

Dietary supplements, exercise, and muscle ageing

Submission date 08/10/2022	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered
		<input type="checkbox"/> Protocol
Registration date 27/03/2023	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
Last Edited 27/03/2023	Condition category Musculoskeletal Diseases	<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims.

Loss of skeletal muscle mass and function is strongly associated with frailty, trips and falls, and a reduction in quality of life in elderly people. There are currently limited effective treatments for reducing loss of muscle and muscle function with ageing, and as we have an ageing population, addressing this issue is an important challenge. Current treatment options are limited to undertaking exercise and increasing protein intake, although these interventions are not effective for everyone. Nitrate supplementation has been suggested to have benefits for muscle function, but this has not been fully tested throughout the human life course. This study aims to determine the effect of nitrate and protein supplementation in young, middle-aged and aged participants, and the effect of exercise, nitrate and exercise, or protein and exercise in aged participants, on skeletal muscle function. The study will also assess some markers of cellular damage to gain insight into how any effects seen may be working.

Who can participate?

Adults aged 18 years or older who are healthy

What does the study involve?

Participants will undertake a selection of baseline measurements (e.g., height, weight, blood pressure, body composition), answer some questionnaires (about diet and quality of life) and undertake a battery of physical function tests. Blood samples and (if participants are happy to do so) a muscle biopsy will be taken. They will then be assigned to an intervention group (nitrate only, protein only, exercise only, nitrate and exercise, or protein and exercise). Participants will take the assigned intervention for 12 months, with follow-up visits at 3, 6, 9, and 12 months, where they will do the physical function tests, blood sampling, and (if happy to do so) muscle biopsy sampling, at each follow-up visit.

What are the possible benefits and risks of participating?

The study aims to understand muscle ageing across the human life course, and the effect of nitrate, protein and exercise on muscle function. This study will provide insight into the use of nitrate and/or protein supplementation, and exercise, as a way of reducing the debilitating effects of muscle ageing on quality of life, particularly in the elderly. Increased protein and exercise have previously been suggested to improve muscle mass and function (at least in some

people), so participants doing these interventions in this study may benefit from these effects. The study is making use of commercially-sourced nitrate and protein supplements, which are generally well-tolerated by the general population. However, there is a small risk these supplements may not agree with you. The researchers will also be asking participants if they would be happy for a muscle biopsy to be taken at each visit. This can feel a bit uncomfortable afterwards, and there is a small risk of infection associated with these biopsies.

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

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

Who is funding the study?
University of Bradford (UK)

Who is the main contact?
Dr Huw Jones, H.S.Jones@bradford.ac.uk

Contact information

Type(s)
Principal Investigator

Contact name
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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
312170

ClinicalTrials.gov number
Nil known

Secondary identifying numbers

IRAS 312170

Study information

Scientific Title

Developing interventions and investigating molecular markers of age-related sarcopenia

Acronym

DIMMAS

Study objectives

Dietary interventions (e.g. protein and nitrate) and exercise can modulate muscle ageing throughout the lifecourse.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approved 16/01/2023, London - Brighton & Sussex Research Ethics Committee (Health Research Authority, 2 Redman Place, Stratford, London, E20 1JQ, UK; +44 (0)2071048202; brightonandsussex.rec@hra.nhs.uk), ref: 22/PR/1028

Study design

Single-centre randomized parallel trial

Primary study design

Interventional

Secondary study design

Randomised parallel trial

Study setting(s)

Other

Study type(s)

Other

Participant information sheet

Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied

Skeletal muscle ageing throughout the life course (aged 18+ years)

Interventions

Participants will undertake the intervention for up to 12 months. For single interventions (e.g. nitrate only, protein only, exercise only) participants will not be randomised. For comparisons with combined interventions, randomisation will occur. All participants will act as their own baseline control.

Randomisation of sub-group allocation for the older participants will be implemented by assigning the exercise intervention to every other participant aged 69+ years recruited to the study. This approach ensures no bias from the study team and that the intervention is assigned pre-sarcopenia assessment and baseline testing.

1. Nitrate only (commercial beetroot extract - oral)
2. Protein only (commercial protein supplement - oral)
3. Exercise only (graded based on isokinetic dynamometer results). Participants undertake a graded mixed modal protocol that gets progressively more intense over 3 months and is reviewed every 3 months. Exercise for 1 hour, 3 times a week)
4. Exercise and protein (as above)
5. Exercise and nitrate (as above)

Intervention Type

Mixed

Primary outcome measure

Physical function measured using isokinetic dynamometer of knee extension and flexion at baseline and follow-up visits (baseline, 3, 6, 9, and 12 months)

Secondary outcome measures

1. Hand grip strength quantified using an isometric dynamometer at baseline, 3, 6, 9 and 12 months
2. Rate of force development, vertical peak force quantified by mid-thigh pulls using force plates, jump height, and concentric peak velocity quantified using a squat jump using force plates at baseline, 0, 3, 6, 9, and 12 months
3. Physical performance assessed using the short physical performance battery at baseline, 3, 6, 9 and 12 months
4. Physical performance assessed using the timed up-and-go test at baseline, 3, 6, 9 and 12 months
5. Body mass index (BMI) calculated by assessment of height and weight at baseline, 3, 6, 9 and 12 months
6. Weight, body mass index, fat mass, fat-free mass and muscle mass measured using bioelectrical impedance analysis (BIA) at baseline, 3, 6, 9 and 12 months
7. Blood and biopsy oxidative stress markers measured at baseline, 3, 6, 9 and 12 months:
 - 7.1. DNA oxidation measured using a liquid chromatography–mass spectrometry (LC–MS) assay for 8-oxo-dG in white blood cells isolated from whole blood and muscle biopsies
 - 7.2. Lipid peroxidation measured using the thiobarbituric acid reactive substance (TBARS) assay and ferrous oxidation xylenol orange (FOX) assay
 - 7.3. Protein carbonyl levels measured using the dinitrophenylhydrazine assay
 - 7.4. Bioavailability of the nitrate intervention measured using plasma nitrate and nitrite levels determined by high-performance liquid chromatography (HPLC)/LC-MS assay

Overall study start date

23/08/2022

Completion date

01/10/2024

Eligibility

Key inclusion criteria

1. Healthy volunteers
2. Asymptomatic
3. 18+ years of age

Participant type(s)

Healthy volunteer

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

A minimum of 30 per category, with 14 subgroups. In total, a target minimum of 420 participants.

Key exclusion criteria

1. Previous history of muscle disorder
2. Cardiac issues
3. Medication which is known to affect muscles, including statins and steroids
4. Contraindications to exercise
5. Pregnant or breastfeeding
6. Known allergies
7. Volunteers on blood thinning medication
8. Known renal impairment
9. Adults lacking capacity (not compos mentis)

Date of first enrolment

30/01/2023

Date of final enrolment

01/10/2023

Locations**Countries of recruitment**

England

United Kingdom

Study participating centre

University of Bradford

Richmond Road

Bradford

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BD7 1DP

Sponsor information

Organisation

University of Bradford

Sponsor details

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Sponsor type

University/education

Website

<http://www.bradford.ac.uk/external/>

ROR

<https://ror.org/00vs8d940>

Funder(s)

Funder type

University/education

Funder Name

University of Bradford

Alternative Name(s)

Funding Body Type

Private sector organisation

Funding Body Subtype

Universities (academic only)

Location

United Kingdom

Results and Publications

Publication and dissemination plan

Planned publication in a high-impact peer-reviewed journal and presented at conferences.

Intention to publish date

01/01/2028

Individual participant data (IPD) sharing plan

Blinded raw data will be made available on request if necessary (e.g. part of publication process). Participant identifiers will not be shared.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No