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Evaluating mobility and strength training with and without protein supplements in pre-frail /frail older adults with low protein intake

Submission date 12/10/2022	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol
Registration date 18/10/2022	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 14/08/2024	**Condition category** Other	[_] Individual participant data [X] Record updated in last year

Plain English summary of protocol

Background and study aims

As people age, loss of muscle size and strength, slower walking, low activity levels, weight loss and feeling tired are common. Older people reporting some or all of these problems may be called frail. Frail people find it harder to get over illness and are more likely to fall or need hospital care. We need to find ways to stop people becoming frail and allow them to live independently without care and support.

Exercise is a treatment for frailty that can improve muscle strength and walking. Including extra protein in an older person's diet may also help. Protein provides the building blocks for muscles but many older people do not eat enough protein. Taking extra protein while exercising may increase the benefits of exercise. However, we do not know if this approach reduces frailty or improves walking and quality of life.

The aim of this study is to find out if it is possible to carry out a larger trial comparing exercise plus extra protein to exercise alone, in older people with low protein intake. We will find out if we can find enough people with a low protein diet willing to take part; whether participants are happy to take the protein supplements; and whether NHS physiotherapy departments can provide the exercise sessions. We will work with NHS physiotherapy departments to recruit 50 older people living in the community who are frail or at risk of becoming frail and have low protein intake. Participants will be randomly allocated to exercise plus protein or exercise only. All participants will undertake exercise twice a week with support from a physiotherapist for 6 months. The exercise programme involves muscle strengthening, balance and walking. Participants will be invited to attend 16 weekly group exercise classes run by the physiotherapist and to carry out the exercises at home once a week. They will then be asked to exercise at home twice weekly for a further 8 weeks. Half the participants will also take protein supplements for 6 months. At enrolment and 8 months later, we will measure walking ability, balance, muscle strength and size. We will ask participants about QoL and use of health and social care services.

Who can participate?

People aged 65 years and older who are frail or pre-frail (as defined by the Fried Frailty criteria) and have a slow walking speed or difficulty walking.

What does the study involve?
For patients identified as potentially eligible and interested in the trial, there are three eligibility checks. Firstly, a telephone call with a research nurse to do an initial check of eligibility. Then, a visit to a local study centre for an assessment including a dietary assessment to work out the current level of protein intake. This appointment also includes a small blood sample and some physical measurements. The final check is a second dietary assessment done via the computer or over the phone. If all three checks are passed, participants will be enrolled in a 24-week exercise programme designed especially for them by a physiotherapist, to improve walking. Participants will attend a weekly exercise class for 16 weeks at their local site, and exercise at home once a week. When the classes finish, participants will do 8 weeks of home exercises twice a week, with telephone support from the physiotherapist. Half of participants will take daily protein drinks. These will be delivered to their home, free of charge. The drinks are not suitable for people with milk or soya allergies or who are intolerant to lactose. A physiotherapist or dietitian will review participants regularly throughout the study. Eight months after starting the study, participants will go to the study centre for a final assessment and blood sample.

What are the possible benefits and risks of participating?
We have already tested this exercise programme in another study, and it improved participant's walking. We hope MMoST participants will have similar benefits. We do not know whether taking the protein supplements will improve participants' strength and walking, as this is the reason we want to conduct a study. Participants are unlikely to be harmed by doing the exercises. A physiotherapist will conduct an initial assessment to make sure that the exercises are at the right level for each participant. Participants may experience muscle soreness after completing some of the exercises. This is normal and the physiotherapist will offer advice on how to manage this. Protein supplements may cause mild gastrointestinal complaints including diarrhoea, constipation and bloating. These types of complaints are usually short lived as your body adjusts to the supplements. The supplements may cause some loss of appetite and weight loss so we will monitor participants' weight regularly and adjust the dose, if needed. We will ask for a blood sample which will be taken using a finger prick test. There is a possibility of bruising to the finger and/or fainting, but care will be taken to avoid this happening.

Where is the study run from?
University of Oxford (UK)

When is the study starting and how long is it expected to run for?
April 2022 to July 2024

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK)

Who is the main contact?
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Study website
https://mmost.octru.ox.ac.uk/

Contact information

Type(s)

Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
317330

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 54164, IRAS 317330

Study information

Scientific Title
A feasibility trial evaluating mobility and strength training with and without protein supplements in pre-frail/frail older adults with low protein intake

Acronym
MMoST

Study objectives
The aim of this multicentre, parallel, two-group, randomized controlled feasibility study is to find out if it is possible to carry out a larger trial comparing exercise plus extra protein to exercise alone, in older people with low protein intake. The study will find out if we can find enough people with a low protein diet willing to take part; whether participants are happy to take the protein supplements; and whether NHS physiotherapy departments can provide the exercise sessions.

Ethics approval required

Old ethics approval format

Ethics approval(s)
Approval pending, London - Surrey Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS; +44 (0)2071048088; surrey.rec@hra.nhs.uk), ref: 22/LO/0672

Study design
Randomized; Interventional; Design type: Treatment, Dietary, Psychological & Behavioural, Physical

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

Health condition(s) or problem(s) studied
Pre-frail/frail older adults with low protein intake

Interventions
A multicentre, parallel, two-group, randomized controlled feasibility trial conducted in NHS community and secondary care trusts. Participants will be frail and pre-frail community dwelling older adults with low protein intake. Participants will be randomized (1:1) to mobility and strength training with or without protein supplements.

Participants will be identified by clinical staff working in NHS rehabilitation services such as physiotherapy and falls clinics at three to five NHS sites in England and with the patient's permission will be referred to site research staff for consent, screening and eligibility assessment. We will also identify potential participants from an existing cohort study (Oxford, Pain, Activity and Lifestyle (OPAL) cohort study). Potential participants will be identified from their most recent OPAL questionnaire and invited by the OPAL study team to undergo screening for the trial. Interested participants will be referred to site research staff for screening and eligibility assessment. OPAL participants have given consent to be contacted about the opportunity to take part in other studies. We will ensure that we clearly identify the recruitment path for each MMoST participant to enable us to understand the numbers of potential participants expected to be identified from the OPAL cohort and those from normal NHS referral routes should we move forward to a larger study.
Consent, screening, eligibility assessments and randomization will be undertaken by site research staff. Following initial screening via telephone, potentially eligible participants will

attend an in-person eligibility assessment. As part of the eligibility assessment, participants will be asked to complete a 24-hour recall dietary assessment to confirm eligibility. Participants will be consented prior to undertaking this study specific assessment.

If, following this assessment, they are still eligible then they will complete the baseline questionnaire and physical assessment to avoid having to attend an additional appointment. Participants will still require final confirmation of eligibility before randomization occurs. They need to complete a second 24-hour recall dietary assessment and have a blood test to check they do not have impaired renal function (protein supplements would be contraindicated). We will obtain consent to request or access existing blood test results, if participants have had one in the last 3 months, to avoid a repeat test where possible. After all eligibility checks are completed, eligible participants will be randomized.
Each participant will be enrolled in the study for an 8-month period. All participants will receive mobility and strength training. Half of the participants will be randomized to also receive protein supplements.

Once randomized, all participants will attend an initial assessment with a physiotherapist (within 6 weeks of their original referral if possible) and will then be invited to attend weekly mobility and strength training classes for 16 weeks and to perform weekly home exercises. On completion of the 16 weeks of supervised classes, participants will be asked to carry out a further 8 weeks of twice weekly independent home exercises with the support of the physiotherapist.

Participants allocated to protein supplements will have an additional 30 minute initial appointment with the physiotherapist or dietitian to receive instruction on how to take the protein supplements including the amount they should take each day. The participants will receive their protein supplements via home delivery. The protein supplement is a powdered supplement (Nutricia Fortifit), provided in tins, including a scoop measure, for mixing up with cold water in shaker that will also be provided. Each serving of the protein powder contains 149 kcal, 20.7g whey protein, 2.8 g leucine, 20 ug/800iu vitamin D and 501 mg of calcium. Two flavours are available (strawberry and vanilla). Participants will be able to try the flavours at the initial appointment and will be given the option of selecting a mix of flavours or choosing a single flavour.

Following this appointment, the delivery company will be informed of the participant's requirements. The physiotherapist will monitor participants allocated to protein supplements when attending the weekly exercise groups including checking they are taking them, any side-effects, and monitoring their weight. The physiotherapist will trigger a new delivery of protein supplements when required. We plan to provide three deliveries to each participant over the course of the study, the size of these deliveries will be dependent upon the number of servings the individual participant is calculated to require, but this can be modified if required (for example, lack of space to store the tins).

At 8 months post randomization, participants will be invited to a final follow-up appointment with research staff at the study site to collect follow up data. If a participant is unable to attend an appointment at the study site, then, if possible, a home visit will be arranged by the site researcher or from the main study team to collect follow up data. Individuals from the main study team undertaking these visits will have a research passport.

Participants will be encourage to continue regular exercise beyond the study. They will be provided with information regarding community based exercise groups in their local area. They will also be provided with information about a digital exercise options including Good Boost

https://www.goodboost.ai/. This particular app was developed with the support of Sport England, co-designed with people living with musculoskeletal conditions, undergone extensive usability testing, and is endorsed by Versus Arthritis and the National Rheumatoid Arthritis Society to help people exercise at home.

Intervention Type
Mixed

Primary outcome measure
Feasibility will be assessed taking into account the following and using pre-defined stop/go criteria:
1. Recruitment rates, recorded as the number of participants recruited within 6 months.
2. Intervention fidelity, recorded as the percentage of participants that undergo their individual assessment and are allocated to their group sessions, the percentage of key criteria are met during observed sessions, and percentage of participants that receive the protein supplements via home delivery as intended.
3. Intervention adherence, assessed by the number of exercise sessions attended by participants, and percentage of days over the intervention period that participants report taking their protein supplement.
4. Study retention at 8 months follow up, assessed by percentage of participants lost to follow up at 8 months, in either study arm.

Secondary outcome measures
A secondary aim of the study is to trial the data collection procedures to be used in a main trial. We will collect the following data at 0 and 8 months unless indicated otherwise::
1. Date of birth, sex, ethnicity, relationship status, height and weight (body mass index), index of deprivation (from postcode), type of housing, work status, education, requires a carer or not (and type of carer – paid/unpaid), household income measured using self-reported questions (baseline only)
2. Physical capacity measured using Short Physical Performance Battery (SPPB) (proposed primary outcome)
3. Mobility measured using 6-minute Walk Test
4. Hand grip strength measured using a hand held dynamometer
5. Quadriceps strength measured using a hand held dynamometer
6. Sarcopenia measured using SARC-F Questionnaire
7. Frailty measured using Tilburg Frailty Indicator
8. Frailty measured using Clinical Frailty Scale Health Questionnaire
9. Frailty measured using Estimate of the Fried Frailty Index
10. Falls measured using Prevention of Falls Network Europe (ProFANE) self-report of falls and fall related injuries
11. Pain measured using Nordic pain questionnaire
12. Self-reported health conditions taken from the Clinical Frailty Scale
13. Assessment of daily dietary protein intake (myfood24.org)
14. Blood test to evaluate Estimated Glomerular Filtration Rate (eGFR)
15. Health related quality of life measured using EQ-5D-5L
16. Health and social care resource use measured using the Client Service Receipt Inventory (8 months only)

Overall study start date
01/04/2022

Completion date
31/07/2024

Eligibility

Key inclusion criteria
1. Aged 65 years and older
2. Frail (at least three criteria) or pre-frail (one or two criteria) as defined by the Fried Frailty criteria and must include slow walking speed (or difficulty walking).
3. Low protein intake (<1 g protein/kg body weight/day) measured by the average of two 24-hour dietary recall assessments.
4. Willing and able to provide informed consent to participate

Participant type(s)
Patient

Age group
Senior

Lower age limit
65 Years

Sex
Both

Target number of participants
Planned Sample Size: 50; UK Sample Size: 50

Key exclusion criteria
1. Dementia or cognitive impairment (defined as an Abbreviated Mental Test score of 6 or less)
2. Inability to walk 3 m without assistance (walking aid permitted)
3. Unable to follow verbal instructions which would make participation in the exercise group impractical including severe hearing impairment not corrected by a hearing aid or inability to follow simple safety instructions (e.g. English comprehension)
4. Living in a residential care or nursing home
5. Pre-existing diagnosis of:
5.1. Stroke in the last 6 months
5.2. Parkinson’s Disease
5.3. Acute, unstable physical illness that would make participation in the exercise programme unsafe
5.4. Dysphagia or swallowing problems that requires a modified diet
5.5. Type 1 diabetes or Type 2 diabetes on insulin
5.6. Severe kidney disease (stage 4 or 5)
6. Already taking protein supplements
7. Known allergies to ingredients of protein supplement (milk, soya) or lactose intolerant
8. Poor kidney function defined by an Estimated Glomerular Filtration Rate (eGFR) of <30 (blood test)
9. High risk of developing refeeding problems based on NICE guidance

Date of first enrolment

01/11/2022

Date of final enrolment
31/03/2023

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Birmingham Community Healthcare NHS Foundation Trust
3 Priestley Wharf
Holt Street
Birmingham Science Park, Aston
Birmingham
United Kingdom
B7 4BN

Study participating centre
Leeds Community Healthcare NHS Trust
Stockdale House
8 Victoria Road
Leeds
United Kingdom
LS6 1PF

Study participating centre
Bradford District Care Trust
New Mill
Victoria Road
Shipley
United Kingdom
BD18 3LD

Study participating centre
Oxford Health NHS Foundation Trust
Warneford Hospital
Warneford Lane
Headington
Oxford

United Kingdom
OX3 7JX

Sponsor information

Organisation
University of Oxford

Sponsor details
Research Governance, Ethics and Assurance
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OX3 7GB
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Sponsor type
University/education

Website
http://www.ox.ac.uk/

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Government

Funder Name
NIHR Central Commissioning Facility (CCF); Grant Codes: NIHR202733

Results and Publications

Publication and dissemination plan

The study protocol and results will be published in open-access peer-reviewed journals. Study results will also be presented at conferences. A lay summary of the study outcomes will be posted to all study participants who request to receive this and placed on the study website.

Intention to publish date
31/07/2025

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Protocol article		08/04/2024	14/08/2024	Yes	No