

# Steroid hormone metabolism and muscle loss in chronic kidney disease

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		<input type="checkbox"/> Protocol
<b>Registration date</b> 11/04/2022	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan
		<input type="checkbox"/> Results
<b>Last Edited</b> 19/05/2022	<b>Condition category</b> Urological and Genital Diseases	<input type="checkbox"/> Individual participant data
		<input type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

People with chronic kidney disease (CKD) develop muscle loss as a complication of their disease. Not only do they experience weakness and fatigue as a result, but they are also at greater risk of injury from falls, admissions to hospital, needing care and early death. We do not fully understand what causes muscle loss in kidney disease. This has made it difficult to develop treatments and other ways to help people with this problem.

In kidney disease, muscles do not respond normally to exercise to maintain their size, strength and function. We know that kidney disease causes problems with the way in which our cells generate energy through the process of metabolism. Specifically, it means that the muscles generate energy less efficiently, and thus are not able to maintain muscle mass and strength. Previous research suggests that excessive signalling of the hormone cortisol plays an important role in this disease process. The aim of our study is to learn about hormone changes that occur in chronic kidney disease and their role for muscle loss. The findings from this study will help us to understand why patients with kidney disease experience muscle loss and guide the development of new treatments for these patients.

### Who can participate?

The study will invite 60 - 80 year old adults with chronic kidney disease and healthy volunteers to participate.

### What does the study involve?

Participation will involve a single research visit for sharing information on health and lifestyle, testing muscle function, and donating blood, urine, and muscle tissue samples. Samples will then be tested in the laboratory to study how metabolism changes in kidney disease.

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

Travel expenses related to study participation will be reimbursed and participants will receive a light meal during the study visit.

Collecting the blood sample can leave a small bruise for a few days. There is an extremely low risk of infection or bleeding from the muscle biopsy and of an allergic reaction to local anaesthetic. Pain and numbness has been reported once in many thousands of otherwise

uncomplicated biopsies. Participants may notice a small scar at the site of the biopsy, but scars should improve within 6-12 months after the biopsy.

Where is the study run from?

University Hospital Birmingham and the University of Birmingham (UK)

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

February 2022 to August 2025

Who is funding the study?

Medical Research Council (UK)

Who is the main contact?

Dr Michael Sagmeister, m.sagmeister@bham.ac.uk

Prof. Lorraine Harper, l.harper@bham.ac.uk

## Contact information

### Type(s)

Scientific

### Contact name

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Principal Investigator

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## Additional identifiers

### EudraCT/CTIS number

Nil known

### IRAS number

288991

### ClinicalTrials.gov number

Nil known

### Secondary identifying numbers

IRAS 288991, CPMS 52504

## Study information

### Scientific Title

The role of cortisol and steroid hormone metabolism for sarcopenia in chronic kidney disease; a cross-sectional study

### Acronym

SMK study

### Study objectives

Our study will address how shifts in steroid hormone metabolism in humans with CKD affect skeletal muscle. Our hypothesis proposes that elevated glucocorticoid activation in skeletal muscle tissue contributes to muscle protein loss in patients with CKD.

### Ethics approval required

Old ethics approval format

### Ethics approval(s)

Not provided at time of registration

### Study design

Single-centre observational cross-sectional study

### Primary study design

Observational

### Secondary study design

Cross sectional study

### Study setting(s)

Hospital

### 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**

Aetiology of sarcopenia in patients with chronic kidney disease

## **Interventions**

Participation will involve a single research visit for sharing information on health and lifestyle, testing muscle function, and donating blood, urine, and muscle tissue samples. Samples will then be tested in the laboratory to study how metabolism changes in kidney disease.

Data collection procedures:

- a) Person characteristics and medical history
- b) Short Nutrition Assessment Questionnaire
- c) International Physical Activity Questionnaire – short form
- d) Body-mass-index
- e) Body composition by bioelectrical impedance assessment
- f) Hand grip strength
- g) Short Physical Performance Battery

Sample collection procedures:

- a) Blood sample (for profiling of biochemical, metabolic, endocrine and inflammatory markers)
- b) Quadriceps muscle biopsy (for ex vivo metabolic steroid activation assays, markers of anabolic /catabolic balance, histology and primary cell culture experiments)
- c) 24-hour urine sample (for urinary steroid profile and creatinine clearance)

## **Intervention Type**

Other

## **Primary outcome measure**

Conversion rate of cortisone to cortisol measured in skeletal muscle biopsies ex vivo at baseline using a radiolabelled tracer assay.

## **Secondary outcome measures**

1. Urinary steroid metabolome measured using liquid-chromatography/mass-spectrometry at baseline
2. Handgrip strength measured using a handheld dynamometer at baseline
3. Body composition measured using bioelectrical impedance analysis at baseline
4. Physical function measured using the Short Physical Performance Battery test at baseline
5. Malnutrition measured using the Short Nutrition Assessment Questionnaire at baseline
6. Physical activity measured using the International Physical Activity Questionnaire (short form) at baseline)
7. Serum cytokine and hormone levels measured by ELISA and LUMINEX assays at baseline
8. Expression of anabolic and catabolic markers in skeletal muscle biopsies using qPCR and Western blot analysis at baseline

## **Overall study start date**

24/02/2022

## **Completion date**

01/08/2025

## Eligibility

### Key inclusion criteria

1. Men and women
2. Age 60-80 years
3. For CKD group (recruitment target 30): chronic kidney disease stage IV or V (eGFR less than 30ml/min for more than 3 months)
4. For control group (recruitment target 20): no history of kidney disease or other major chronic illness
5. Willing and able to provide informed consent

### Participant type(s)

Mixed

### Age group

Adult

### Sex

Both

### Target number of participants

50

### Key exclusion criteria

1. Receive steroid medications or hormone replacement therapy other than thyroxine for well-controlled hypothyroidism
2. Have a primary neurological or muscle disease that impairs muscle function
3. Be at extremes of body weight (BMI <18 or >35kg/m<sup>2</sup>)
4. Have a diagnosis of cancer in the past 5 years (except non-melanoma skin cancer)
5. Suffered an acute illness requiring hospital admission within the past month
6. Have a bleeding predisposition or receive anticoagulation (except aspirin that can be suspended for 3 days without significant clinical risk)
7. Be enrolled in another clinical trial with a treatment intervention within past four months

### Date of first enrolment

01/04/2022

### Date of final enrolment

01/04/2023

## Locations

### Countries of recruitment

England

United Kingdom

**Study participating centre**  
**Queen Elizabeth Hospital**  
University Hospitals Birmingham NHS Foundation Trust  
Mindelsohn Way  
Edgbaston  
Birmingham  
United Kingdom  
B15 2GW

## Sponsor information

### Organisation

University of Birmingham

### Sponsor details

Research Governance  
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+44 7814650003  
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### Sponsor type

University/education

### Website

<http://www.birmingham.ac.uk/index.aspx>

### ROR

<https://ror.org/03angcq70>

## Funder(s)

### Funder type

Research council

### Funder Name

Medical Research Council

### Alternative Name(s)

Medical Research Council (United Kingdom), UK Medical Research Council, MRC

**Funding Body Type**

Government organisation

**Funding Body Subtype**

National government

**Location**

United Kingdom

## Results and Publications

**Publication and dissemination plan**

The study results will be disseminated among the scientific community through discussion in regional academic networks, presentation at international conferences and publication in peer-reviewed scientific journals. A lay summary of the study results will also be shared with study participants and published in the newsletter of the local Kidney Patients' Association.

**Intention to publish date**

01/01/2026

**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