

# Can metformin prevent worsening of muscle weakness and frailty in older people who are showing early signs of frailty?

<b>Submission date</b> 10/04/2020	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 21/01/2021	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 28/04/2026	<b>Condition category</b> Signs and Symptoms	<input type="checkbox"/> Individual participant data

## Plain English summary of protocol

### Background and study aims

Frailty is a condition where the body isn't able to cope with a problem such as an injury, mild infection or other illness. Some of the first signs are losing muscle strength and slower walking. It is not yet known how best to prevent the onset of frailty. Exercise can help, and diet may also play a part. These approaches only go so far though, and new approaches including medication are also needed. Metformin is a medication that may be promising to prevent frailty by improving muscle function.

This project will test whether metformin, a medicine normally used to treat diabetes, can improve physical function in older people without diabetes at risk of developing frailty or sarcopenia (muscle weakness).

### Who can participate?

People living in the North East of England aged 65 years or older who walk slowly and have low muscle strength, which means they are at risk of becoming frail, and who do not have diabetes.

### What does the study involve?

Participants will be randomly allocated to one of two groups. One group will take a metformin tablet three times a day for 4 months. The other group will take a placebo (dummy) tablet three times a day for 4 months. Neither the participants nor the research team will know who is taking which tablet until the end of the study.

The researchers will measure walking speed, handgrip strength and other aspects of frailty and muscle weakness at the start and after 4 months of treatment. They will also measure activities of daily living, quality of life, muscle size, side effects of medication, and a series of blood tests to understand who might respond best to metformin to help select participants for a future large study.

### What are the possible benefits and risks of participating?

Metformin is a safe medication that has been used by millions of people for over 50 years. It can cause loose bowel motions or nausea in some people, but the researchers will minimise the chances of this happening by using a low dose, and excluding anyone with recent diarrhoea. Very

rarely, metformin can cause a build up of acid in the blood (acidosis). The researchers will monitor this at the monthly visits, and they will also exclude people with poor kidney function, who may have problems expelling metformin from the body, which can increase the chances of metformin causing a build-up of acid.

Where is the study run from?

Newcastle upon Tyne Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?

April 2020 to August 2023

Who is funding the study?

NIHR Newcastle Biomedical Research Centre (UK)

Who is the main contact?

Professor Miles Witham, Miles.Witham@newcastle.ac.uk

## Contact information

### Type(s)

Public

### Contact name

Prof Miles Witham

### ORCID ID

<https://orcid.org/0000-0002-1967-0990>

### Contact details

Campus for Ageing and Vitality

Newcastle

United Kingdom

NE4 5PL

+44 (0)1912081317

Miles.Witham@newcastle.ac.uk

## Additional identifiers

### Clinical Trials Information System (CTIS)

2020-004023-16

### Integrated Research Application System (IRAS)

275219

### Central Portfolio Management System (CPMS)

47772

## Study information

Scientific Title

Metformin to prevent progression of sarcopenia and frailty for older people – a randomised controlled proof of concept trial

**Acronym**

MET-PREVENT

**Study objectives**

4 months of metformin 500 mg three times a day will improve measures of physical performance in older people with sarcopenia and prefrailty.

**Ethics approval required**

Old ethics approval format

**Ethics approval(s)**

Approved 07/01/2021, North West - Liverpool Central Research Ethics Committee (\*\*Currently being held remotely via Teleconference/ZOOM\*\* Liverpool Women's Hospital, +44 (0)207 104 8197, +44 (0)2071048387; liverpoolcentral.rec@hra.nhs.uk), ref: 20/NW/0470

**Study design**

Randomized, placebo-controlled, double-blind, parallel-group trial

**Primary study design**

Interventional

**Study type(s)**

Prevention

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

Frailty and sarcopenia in older people

**Interventions**

Participants will be randomised 1:1 into the metformin or placebo arms using a web-based randomisation system. They will receive metformin hydrochloride 500 mg or matching placebo three times a day for 4 months. Assessments will be conducted at baseline and 4 months (all outcomes) with an additional safety assessment visit at 1 month.

**Intervention Type**

Drug

**Phase**

Phase IV

**Drug/device/biological/vaccine name(s)**

Metformin hydrochloride

**Primary outcome(s)**

4-m walk speed at 4 months

**Key secondary outcome(s)**

1. Fried frailty score, including individual components:
  - 1.1. Activity level assessed using self-report questionnaire at baseline and 4 months
  - 1.2. Exhaustion assessed using self-report questionnaire at baseline and 4 months
  - 1.3. Grip strength assessed using Jamar handgrip dynamometer at baseline and 4 months
  - 1.4. 4-m walk speed assessed using timed walk test over 4 m at baseline and 4 months
  - 1.5. Weight assessed using calibrated scales at baseline and 4 months
2. Transitions from pre-frail to frail, death, inability to continue in trial, or to non-frail from baseline to 4 months
3. Lower limb muscle power measured using Short Physical Performance Battery at baseline and 4 months
4. 6-min walk distance assessed at baseline and 4 months
5. Total body muscle mass measured using bioimpedance at baseline and 4 months
6. Ability to perform activities of daily living assessed using the Nottingham Extended Activities of Daily Living Scale (EADL) at baseline and 4 months
7. Health related quality of life assessed using the EQ5D and SF-36 scales at baseline and 4 months
8. Trial metrics:
  - 8.1. Conversion from screening to randomisation assessed using study records at screening and baseline study visits
  - 8.2. Recruitment rate assessed using study records over the 10-month recruitment period
  - 8.3. Retention rate assessed using study records over the 4-month participation period

**Completion date**

31/08/2023

## Eligibility

**Key inclusion criteria**

1. Aged 65 years or over
2. Low maximum handgrip strength (<16 kg for women, <27 kg for men)
3. Walk speed <0.8 m/s on 4-m walk test

**Participant type(s)**

Patient

**Healthy volunteers allowed**

No

**Age group**

Senior

**Lower age limit**

65 years

**Upper age limit**

100 years

**Sex**

All

## **Total final enrolment**

72

## **Key exclusion criteria**

1. Diabetes mellitus (type 1 or type 2)
2. eGFR <45 ml/min/1.73 m<sup>2</sup> by MDRD4 or CKD-EPI equation
3. History of diarrhoeal illness within the last 3 months (>48 h of Bristol stool chart grade 6 or 7)
4. Alcohol intake >21 units/week (women) or >35 units/week (men)
5. Symptomatic chronic heart failure, diagnosed according to European Society of Cardiology guidelines (asymptomatic left ventricular systolic dysfunction will not be an exclusion criterion)
6. Liver function tests (bilirubin, alanine aminotransferase or alkaline phosphatase) >3x upper limit of normal
7. Oral steroid dose >7.5 mg prednisolone equivalent per day
8. Unable to mobilise without human assistance
9. Life expectancy of <3 months as adjudicated by the local investigator
10. Unable to give written informed consent
11. Previous intolerance of metformin or taking metformin for another condition
12. Currently participating in, or participated within 30 days, another intervention study (observational studies and registries are permitted)

## **Date of first enrolment**

01/04/2021

## **Date of final enrolment**

30/09/2022

## **Locations**

### **Countries of recruitment**

United Kingdom

England

### **Study participating centre**

**Campus for Ageing and Vitality**  
Biomedical Research Building  
Newcastle University  
Newcastle upon Tyne  
England  
NE4 5PL

### **Study participating centre**

**Queen Elizabeth Hospital**  
Queen Elizabeth Ave  
Gateshead  
England  
NE9 6SX

# Sponsor information

## Organisation

Newcastle upon Tyne Hospitals NHS Foundation Trust

## ROR

<https://ror.org/05p40t847>

# Funder(s)

## Funder type

Research organisation

## 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 the current study will be available upon request from the Chief Investigator (Professor Miles Witham, [Miles.Witham@newcastle.ac.uk](mailto:Miles.Witham@newcastle.ac.uk)). Deidentified, individual participant-level data will be available to bona-fide academic research teams from 12 months after the end of the trial, subject to submission of an outline of the purpose for which it will be used, and subject to approval by a Data Access Committee process hosted by the trial funder (NIHR Newcastle Biomedical Research Centre). Consent will be obtained from participants for this data sharing.

## IPD sharing plan summary

Available on request

## Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Results article</a>		24/03/2025	28/04/2026	Yes	No
<a href="#">Protocol article</a>		18/07/2022	18/08/2023	Yes	No
<a href="#">Basic results</a>		19/12/2023	19/12/2023	No	No
<a href="#">HRA research summary</a>			28/06/2023	No	No
<a href="#">Other publications</a>	Post hoc secondary analysis	10/04/2026	10/04/2026	Yes	No
<a href="#">Plain English results</a>		23/01/2024	23/01/2024	No	Yes