ISRCTN23294745 https://doi.org/10.1186/ISRCTN23294745

Dietary supplements, exercise, and muscle ageing

Submission date
08/10/2022

Recruitment status
No longer recruiting

Registration date
27/03/2023

Overall study status
Completed

Last Edited
27/03/2023

Condition category
Musculoskeletal Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] 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
Dr Huw Jones

ORCID ID
https://orcid.org/0000-0001-9846-5268

Contact details
Institute of Cancer Therapeutics
University of Bradford
Richmond Road
Bradford
United Kingdom
BD7 1DP
+44 (0)1274 234217
h.s.jones@bradford.ac.uk

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
312170

Protocol serial number
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

Study type(s)
Other

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

Key secondary outcome(s))
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

Completion date
01/10/2024

Eligibility

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

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit

18 years

Sex
All

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
United Kingdom

England

Study participating centre
University of Bradford
Richmond Road
Bradford
United Kingdom
BD7 1DP

Sponsor information

Organisation
University of Bradford

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

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