow.

A swallow programme including strengthening exercises (Swallow-STRONG) uses tongue strengthening exercises (Rogu-Pulia 2016) and the Shaker manoeuvre, Neck exercises (Shaker et al., 2002)) have been shown to improve swallow mechanics. Shaker and colleagues developed a system of isometric resistance exercises to strengthen the hyoid group of muscles and neck muscles (Shaker et al., 2002). The exercise programme consists of 3 isometric head lifts, held for 60 seconds each and then rapid neck flexion for 30 times daily for six weeks. They also involve activation of muscles (sternocleidomastoid) and abdominal muscles not directly related to swallowing. The exercise programme strengthens the suprahyoid muscles resulting in improved upper oesophageal opening ($p<0.01$), laryngeal anterior excursion ($p<0.05$) and reduction in post-swallow aspiration ($p<0.05$; Shaker, 2002).

Mapani et al (2009) found that the Shaker Exercise resulted in an increase in thyrohyoid shortening after 6 weeks compared to tongue exercises and swallowing manoeuvres. Some studies suggest that this type of exercise causes increased contraction pressure in the pharynx, increased pressures in the pyriform sinuses and shortened opening times of the UES. However, this is in contrast to some other studies (Balou, 2013; Park et al., 2010). Balou et al (2013) suggest that more data is required to determine how chin tuck affects the physiology of swallowing.

In frail older people, the Shaker Exercise may not be technically feasible due to muscle weakness, fatigue or co-existing morbidities. Sze et al (2016) showed that it was possible to do this type of exercise by placing a partially-inflated ball beneath the chin and then pressing down against the ball. This exercise - Chin Tuck Against Resistance (CTAR) - generated similar EMG results and greater benefits than Shaker. Recently Shaker and colleagues have suggested an alternative approach – ‘Laryngeal Resistance’.

The chin tuck is a swallowing exercise that is often deployed where the swallowing problem is secondary to a delay in onset of the pharyngeal swallow. It is generally accepted that the exercise pulls the larynx up and forwards and at the same time opens the UES (Shaker et al., 2002; Welch et al., 1993). Such a system is being utilised as part of the Ampcare neuromuscular stimulation programme. However, at present it is not possible to perform the chin tuck exercise in a consistent way, with controlled effort because there is no means by which effort can be regulated by the patient. The advantage of the chin tuck exercise, over the Shaker movement, is that the effects are more localised and less likely to unnecessarily recruit the muscles of the neck. Yoon et al (2018) studied stroke patients and showed positive clinical benefits of CTAR in a small randomised study.

Pogus-Pulia et al (2016) used isometric progressive resistance oropharyngeal therapy (Robbins et al., 2007) to demonstrate improved FOIS score (effect estimate 0.4, $p<0.02$), reduced incidence of pneumonia and reduced number of hospital admissions, in a cohort that was mixed in aetiology of dysphagia. However, previous exercise interventions have not been

carefully-controlled. The ability to control one's own effort during rehabilitation is essential in order to undertake the exercise in a consistent and regulated way, especially if it is to be performed by the patient at home. No exercise rehabilitation devices provide feedback that allows the patient to carefully control their effort when exercising at home. Furthermore, no previous exercise programmes allow logging of exercise data for subsequent review by the therapist in the clinic.

2. Assessment and management of risk

The study will be managed and monitored by the Trial Management and Steering Group (TMSG) which will be responsible for 'assessment and management of risk'. This group will comprise all members of the study team. In addition this group will include at least two patient representatives. The chief investigator and other research team members will meet periodically with the Acute and Emergency Medicine (AEM) Governance team to assess and manage study risks.

The device is an air filled bladder (typically a small ball) with a solid state electronic battery powered pressure gauge that connects to an Android Smartphone/tablet by Bluetooth. This will be in a plastic housing. We have no published studies on the safety, but the preliminary experience with staff members and family members is that there are no concerns regarding safety. Papers using the ball alone have not reported any safety concerns. The external casing of ExerPhager can be wiped and replaced.

There are many unknowns with respect to swallowing physiology and the anatomical structures that are involved in the chin tuck exercise and how this exercise results in an improvement in swallowing and a reduction of aspiration. With active swallow rehabilitation, the appropriate dose of exercise is required for benefit is not known, i.e how frequently the exercise should be undertaken, how many repetitions should be performed per session and at what force/pressure change the exercise should be carried out, is required for patient benefit and optimal compliance with an exercise rehabilitation intervention.

3. OBJECTIVES AND OUTCOME MEASURES/ENDPOINTS

3.1 Primary objectives

Establish whether it is feasible to recruit enough patients to assess the effectiveness of this intervention in reducing dysphagia and community-acquired pneumonia, in a larger-scale multi-centre randomised controlled trial (Hooper 2017; Lancaster et al 2004; Sim and Lewis 2012).

Assess the recruitment rates across each of the two NHS hospital sites

Assess willingness of patients to participate in, and complete the intervention.

Assess the compliance with the home-based daily exercise programme.

Establish the measurement variability of the tools for assessing outcome. Eg. FOIS, Quality of life (SWAL-Qol, EQ5D) and Swallow Speed.

Assess the ease-of-use and acceptability of the intervention (including the ExerPhager feedback ball).

Determine whether patients are willing and able to undergo videofluoroscopy.

Identify the optimum dose of CTAR-SwiFt training (frequency - daily vs twice-a-day).

3.2 Secondary objectives

These are physiological changes as measured using videofluoroscopy

Assess changes in bolus flow rates.

Measure the % change in laryngeal elevation.

Measure the % change in base-of-tongue retraction during a swallow.

Establish whether there is a reduction in the pharyngeal residue after the intervention.

Observe the timing of UES opening, before and after the intervention.

3.3 Outcome measures/endpoints

1. Recruitment rates across two NHS hospital sites
2. Willingness to be recruited to the study.
3. Study retention (<30% drop out)
4. Compliance: 80% of exercises undertaken daily
5. The absence of adverse incidents.
6. Acceptability of intervention.
7. Videofluoroscopy measurement (Reduced PTT; reduced residue post swallow)
8. Change in laryngeal movement, UES opening and Tongue base retraction.
9. Improvement in swallowing speed as assessed by timed swallow.
10. Ease of use of the CTAR-SwiFt feedback system.
11. FOIS (Food oral intake score)
12. Swal-Qol/ED5Q Questionnaires.
13. Timed Up and Go (stand from sitting. Walk 3 metres, turn around and sit down again).
14. Reduction in TWST (Time taken to drink a 90mls of water).

4. TRIAL DESIGN

The study is a randomised controlled study. Once recruited people will be randomised to one of three groups

1. Usual standard care (as defined by the clinical team including the speech and language therapist)
2. Low intensity rehabilitation (once daily CTAR-SwiFt exercise)
3. High intensity rehabilitation (twice daily CTAR-SwiFt exercises)

4.1 TRIAL SETTING

The study will be undertaken at two sites. The Queen Elizabeth Hospital, Woolwich, SE18 4QH, and Southmead Hospital, Bristol. Participants will be identified from those admitted acutely to hospital.

5. PARTICIPANT ELIGIBILITY CRITERIA

5.1 Inclusion/ exclusion criteria

- Medically stable (systolic BP >110; Heart rate >60 bpm, MEWS ≤1)
- Over the age of 75 years
- Clinical Frailty Score of ≥4 <8
- MOCA >14
- Able to provide consent (Different media will be provided to patients to enable consent to occur e.g. pictures; Speech Therapy support)
- No significant breathlessness (St Georges COPD Score)
- Not requiring oxygen
- No past history of stroke or neurological disease
- No evidence of severe rheumatoid arthritis (risk of neck instability)

5.2 Exclusion criteria

- Failure to provide consent to take part in the study
- Progressive medical conditions (some malignancy, neurological disease)
- MOCA <14
- Dysphagia requiring active intervention at the time of assessment
- Dysphagia secondary to surgical treatment of head and neck cancer

6. TRIAL PROCEDURES

The study will run for a total of 24 months. The intervention period is three months, with three months follow up.

6.1 Recruitment

This is a feasibility study. One of the outcomes is the ability to recruit. The TSMG will monitor recruitment monthly. Information will be gathered form researchers, participants and those refusing to take part to optimise the recruitment process.

The clinical teams will be approached to identify possible participants. These teams will be reminded and updated on a regular basis at departmental and governance meetings.

6.2 Participant identification

Patients will be identified on the acute frailty wards of the participating hospitals.

The responsible medical team will identify the patients to the research team, who will be based on the ward.

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6.3 Screening

Identified patients will be screened against study eligibility criteria by the research team, prior to consent being sought.

6.4 Consent

Consent will be obtained by either the research staff or the responsible medical consultant. All patients participating in the study will be asked to provide informed consent. A patient information sheet will be provided prior to consent being sought. Participants will be given at least 24 hours to consider whether they wish to be involved in the study.

6.5 The randomisation scheme

Sixty patients will be recruited across two centres (30 per centre) to study the feasibility of the 12-week CTAR-SwiFt intervention programme. Patients will be randomly allocated to one of 3 groups:

1. Usual treatment group (CON).
2. Exercise rehabilitation ‘once-per-day’ group (EXR1).
3. Exercise rehabilitation ‘twice-per-day’ group (EXR2).

Randomisation support will be provided by the Clinical Trials Unit at King’s College. Randomisation will be at individual participation level.

6.5.1 Method of implementing the randomisation/allocation sequence

- A web based randomisation system will be designed, using the bespoke KCTU randomisation system. The randomisation system will be created in collaboration with the

trial analyst/s and the CI and maintained by the King's Clinical Trials Unit for the duration of the project. It will be hosted on a dedicated server within KCL.

- The CI or delegate will request usernames and passwords from the KCTU. System access will be strictly restricted through user-specific passwords to the authorised research team members. It is a legal requirement that passwords to the randomisation system are not shared, and that only those authorised to access the system are allowed to do so. If new staff members join the study, a user-specific username and password must be requested via the CI or delegate (e.g Trial Manager) from the KCTU team and a request for access to be revoked must be requested when staff members leave the project. Study site staff experiencing issues with system access or functionality should contact the CI or delegate (e.g Trial Manager) in the first instance.

- Participant initials and date of birth will be entered on the randomisation system, NHS number, email addressed, participant names and addresses and full postcodes will not be entered into the randomisation system. No data will be entered onto the randomisation system unless a participant has signed a consent form to participate in the trial. Randomisation will be undertaken centrally by the co-ordinating study team, by authorised staff onto the randomisation system by going to www.ctu.co.uk and clicking the link to access the randomisation system. A full audit trial of data entry will be automatically date and time stamped, alongside information about the user making the entry within the system.

- The Trial Safety and Management Team will undertake appropriate reviews of the entered data, in consultation with the project analyst for the purpose of data cleaning. No data can be amended in the system, however CI or delegate (e.g. Trial Manager) may request King's Clinical Trials Unit to add notes against individual subject entries to clarify data entry errors.

- Upon request, KCTU will provide a copy of the final exported dataset to the CI in .csv format and the CI will onward distribute as appropriate.

- Randomisation will be at the level of the [individual] using the method of [block randomisation with {fixed/ } stratified by {x (a,b), y (a,b,c)}].

6.6 Baseline data

Data will only be collected if it affects the trial outcome. We will collect
Age
Sex
Co-morbidities which may affect the ability to use the ExerPhager (e.g. severe rheumatoid arthritis)
Medication use:
Swallowing Assessment
Plus those Assessments of study outcome parameters (see table below 7)

7 Trial assessments

Procedure	Enrolment	Baseline/ Week 0*	Week 4	Week 8	Week 12*	Week 16	Week 20	Week 24*
Consent	x							
Clinical Swallow Assessment		x			x			x
Timed Water Swallow Test		X	x	x	x	x	x	x
Videofluoroscopy (for those randomised to this arm)		x			x			
EAT-10		x	x	x	x	x	x	x
4QT		x	x	x	x	x	x	x
FOIS		x	x	x	x	x	x	x
Timed Up and Go (TUG)		x	x	x	x	x	x	x
QoL		x			x			x
EQ 5D		X			X			X

*CON group review dates

8 Trial Treatments

8.1 Clinical Swallowing Assessment:

Each participant will undergo a standardised clinical swallowing assessment by a speech and language therapist (SLT), and if clinically indicated advice on management of dysphagia and swallowing will be offered. Those people where the presence of dysphagia is pre-existing or where there is a clinical concern will be excluded from the study.

8.2 Exercise Rehabilitation Optimisation:

The exercise rehabilitation intervention will last for 12 weeks and will involve performing chin tuck exercises against resistance with feedback (CTAR-SwiFt), using the ExerPhager device (a rubber ball with pressure gauge, linked to a tablet via Bluetooth). It will be possible to set a 'target' level of effort (using feedback, during exercise) so that the exercise can be carried out safely. Part of the purpose of the feasibility study will be to establish appropriate target effort levels for each patient. The target effort will be set through an 'exercise rehabilitation optimisation' assessment, prior to the exercise rehabilitation intervention.

An SLT or physiotherapist will describe and demonstrate the ExerPhager device. Each patient will be shown how to use the device and how to perform the exercises correctly. The use of a 'target' effort level will be explained and each patient will be shown how to use the feedback

provided, to ensure that the target effort level is maintained. The device will be constructed of a suitable material that can be cleaned between use.

The 'exercise rehabilitation optimisation' will be conducted to determine the optimum dose of CTAR-SwiFt exercise therapy that is acceptable to each patient. First, each patient will be invited to perform 3 x chin tuck exercises, of brief but maximal effort (3 to 5 seconds). The mean measured strength value, derived from these 3 brief efforts, will be used to calculate the 'target' 30% effort level. This initial target level (30%) is based on our pilot data (acquired in healthy older participants). After determining the individual's target level, patients will be invited to attempt to perform the 'standard dose' derived from previously-published study exercise protocols (3 times 60 seconds of sustained effort at 30% of the participant's individual maximal volitional effort). If patients are not able to complete this 'standard dose', a lower effort level or duration will be adopted. During the 12-week intervention period, the dose will be assessed at the monthly review (control and intervention arms), to allow adjustment as participants improve or in case of difficulty performing the exercise.

8.3 Videofluoroscopy:

Thirty patients will undergo videofluoroscopy examination of their swallow. Each patient will be invited to undergo videofluoroscopy (pre and post-exercise programme) in the lateral plane, with the exposure field set between the lips and the back of the neck. The examination will consist of recording fluoroscopic images which appear on a monitor during oral intake of a bolus coated with barium. The procedure will enable a precise evaluation to be made, not only of the morphological features and dynamics of the swallowing act but also the timing of the oral and pharyngeal phases of the swallow.

Videofluoroscopy will be conducted at the study sites, following standard clinical procedures and protocols, by a SLT and radiographer. Six swallows will be assessed using three consistencies twice; Of the two swallows per consistency once will be performed whilst using the ExerPhager, undertaking a CTAR and one without. The examination will begin with the administration of barium (liquid consistency). If no signs of aspiration are observed, the examination will continue with the administration of boluses of variable consistencies: liquid (barium and water), semi-solid (yoghurt) and solid (biscuit). The timing of the transit of the various consistencies will be measured. The oral transit time (OTT) is defined as the time elapsed between the bolus starting to move inside the mouth and the time point at which the head of the bolus passes into the pharynx, beyond the base of the tongue. The pharyngeal transit time (PTT) is defined as the time elapsed between the head of the bolus going past the base of the tongue, and the tail of the bolus going through the UES (Rugiu, 2007).

Additionally, the sequence of fluoroscopic images will be processed in order to extract the motion of the passage walls as well as the bolus. The data will be analysed in two different ways:

1. The physiological effects of the chin tuck exercise rehabilitation intervention on the base of the tongue, posterior pharyngeal wall and laryngeal movement has not been fully clarified. Therefore we will examine the changes in the movements of these three structures, with and without CTAR.

2. This data will be used as input to computational fluid dynamics simulations in order to determine the precise values of pressure, velocity, efficiency of bolus mixing, and the stress exerted on the passage walls by the transiting bolus. This will establish the quantitative measures that will be important in establishing the repeatability of swallows and in evaluating the efficacy of the chin tick exercise.

Such analysis of the videofluoroscopy data through the use of numerical simulations provides a wealth of quantitative data. Additionally, subsequent simulations of different swallowing scenarios, such as different viscosity foods or alternative postures, can provide a prediction of the swallowing outcome, and therefore guide the definition of a protocol as well as tailoring treatment to individual patients.

By undertaking two swallows we will be able to determine the structural and relationship changes in the pharyngeal anatomy as well as changes in pressure and fluid dynamics induced by chin-tuck. Total exposure to radiation will be 5 minutes per subject.

8.4 Timed Water Swallow Test:

A simple assessment of swallowing speed. The subject will be provided with 90 ml of water to drink. They will be timed as to how long it takes to drink the 90 ml and how many sips were taken. If the total volume was not drunk, the residual will be recorded.

8.5 Questionnaires

EAT-10: a validated questionnaire swallow screen. There are 10 variables with scores of 0-4. A score of >3 is indicative of dysphagia.

4QT: A simple 4 question swallow screening tool.

QoL: The two scales recommended are the EQ-5D and Swal-Qol.

8.6 FOIS: A functional score of the amount that can be eaten, type and consistency.

8.7 Timed Up and Go (TUG). The time taken to rise from a chair, walk 3 metres, turn around and sit back down.

8.8 EQ 5D A quality of life measure

All participants will be assessed at base line, week 12 and week 24.

9. The CTAR Exercise rehabilitation Intervention Programme (12 weeks).

Sixty patients will be recruited across two centres (30 per centre) to study the feasibility of the 12-week CTAR-SwiFt intervention programme. Patients will be randomly allocated to one of 3 groups:

1. Usual treatment group (CON).

2. Exercise rehabilitation 'once-per-day' group (EXR1).

3. Exercise rehabilitation 'twice-per-day' group (EXR2).

Each patient who is allocated to either of the Exercise Rehabilitation Intervention Groups will be asked to perform Chin Tuck Against Resistance exercises (either once, or twice per day) using the ExerPhager device.

- One exercise session per month will be performed in a supervised way, at the Queen Elizabeth Hospital and Bristol Northern Hospital, and the other daily exercise sessions will be performed at home.
- The "Chin Tuck Strength Assessment" will be used to assess the maximum chin tuck strength (MCTS). This will involve 3x chin tuck for 3-5 seconds during which the patient will be asked to exert as much chin tuck force against the rubber ball as possible.
- The MCTS value will be used to determine a 'target' chin tuck exercise intensity usually 30% of maximum chin tuck strength (MCTS).
- The number of repetitions and the duration of each bout of exercise will be set according to that which was identified as most 'suitable' via the previous 'exercise rehabilitation optimisation' procedure.
- Patients will be asked to use the feedback (provided on a visual display screen) to adjust their effort until it matches the 'target intensity' (effort). Patients will be asked to maintain this effort until the specified time period has elapsed (e.g. 1 minute).

There will be approximately 1 minute of rest in between each of the 3 exercise periods (depending on that which is identified as most 'appropriate' via the exercise rehabilitation optimisation procedure'..

Each patient will then be asked to complete (at home) either one (EXR1 group), or two (EXR2 group) sessions of chin tuck exercises per day, for 12 weeks, in the format established during the previous supervised hospital-based exercise session. The overall ease with which each exercise session is completed, will be assessed by asking patients to complete a simple exercise 'comfort rating scale' (CR-10; Borg, 1974). The ease of completion will be used by the patient and clinic staff, to decide whether 'progression' is appropriate. 'Progression' will be achieved in monthly supervised sessions, by increasing the chin tuck exercise dose, by increasing either the number of repetitions, the %MCTS intensity, or the time period (see list of doses given in the 'exercise rehabilitation optimisation' process).

10. Data Collection

Data generated will be collated by the research assistants. The study is not blinded. The assessments are objective and do not require subjective interpretation from the RAs or other members of the research team. All data will be entered onto an electronic database, kept secure in a password protected file.

Quantitative data will be obtained via the set assessments on validate proformas.

The Qualitative data will obtained by interview by both formal and informal methodology.

11. Qualitative assessments

Semi-structured qualitative interviews with study participants will be conducted to determine key issues of concern for participants. Twelve participants (20% of the entire sample) will be purposively recruited, to represent: participants from all 3 study arms; even gender split; old and very old participants; those with good exercise completion and those with low exercise completion; those with informal care support at home and those without. Qualitative data will be transcribed and analysed thematically, allowing the research team to understand participants' experiences of study participation, and identification of common and variable points.

This should be able to provide data covering all relevant points; and to enable the research team to understand how a phenomenon is seen and understood among different people, in different settings and at different times. It will permit the identification of common and variable points (Green & Thorogood, 2018, 4th edition, Sage).

All participants will be provided with a feedback questionnaire. The questionnaire will ask about the organisation of the study and how it could have been "run better". This will be developed with the PPI representatives.

Participants will be approached to provide feedback about the ExerPhager; including ease of use of the device and App and what instructions should be included with the device. This will be conducted by survey with closed and open questions.

12. Withdrawal criteria

People recruited to the study will be free to withdraw at any stage. Withdrawing from the study is an end point. The numbers withdrawing and reason for withdrawing will be documented.

13. End of trial

The study will recruit 60 patients. The intervention will last 12 weeks, and participants will be reassessed at 6 months (24 weeks), 3 months after the intervention has ceased. The study will end when the last person has been followed up. Recruitment will cease when the last person has been recruited.

14. Name and description of investigational Device

With the help of patients, clinicians and therapists, we have developed a simple chin tuck feedback-enabled exercise (small rugby) ball, which works by squeezing and which is placed under the chin as originally developed by Yoon et al., 2016. However, our exercise ball allows the level of pressure that is exerted (during the chin tuck squeeze) to be monitored by a small pressure gauge. This exertional pressure can be sent to a monitoring and display device (Smart phone or tablet/ipad), which provides feedback to the participant. By adjusting the level of effort exerted in squeezing the ball, the participant can match a predetermined safe 'target' (which is determined by the clinician and researchers). This feedback system thereby ensures that repeated periods of chin tuck exercise are performed by the patient at a safe and consistent effort level each time.

This is a study looking at the benefit of a form of neck exercises. The device used (**ExerPhager**) is a novel device that allows the participant to undertake consistent exercise. The Device will consist of a ball fitted with a pressure gauge and an app installed on a Smart phone or tablet/ipad. The feedback will be activated by tapping tapping on the app and then tapping start. Also, the duration, frequency and compliance with the programme of chin tuck exercises can be recorded on the Smart phone or tablet/ipad. Where appropriate, this recorded data could be opened/downloaded by the therapist, either virtually via the internet or in the clinic setting, for discussion with the patient. No passwords will be required by the participant. The ExerPhager will be provided to the participant for the 12 weeks of the study. After the study the ExerPahger ball will be returned to the local trial team. This will be cleaned and reused if needed for purposes of the trial.

15. Assessment of compliance with treatment

The software will record compliance, i.e. the frequency and nature of the chin tuck exercises actually undertaken by the participant, and compared with the recommend allocated exercise sessions provided at the outset of the programme.

16. Adverse Events

1. Any adverse event should be reported to the study co-ordinator/ Chief Investigator within 7 working days.

2. Serious Adverse Events should be reported to the chief investigator within 24 hours.

3. Unexpected serious untoward events should be reported to the chief investigator within 24 hours

A standard reporting form will be provided. This will be kept on laptop held by the local research team. The form will record the trial number, age and sex of the patient.

A description of the adverse event and the outcome to the event will be kept on file. Where appropriate serious adverse events should be reported through the local governance procedures.

16.1 Notification of deaths

A death of a trail participant will be treated as an SAE/SUSAR. The Chief Investigator should be notified immediately and the Sponsor within 24 hours. The Sponsor will be notified by direct contact with the Operations Manager of R&D and subsequently the Director of R&D. They will be responsible for forwarding the information to the Director of Governance if the investigation warrants referral.

17. Study Responsibilities

17.1 Principal Investigator responsibilities

The site PI will be responsible for the day to day management of the study on their site. They will have oversight of the running of the study and the RA on their site. They will be responsible for ensuring governance and GCP requirements are met.

17.2 Research Assistants

It is the responsibility of the research assistants to identify the participants on the ward, assess their eligibility for the study. The RA will undertake the initial approach and provide the Patient Information sheet and consent form. Consent will be taken by the person delegated at the time, either the RA or the PI.

The RA shall keep a screening log of people admitted with pneumonia (who may subsequently be screened, and consented). This will permit an estimate of the population the study subset is drawn from.

CI (DS)	Overall study management Commencement and completion of the study Timing of the study Adherence to the protocol. Recruitment to time Governance Investigation of AE and reporting to Sponsor
TSMG DGS, ILS, DH, RW, ELD, SA, AG	To provide Governance Oversight Reports to the CI and Research Governance
Local PI	Delegated site responsibility for the above Consenting Participants Randomising

	Initial investigation of AE and reporting to CI
RA	Day to day running of the study. Screening Log Participant Log Identification of participants Provision of the PIS and Consent Form Collection of Data Entry of data into CRF Training the Patient in using the ExerPhager Arranging hospital/home visits/ reviews and undertaking such reviews as per protocol
SLT (RW/DH)	Overseeing the video fluoroscopy, following the agreed protocol Collecting images and forwarding for analysis to Bristol University
AG	Reviewing and reporting the VFs.
SA	Advice on trial management and data analysis
PPI	Advice on trial conduct and design
R&D	Study Governance reports Clinical Safety Committee Financial management with Finance Manager
CTU	Randomisation Data Management Statistical analysis

18. STATISTICS AND DATA ANALYSIS

18.1 Sample size calculation

CTAR-SwiFt is a feasibility study and as such is not powered to detect a significant difference. Sixty participants will be recruited which was considered to be adequate to identify the possibility of progressing to a larger definitive study, and is a generally recommended sample size (Ref) for feasibility studies. The objective measures, process mapping and qualitative data collected will aid in that decision.

18.2 Planned recruitment rate

The study is aiming to recruit 60 patients. The study would aim to recruit a minimum of 10 participants per site per month.

18.3 Statistical analysis plan

On the completion of the study, the data will be cleaned and then analysed. The study is a feasibility study. Recruitment rate, retention and attrition are simple percentages of those recruited. There will be comparisons between the three arms of the study. Non parametric tests will be utilised to compare between groups. Improvements in FOIS, TWST, TUG will use parametric tests to compare groups and within subject changes.

19 DATA MANAGEMENT

19.1 Source Data

Original data/ source data will be recorded directly into an electronic record. No paper source documents will be kept. Videofluoroscopy data will be stored on a high definition DVD or USB device and transferred to the University of Bristol by secure parcel post or electronically if this is deemed secure enough.

19.2 Case report forms

There will be no paper case report forms. All Case Reports will be digital.

19.3 CRFs as Source Documents

A copy of all data will be kept at the trial site for the duration of the trial.

19.4 INSPECTION OF RESEARCH RECORDS

The CI, PIs and all institutions involved in the study will permit study related monitoring, audits, and REC review. The CI agrees to allow the Sponsor or, representatives of the Sponsor, direct access to all study records and source documentation. These inspections will be planned, but may be required to be undertaken at short notice should there be a serious untoward event or trial irregularity.

20 GOOD CLINICAL PRACTICE

20.1 ETHICAL CONDUCT OF THE STUDY

The study will be conducted in accordance with the principles of good clinical practice (GCP). All research staff will be GCP compliant and hold a recent Certificate to verify this.

In addition to Sponsorship approval, a favorable ethical opinion will be obtained from the appropriate REC and appropriate NHS R&D approval(s) will be obtained prior to commencement of the study at each site.

20.2 Confidentiality

All CRFs, evaluation forms, reports, and other records will be identified in a manner designed to maintain participant confidentiality. All records will be kept in a secure storage area with limited access to study staff only. Clinical information will not be released without the written permission of the participant, except as necessary for monitoring and auditing by the Sponsor or its designee. The CI and study staff involved with this study will not disclose or use for any purpose other than performance of the study, any data, record, or other unpublished, confidential information disclosed to those individuals for the purpose of the study. Prior written agreement from the Sponsor or its designee will be obtained for the disclosure of any said confidential information to other parties.

Participant identifiers will not be held on the central study database; a unique study identifier will be assigned to each participants' data. Participant identifiers will be held at each site on a hard-copy form; this will allow participants to be re-contacted by the clinical research team at each site (for follow up and invitation for future studies) without identifiers being held outside the local recruiting organization.

20.3 Data Protection

The CI and study staff involved with this study will comply with the requirements of General Data Protection Regulation 2016 with regard to the collection, storage, processing and disclosure of personal information and will uphold its core principles. Access to collated participant data will be restricted to the CI and appropriate study staff.

Computers used to collate the data will be NHS and University networked computers and have limited access measures via user names and passwords. Hard copies of documents containing person-identifiable information (e.g. Informed Consent Form) will be stored securely in a locked filing cabinet in access-restricted offices at the study sites.

Published results will not contain any personal data that could allow identification of individual participants.

21 Data handling and record keeping

Data integrity is the responsibility of the CI and CTU. Data supplied at the end of the study for analyses and cleaning will be a copy with the original database stored in a locked room and filing cabinet.

Data will be obtained by the research team (RA/PI) and entered into an electronic CRF/ data form. Once entered the RA will be unable to change data.

21.1 Access to Data

Access to data during the trial will be via the Sponsor and the CTU. Access will be granted when there are serious safety concerns with respect to the advice

21.1.1 Access to the final trial dataset

- The data collected will be stored in a password protected file on a lap top.
- At the end of the trial data will be centralised and combined by the clinical trials unit.
- Access to the final dataset will be limited to the TSMG including the trial statistician..
- The computer files will be stored in a password protected file, on a memory stick and kept in a locked filing cabinet.
-

At the end of the study, all data will be released to the CI. The data will be backed up. A copy of the data will be forwarded to the trial statistician for analysis. The copy will be kept in a locked drawer in a locked room

21.2 Archiving

- All source records will be electronic with no paper copies. All records will be kept on an external storage device and kept for 15 years.

21.3 Data protection and patient confidentiality

- Every one taking part in the study will be allocated a study number. The patients name and details with their recruitment number will be kept separate from trail data and will not be accessible to the research team.
- Data will be stored in computer files protected by an encrypted password.
- At the end of the study, data will be transferred to a memory stick and the data centralised.
- Files (memory stick) will be kept for 10 years in a locked filing cabinet in a locked office.

22. ETHICAL AND REGULATORY CONSIDERATIONS

22.1 Research Ethics Committee (REC) review& reports

- before the start of the trial, approval will be sought from the Health Research Authority (HRA) and a REC for the trial protocol, informed consent forms and other relevant documents e.g. advertisements and GP information letters
- substantial amendments that require review by REC will not be implemented until the REC grants a favourable opinion for the trial (note that amendments may also need to be reviewed and accepted by the MHRA and/or NHS R&D departments before they can be implemented in practice at sites)
- all correspondence with the REC will be retained in the Trial Master File/Investigator Site File
- an annual progress report (APR) will be submitted to the REC within 30 days of the anniversary date on which the favourable opinion was given, and annually until the trial is declared ended
- it is the Chief Investigator's responsibility to produce the annual reports as required.
- the Chief Investigator will notify the REC of the end of the trial
- if the trial is ended prematurely, the Chief Investigator will notify the REC, including the reasons for the premature termination
- within one year after the end of the trial, the Chief Investigator will submit a final report with the results, including any publications/abstracts, to the REC

22.2 Peer review

The study has been peer reviewed by the study participants, sponsor R&D office, the NIHR for funding purposes and latterly the Ethics Committee:

22.3 Amendments

Any amendments required to the study protocol will be notified to the ethics committee and the relevant R&D offices of the Sponsor and participating centres. Approval will be required before they can be adopted formally and actioned

22.4 Protocol compliance

The protocol is the definitive document for the trial. It sets out how the study should run. Compliance with the protocol will be the PIs responsibility. Should evidence of non-compliance/ deviation become aware to the TSMG and Sponsor, a full investigation will take place. Repeated deviation from the protocol may mean that the study has to cease recruiting on that site and the deviations will be classified as a serious breach of protocol..

Any one not meeting the inclusion criteria should not be included.

If a change to the protocol becomes apparent an amendment will be sought via the ethics committee.

23. Indemnity

The study will be undertaken in peoples' homes and on the hospital site. The risks are small. The study will be covered by NHS indemnity at the relevant participating centre.

24 DISSEMINIATION POLICY

All data and IP generated by the trial will be the property of Lewisham and Greenwich Health Care Trust. Where appropriate agreements will be agreed with collaborating organisations regarding access to particular parts of the data set (e.g. videofluoroscopy data).

25 REPORTING, PUBLICATIONS AND NOTIFICATION OF RESULTS

25.1 AUTHORSHIP POLICY

Ownership of the data arising from this study resides with the study team and their respective employers. On completion of the study, the study data will be analysed and tabulated, and a clinical study report will be prepared.

Eligibility for authorship will be based on fulfilling the International Committee of Medical Journal Editors criteria for authorship. The opportunity to co-author publications will be extended to the core applicant team, local investigators, and others deemed by the core applicant team to have made a significant intellectual contribution to the study.

25.2 PUBLICATION

The clinical study report will be used for publication and presentation at scientific meetings. Investigators have the right to publish orally or in writing the results of the study.

Summaries of results will also be made available to Investigators for dissemination within their clinical areas (where appropriate and according to their discretion).

Summaries of the results of the project will be sent to all participants at the end of the study, and interim reports / newsletters (both for information and to encourage continued participation) will be sent to participants during their participation.

25.3 Monitoring Outputs and Dispute Resolution

The steering group will monitor and ensure the study team adequately report findings arising from the trial. Also, where there is a dispute of authorship or acknowledgement, the steering group agrees to act as arbitrator and the study team agrees to abide by decisions made by the Steering Group.

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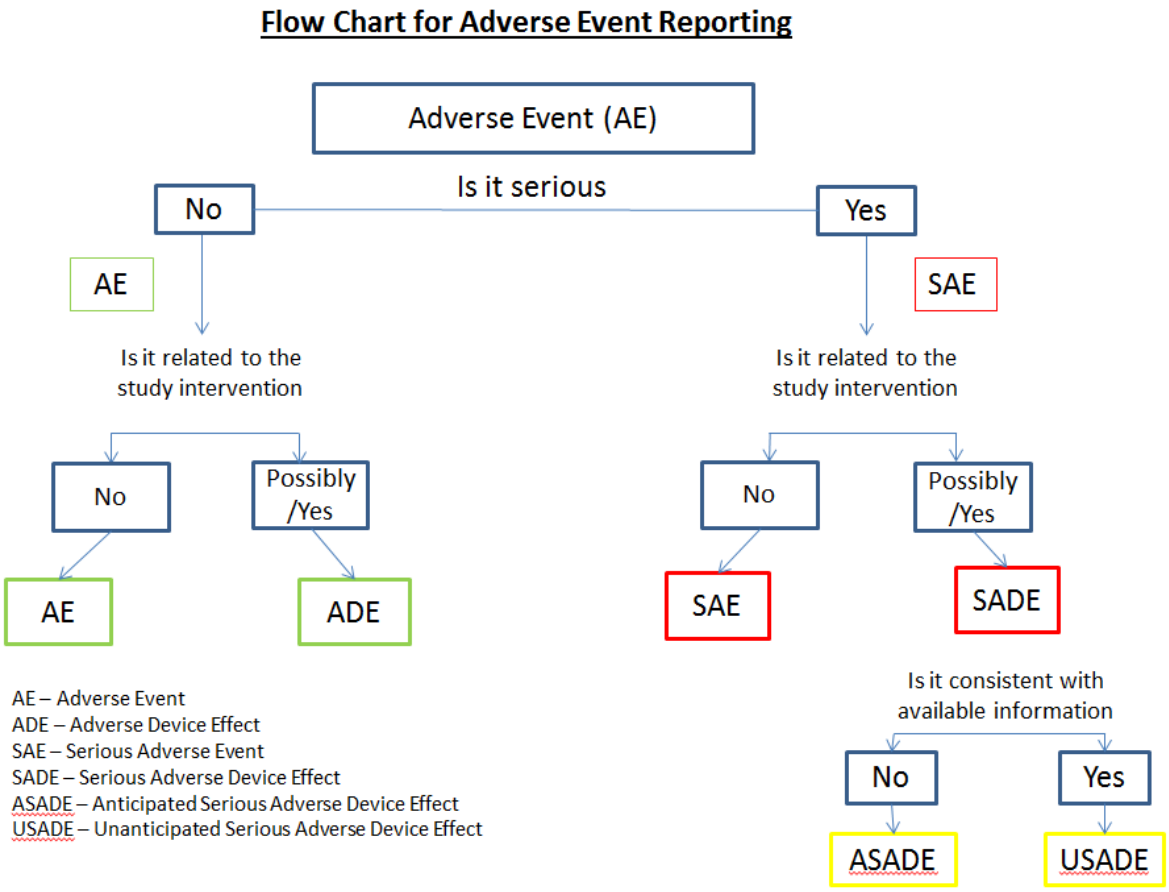
Appendices

Appendix 1 – Safety/ Adverse event Report Flow Chart

Appendix 2 - Protocol Amendments

Appendix 3 – Adverse Events Log

Appendix 1 - Safety/ Adverse event Report Flow Chart



Appendix 2 – Amendment History

Amendment No.	Protocol version no.	Date issued	Author(s) of changes	Details of changes made

List details of all protocol amendments here whenever a new version of the protocol is produced.

Protocol amendments must be submitted to the Sponsor for approval prior to submission to the REC committee or MHRA.

Appendix 3 - Adverse Events Log

Adverse Event Log

Insert Trust logo

Study No.	Date of Reporting	Date of Event	Study Arm (Control/ Exer1/ Exer2)	AE/SAE	Description and Action Taken

Version 1, 27 June 2019