

The use of neuromuscular electrical stimulation as a treatment for sarcopenia in people on haemodialysis

Submission date 24/11/2024	Recruitment status Recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 29/11/2024	Overall study status Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 15/04/2025	Condition category Musculoskeletal Diseases	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

Chronic Kidney Disease (CKD) is an illness where the kidneys gradually lose their ability to work properly. It is relatively common, affecting about 14% of the adult UK population. Sometimes, when kidney function becomes so low, people have to start kidney dialysis, which replaces the function of the kidney. Whilst this is lifesaving, it does have a big effect on people's well-being and their ability to perform everyday tasks as people say they notice their muscles get smaller and weaker (which is a condition called sarcopenia). These symptoms are not only troubling to the individual but having sarcopenia means the person has poorer health in the long term. Therefore, any intervention that is capable of building muscles back up again would have a beneficial effect on physical function, quality of life, well-being and health in the long term. Traditional type exercise holds lots of benefits for people, including people on dialysis, but a large number of people do not want to exercise or are not well enough. Therefore, it is important to find an alternative intervention capable of delivering some of the same benefits as exercise, but that is easier for people to manage. Neuromuscular electrical stimulation (NMES), is a well-tolerated rehabilitation technique that increases muscle mass and strength. It's a small device that delivers tiny electrical impulses to the muscles via electrodes placed on the skin, a bit like a 'Slendertone' device. It's so widely used that these devices are available to buy in high street shops. NMES might be a good way to help people on dialysis build up muscle mass and strength, but there is not enough research to confirm this. This study aims to find out if 3-months of neuromuscular electrical stimulation (NMES) can improve muscle strength in people on dialysis.

Who can participate?

Adults aged >18 years, undertaking haemodialysis for >3-months (home or unit-based), with sarcopenia diagnosed by low muscle strength on patient screening (<27kg for men and <16kg for women for handgrip strength), and able to give written informed consent.

What does the study involve?

228 haemodialysis patients across three centres who have been diagnosed as having some level of sarcopenia will be randomly assigned to either receive the NMES intervention or continue

with their usual care. Before people start the study, several tests will be performed that provide information on the participant's muscle mass and strength, physical function, activity levels and quality of life. The NMES intervention will be given 3 times a week during dialysis for 3- months with each session building up to 30-minutes, if that is tolerated. Patients will be in control of the strength of the electrical pulse delivered, and they will be asked to gradually increase it over time to the most that they can manage. After three months, the tests will be repeated to see if anything has improved and how well the impact is sustained over time.

What are the possible benefits and risks of participating?

There are no direct benefits to taking part in this research. However, the results will provide valuable data about whether NMES can be used to improve muscle strength in people on dialysis. If the results are positive, they could help to implement NMES into clinical care guidelines.

There are possible risks, disadvantages and inconveniences with any research study. The individual risks of each procedure and investigation are described fully in the participant information sheet. Participating in the study involves a time commitment for additional hospital visits, for which transport can be arranged. Some procedures, like NMES and electromyography, may cause mild discomfort, soreness, or slight bruising, but these effects are typically brief or temporary. All tests and procedures are supervised by trained staff, and participants can stop any activity at any time if they feel uncomfortable.

Where is the study run from?

STIM-HD is organised by the Department of Cardiovascular Sciences at the University of Leicester. The University of Leicester is the Sponsor for this study and is the organisation responsible for ensuring that the study is carried out correctly. This study is linked to an external pilot, i.e. STIM-HD Work Package 1 (IRAS 347115), led by Loughborough University.

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

September 2024 to February 2028 (recruitment to commence April 2025).

Who is funding the study?

Both the STIM-HD main study and the external pilot studies are funded by the National Institute for Health and Care Research (NIHR) through the Efficacy and Mechanism Evaluation (EME) Programme

Who is the main contact?

Central Coordinating Team, STIM-HD@leicester.ac.uk

Chief Investigator, Prof James Burton, jb343@leicester.ac.uk

Mechanistic Lead, Dr Emma Watson, emma.watson@leicester.ac.uk

Study website

<https://fundingawards.nihr.ac.uk/award/NIHR158852>

Contact information

Type(s)

Principal Investigator

Contact name

Prof James Burton

ORCID ID

<http://orcid.org/0000-0003-1176-7592>

Contact details

Department of Cardiovascular Sciences
Glenfield Hospital,
Grobby Road
Leicester
United Kingdom
LE3 9PQ
+44 (0)116 258 8043
jb343@leicester.ac.uk

Type(s)

Scientific

Contact name

Dr Emma Watson

ORCID ID

<http://orcid.org/0000-0002-3869-8972>

Contact details

Department of Cardiovascular Sciences
Glenfield Hospital
Grobby Road
Leicester
United Kingdom
LE3 9PQ
+44 (0)116 252 5033
emma.watson@le.ac.uk

Type(s)

Public

Contact name

Ms Niamh Quann

ORCID ID

<http://orcid.org/0000-0001-8870-3437>

Contact details

Department of Cardiovascular Sciences
Glenfield Hospital
Grobby Road
Leicester
United Kingdom
LE3 9PQ
+44 (0)116 252 2893
STIM-HD@leicester.ac.uk

Additional identifiers

EudraCT/CTIS number

Nil known

IRAS number

327885

ClinicalTrials.gov number

Nil known

Secondary identifying numbers

CPMS 55928, Protocol number 0968, NIHR158852

Study information

Scientific Title

Neuromuscular electrical STIMulation for sarcopenia in people on HaemoDialysis (STIM-HD)

Acronym

STIM-HD

Study objectives

Experimental hypothesis: Three months of neuromuscular electrical stimulation (NMES) will create a significant increase in muscle strength compared to the standard care group.

Ethics approval required

Ethics approval required

Ethics approval(s)

Approved 20/11/2024, Wales REC 3 (Merthyr Road, Coryton, Cardiff, CF15 7LH, United Kingdom; +44 (0)2922 940963; Wales.REC3@wales.nhs.uk), ref: 24/WA/0339

Study design

Prospective open-label assessor-blind two-arm multi-centre randomized controlled trial with a health economic evaluation and optional mechanistic study

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Home, Hospital, Medical and other records

Study type(s)

Quality of life, Treatment, Efficacy

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

Sarcopenia in people on haemodialysis

Interventions

- **Treatment method, duration and frequency:** Participants randomised to the intervention group will receive NMES at each dialysis session they attend for 3-months. It will be administered using a commercially available 4-channel portable stimulator with participants either sitting or lying down (however they are usually positioned for dialysis). The skin will be cleaned and then electrodes will be placed upon the thigh muscles. The participants will have control of the NMES device so they can change the current that is administered. During the first two to three sessions participants will be encouraged to find their initial comfortable level of stimulation intensity (the current) and to get used to how it feels. After the first week the training will be progressed by two methods: (1) Increasing session duration up to a maximum of 30 minutes, if this is not initially achievable (excluding warm up and cool down); (2) Increasing stimulation intensity (current) which determines the strength of the muscle contraction that is induced and therefore how uncomfortable it can feel. Participants will be encouraged to increase the stimulation intensity beyond their initial comfort level for a portion of each session. As participants become increasingly familiar with NMES and as they adapt they will be encouraged to progressively increase the stimulation intensity further. This progression will also be guided by their individual rating of perceived exertion (RPE). RPE is a scale that guides exercise intensity. Participants will be familiarised with this in the first few NMES sessions. Participants will be encouraged to achieve a of about '4' or 'somewhat' hard. In addition, a discomfort scale will be shown to the participants to help ensure the stimulation intensity is at the correct level. Exercise intensity will also be monitored through a session using a heart rate monitor to measure heart rate and blood lactate concentrations will be measured at the end of the session. Both of these will be performed once a month to more closely monitor progress.
- **Randomisation:** After consent and baseline measurements have been collected, participants will be randomised by a delegated individual at each participating centre to either the intervention (3-months of NMES) or the control group (standard care) in a 1:1 manner. Participants will be allocated using minimisation factors of age and time on dialysis, this will ensure the external validity of the results. Randomisation will be performed using a validated web-based system (Sealed Envelope) to maintain allocation concealment.
- **Follow-up activities:** All outcome assessments made at baseline will be repeated at -3, 6 and -9 months post-randomisation except the optional outcome measures which will be performed at baseline and 3 months only. It is expected that each participant will partake in the study for 10 months in total. The 3-month timepoint is the end of the intervention period, and 6 and 9 months are follow-up.
- **Health economic evaluation:** Resource use and expenditure data will be collected via participant questionnaires at baseline, 3, 6, and 9 months, supplemented by UK Renal Registry data. To reduce recall bias, participants will be offered an optional diary to keep records of healthcare visits and other relevant costs. Data will primarily capture NHS-related expenses (hospital stays, professional visits, medications) and patient/carer impacts (employment changes, unpaid care). Using standard tools, resource data will be combined with unit costs to estimate per-patient costs, validated against secondary care records. Quality Adjusted Life Years (QALYs) will be calculated from EQ-5D-5L responses at baseline, 3, 6, and 9 months using NICE-recommended utility scores. Differences in costs, resource use, and QALYs between intervention and control groups will determine the cost-effectiveness of the intervention, with

results extrapolated for long-term impact.

- Optional mechanistic study: Optional mechanistic outcomes will be performed in a sub-group (both study arms) to assess the mechanistic effects of neuromuscular electrical stimulation on skeletal muscle morphology and function in haemodialysis patients. Participants will indicate via the consent form whether or not they wish to participate in the following optional assessments. Participants can still take part in the main study without completing these assessments. These assessments will be performed in centres with appropriate capability and capacity, at baseline and 3-month follow-up only. a) Skeletal muscle biopsy using the needle biopsy procedure b) Surface electromyography c) Intramuscular Electromyography d) Femoral nerve stimulation.

Intervention Type

Device

Pharmaceutical study type(s)

Not Applicable

Phase

Not Applicable

Drug/device/biological/vaccine name(s)

Neuromuscular electrical stimulation (NMES) device.

Primary outcome measure

Muscle strength measured using isometric strength at screening (as a familiarisation session) at baseline, 3, 6, and 9 months

Secondary outcome measures

1. Quality of life measured using the Kidney Disease Quality of Life (KDQoL) tool at baseline, 3, 6, and 9 months
2. Cost-effectiveness, within an NHS costing perspective, measured using the EQ-5D-5L and a resource use questionnaire at baseline, 3, 6, and 9 months
3. Muscle size and physical function are measured using the following methods at baseline, 3, 6, and 9 months:
 - 3.1. Muscle mass using ultrasound to assess thickness and cross-sectional area
 - 3.2. Muscle quality and architecture using ultrasound e.g. echo intensity and angle of pennation
 - 3.3. Handgrip strength using dynamometry
 - 3.4. Lower-extremity strength, functional capacity, and balance using the Short Physical Performance Battery (SPPB) and sit to stand 60 (60STS)
 - 3.5. Cardiovascular functional capacity and endurance using the 6-minute walk test or the Incremental Shuttle Walk Test (ISWT) (if space constraints)
 - 3.6. Body composition using bioelectrical impedance
 - 3.7. Muscle endurance using the Sit-to-stand-60 test muscle endurance
 - 3.8. Isometric rate of force development measured using dynamometry at baseline, 3, 6 and 9 months
 - 3.9. Physical activity levels using the GP Physical Activity questionnaire and accelerometry
 - 3.10. Levels of fatigue using SONG-HD Fatigue score
 - 3.11. Indices of sarcopenia using the SARC-F questionnaire
4. Neuromuscular adaptations and changes in muscle phenotype will be measured using the following methods at baseline and 3 months:
 - 4.1. Motor unit recruitment, discharge rate, and conduction velocity using high-density electromyography

- 4.2. Motor unit potential jiggle and segment jitter using intramuscular electromyography
- 4.3. Evoked quadriceps contractile properties measured using electrical stimulation and force transducers at baseline and 3 months
- 4.4. Skeletal muscle fibre size, distribution, morphology, and mitochondrial function analysed from biopsy samples obtained using the needle biopsy technique at baseline and 3 months
5. The safety of the intervention measured using adverse events reporting relating to the intervention at 3 months

Overall study start date

01/09/2024

Completion date

29/02/2028

Eligibility

Key inclusion criteria

1. Undertaking HD for >3-months (home or unit-based).
2. Age >18 years
3. Has sarcopenia diagnosed by low muscle strength on patient screening (<27kg for men and <16kg for women for handgrip strength).
4. Able to give written informed consent.

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Sex

Both

Target number of participants

228

Key exclusion criteria

1. Contra-indications to neuromuscular electrical stimulation therapy including:
 - 1.1. Lower limb amputation
 - 1.2. Active skin ulceration or infection
 - 1.3. Symptomatic lower limb claudication/ ischaemia
 - 1.4. Lower limb deep vein thrombosis <3-months
 - 1.5. Cardiac pacemaker or implantable cardiac defibrillator
 - 1.6. Metallic hip or knee joint
2. Conditions known to cause muscle wasting:
 - 2.1. Known neuromuscular disease
 - 2.2. Active malignancy
3. Scheduled for living donor kidney transplant or plan to change dialysis modality or centre in

the next 6-months

4. Life expectancy of <6-months

5. Current participation in an interventional trial with conflicting therapies or outcomes

6. Unable to give written informed consent

Date of first enrolment

01/05/2025

Date of final enrolment

31/12/2026

Locations

Countries of recruitment

England

United Kingdom

Study participating centre

University Hospitals of Leicester NHS Trust

Leicester Royal Infirmary

Infirmary Square

Leicester

United Kingdom

LE1 5WW

Study participating centre

University Hospitals Coventry and Warwickshire NHS Trust

Walsgrave General Hospital

Clifford Bridge Road

Coventry

United Kingdom

CV2 2DX

Study participating centre

University Hospitals Birmingham NHS Foundation Trust

Queen Elizabeth Hospital

Mindelsohn Way

Edgbaston

Birmingham

United Kingdom

B15 2GW

Sponsor information

Organisation

University of Leicester

Sponsor details

Research Governance Office
Research & Enterprise Division
University Road
Leicester
England
United Kingdom
LE1 7RH
+44 (0)116 373 6508
RGOsponsor@leicester.ac.uk

Sponsor type

University/education

Website

<https://le.ac.uk/research/regi>

ROR

<https://ror.org/04h699437>

Funder(s)

Funder type

Government

Funder Name

National Institute for Health and Care Research

Alternative Name(s)

National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

United Kingdom

Results and Publications

Publication and dissemination plan

Upon completion, the data will be analysed and disseminated at relevant national and international scientific/medical conferences, as well as patient led conferences and workshops. The data will be published in a high impact journal as well as disseminated on social media and via blogs. A video of the results will be made to increase accessibility for patients. In addition, if participants have indicated on the consent form they wish to receive a copy of the results, this will be sent to them upon study completion which will be written in collaboration with our Patient Participation, Involvement, and Engagement (PPIE) group.

Intention to publish date

28/02/2029

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study will be published as a supplement to the results publication.

IPD sharing plan summary

Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 1.0	10/10/2024	29/11/2024	No	No