ISRCTN10801475 https://doi.org/10.1186/ISRCTN10801475

One study, many treatments: a new way to fight muscle loss in later life

Submission date 02/06/2025	**Recruitment status** Recruiting	[X] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 12/06/2025	**Overall study status** Ongoing	
Last Edited 08/07/2025	**Condition category** Musculoskeletal Diseases	

Plain English summary of protocol

Background and study aims
Muscle weakness in older people (known as sarcopenia) is common and can lead to falls, problems with mobility and the ability to look after oneself, poorer quality of life, longer hospital stays and earlier death. We would like to find out if there are treatments for this condition that could be tested in a large clinical trial, but first need to make sure this will work. Therefore this study will test different ways of treating muscle weakness in older people using a ‘platform trial’ design, in which we will run several smaller trials (or 'subtrials') testing a different treatment in each one. This way we hope to find out if any of the treatments seem promising for testing in a larger clinical trial.

Who can participate?
We will identify people aged 65 and over from GP practices, hospital clinics, registries and previous studies.

What does the study involve?
We will do a brief telephone call to check whether the person is likely to be eligible to take part, and if they are, we will do a full screening visit in their own home or in the research centre, involving asking some questions and taking a small sample of blood. Where participants are eligible for more than one subtrial (once more than one subtrial is running) we will give them the choice of which one they wish to take part in.
Once eligibility is confirmed we will invite participants to do two 'baseline' visits. At the baseline visits we will measure all participants' balance, walking speed and muscle strength. We will measure muscle size throughout the body using a scan called a DXA scan. We will also take a blood sample and a small sample of muscle from the thigh (a muscle biopsy). These tests will be performed at the beginning of the trial. We will randomise participants to either get 12 weeks of treatment (each subtrial will have a different treatment) or 12 weeks of usual care. At the end of this 12-week period, we will repeat all the tests that were done at the baseline visits. Each subtrial will recruit approximately 30-40 participants, depending on the treatment being tested.

What are the possible benefits and risks of participating?
It is unlikely that participants will benefit directly from participation, but the findings may lead to treatments for muscle weakness that could indirectly benefit participants in future. There are

very minor risks from the muscle biopsy, involving a minor level of discomfort and a small risk of bleeding or infection. Very rarely, a muscle biopsy can be associated with nerve damage, which can result in a small area of numbness or tingling (approximately the size of the palm of the hand). The team has extensive experience performing this procedure on older individuals, including frail older adults.
Participants in our previous studies have tolerated muscle biopsies very well, and the vast majority have stated that they would be happy to undergo the procedure again. Participants will also undergo a DXA scan, which carries a very minor risk. The scan uses a low dose of x-rays, which carries a minimal increased risk of cancer over many years.

Where is the study run from?
The main study visits will take place at the Clinical Ageing Research Unit in Newcastle, but the initial visit to confirm if people are eligible to participate can be done in their own home if preferred.

When is the study starting and how long is it expected to run for?
June 2025 to March 2028

Who is funding the study?
Newcastle NIHR Biomedical Research Centre (UK)

Who is the main contact?
Philippa Watts, revitalise@newcastle.ac.uk

Contact information

Type(s)
Scientific, Principal investigator

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Additional identifiers

Integrated Research Application System (IRAS)
352708

Protocol serial number
R&D11122

Study information

Scientific Title
Randomised evaluation platform – Interventions to treat older people with sarcopenia

Acronym
REVITALiSE

Study objectives
A wide range of different interventions could potentially be of benefit in sarcopenia, including exercise interventions, other physical methods to stimulate muscle, nutritional interventions, and pharmacological interventions targeting both muscle-specific pathways and broader biological mechanisms underpinning ageing. Using efficient ways to identify which interventions are promising at an early stage is needed to maximise the chance of later-stage trial success. In order to select which interventions should go on to testing in large randomised controlled trials, proof of concept data are needed – to show that interventions have an effect on the expected biological mechanistic pathway in humans, to provide a signal of potential efficacy, and to provide initial data on tolerability and feasibility of delivery of the intervention. This platform trial has been designed to provide these proof-of-concept data in a way that enables interventions to be tested in a standard way, enhances statistical power and maximises the efficiency of recruitment for this underserved group of patients.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 03/07/2025, North East - Tyne & Wear South Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ, United Kingdom; +44 (0)20 7104 8384; tyneandwearsouth.rec@hra.nhs.uk), ref: 25/NE/0102

Primary study design
Interventional

Study design
Single-centre platform trial consisting of multiple parallel-group, individually randomized controlled, open-label, proof-of-concept subtrials

Study type(s)
Treatment, Efficacy

Health condition(s) or problem(s) studied
Sarcopenia

Interventions
The platform trial will be made up of a number of randomised controlled subtrials which will run in parallel with each other. It will start with a single subtrial but then others will be added as further funding is secured. Each subtrial will compare a new treatment with usual care and participants will be randomised. Randomisation will be performed using a web-based randomisation system (REDCap). Randomisation within each subtrial will take place independently and the default randomisation ratio will be 1:1 between the intervention and control arms unless otherwise specified in the protocol subtrial annex information.

Where a single subtrial is open, the participant will automatically be allocated to that subtrial. Where more than one subtrial is currently open to recruitment, the investigator will ascertain which subtrials the participant is eligible to take part in. If the participant is eligible to take part in more than one open subtrial, the participant will be able to choose which subtrial to take part in after discussion with the investigator.

Initially the intervention being tested is Fisetin 400 mg capsules (marketed as a food supplement). Fisetin will be provided in tubs of 60 capsules per tub, with instructions for use provided along with each tub.

Intervention schedule:
Fisetin will be taken by participants once a day for three consecutive days on a 2-week cycle. A diary will be provided to highlight when participants should take fisetin. Fisetin will be taken with a meal.
The dose of fisetin to be taken will be written on the instructions and will vary by body weight:
<=50 kg: 2 capsules (800 mg) per day
50-69.9 kg: 3 capsules (1200 mg) per day
70-89.9 kg: 4 capsules (1600 mg) per day
>=90 kg: 5 capsules (2000 mg) per day
In the event of intolerable side effects or adverse reactions from the trial intervention, fisetin will be stopped.

Intervention Type
Mixed

Primary outcome(s)
4-metre walk speed in m/s measured at baseline and 12-week follow-up

Key secondary outcome(s)
1. Grip strength in kg measured using a handgrip dynamometer at baseline and 12-week follow-up
2. 7-day physical activity measured using a body-worn activity monitor (Axivity AX6). The Mobilise-D algorithm will be used to assess digital mobility outcomes (DMOs):
2.1. Number of walking bouts undertaken per day
2.2. Mean daily walking bout duration (seconds)
2.3. Mean walking speed (metres per second) estimated from short walking bouts

Measured at baseline and 12-week follow-up
3. Balance, lower extremity strength, and functional capacity measured using the Short Physical Performance Battery (overall score from 0 to 12) at baseline and 12-week follow-up
4. Intervention adherence evaluated by comparing the final tablet count at follow-up with the initial tablet allocation. Adherence will be calculated as (the number of tablets taken / the number of tablets expected to be taken by the final study visit) × 100
5. Withdrawal rate: number of participants not completing the 12-week follow-up
6. Number of adverse events: total number of adverse events reported and recorded at baseline, phone calls 2 and 7 days after baseline, and 12-week follow-up
7. Severity of adverse events: for each reported adverse event, an assessment of severity will be made according to the following criteria:
7.1. Mild: an event tolerated by the patient, causing minimal discomfort and not interfering with everyday activities
7.2. Moderate: an event sufficiently discomforting to interfere with normal everyday activities
7.3. Severe: an event that prevents normal everyday activities
Measured at baseline, phone calls 2 and 7 days after baseline, and 12-week follow-up

Completion date
31/03/2028

Eligibility

Key inclusion criteria
1. Age 65 years or over
2. Low maximum handgrip strength (<16 kg for women, <27 kg for men) OR prolonged 5 x sit to stand time (>15 s) (Inability to complete five sit to stands will count as a prolonged sit to stand time)

Participant type(s)
Other

Healthy volunteers allowed
No

Age group
Senior

Lower age limit
65 Years

Sex
All

Key exclusion criteria
General:
1. Unable to give written informed consent
2. Currently enrolled in another intervention study (observational studies are permitted).
3. Currently participating in supervised exercise classes or physiotherapy
4. Any progressive neurological or malignant condition with life expectancy <6 months or with rapid progression judged by the investigator to cause a significant decline in physical function

over the 12-week course of the trial
5. Unwilling or unable to undergo two muscle biopsies

Safety of muscle biopsy:
1. Platelets <100x109/L at screening (contraindication to muscle biopsy)
2. Presence of a bleeding diathesis or use of oral or parenteral anticoagulant medication
3. Antiplatelet agents
4. Allergy to local anaesthetic (lidocaine)
5. Unable to palpate vastus lateralis muscle to enable biopsy localisation
6. Unable to locate safe biopsy site (e.g. due to overlying vasculature)
7. Investigator judges biopsy would be unsafe (e.g. due to immunosuppression)

Other causes of skeletal myopathy:
1. Liver function tests (bilirubin, ALT, alkaline phosphatase) > 3x ULN
2. Estimated glomerular filtration rate <15ml/min/1.73m2 by CKD-EPI equation or on renal replacement therapy
3. Symptomatic (NYHA class II-IV) chronic heart failure (diagnosed according to European Society of Cardiology guidelines)
4. Severe COPD (GOLD stage IV)
5. Known myositis or other established myopathy
6. Self-reported weight loss of >10% in the last 6 months (to exclude significant cachexia)
7. Known uncontrolled thyrotoxicosis
8. 7.5mg/day or greater prednisolone use (or equivalent)

Date of first enrolment
31/07/2025

Date of final enrolment
30/09/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
NIHR Newcastle Clinical Ageing Research Unit (CARU)
Campus for Ageing and Vitality
Newcastle upon Tyne
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NE4 5PL

Sponsor information

Organisation
Newcastle upon Tyne Hospitals NHS Foundation Trust

ROR
https://ror.org/05p40t847

Funder(s)

Funder type
Government

Funder Name
NIHR Newcastle Biomedical Research Centre

Alternative Name(s)
Newcastle Biomedical Research Centre, Newcastle NIHR Biomedical Research Centre, NIHR Newcastle BRC, Newcastle Biomedical Research Centre - NIHR

Funding Body Type
Government organisation

Funding Body Subtype
Research institutes and centers

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the trial will be available upon request from a Data Access Committee, which will have representation from the Funder, Sponsor and CI and will be subject to presenting a clear plan of what the data will be used for, how the data will be analysed, how the results will be disseminated, and who the authors will be.
Data transfer will be subject to completion of a Data Sharing Agreement between Newcastle University and the end users.
Data will not be withheld from bona fide researchers requesting access unless the above criteria for sharing are not met.

IPD sharing plan summary
Stored in non-publicly available repository, Available on request