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MiFoot – reducing heart disease risk in those with a history of diabetic foot ulcers

Submission date 14/09/2023	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 28/09/2023	**Overall study status** Ongoing	
Last Edited 11/09/2024	**Condition category** Nutritional, Metabolic, Endocrine	

Plain English Summary

Background and study aims
People with Type 2 diabetes and either a current or previous diabetes-related foot ulcer are often at high risk for future heart problems, such as heart attacks or strokes. This may be caused by different factors such as difficulty in being physically active, or managing their often complex condition. People might also find it more difficult to do every-day activities that are important to them, feel more anxious or depressed, and may need to use healthcare services more often. Healthcare for people with diabetes-related foot ulcers is usually focussed on treating the ulcer, and not preventing long-term heart problems.

What is MiFoot RCT?
The MiFoot RCT is a research study that will test a programme designed to improve heart health in people with diabetes and diabetes-related foot ulcers.
MiFoot programme aims to help people to better manage their condition, receive the most up to date care and be more physically active.
The MiFoot programme will include:
• Group-based education and exercise sessions
• One to one session with a health care professional
• An online platform designed to support patients to live a healthy lifestyle

We want to see whether the MiFoot programme can improve the health of people with current or previous diabetes-related foot ulcers, and if it is good value for money.

Who can participate?
Adults over 18 years, with type 2 diabetes and current or previous diabetes-related foot ulcers.

What does the study involve?
The study lasts 2 years, involves face-to-face visits to participants local hospital, the completion of questionnaires and the wearing of an activity monitor to measure your physical activity.

What are the possible benefits and risks of participating?
Taking part in this research study could potentially benefit other people with diabetes and diabetes-related foot ulcers by providing information on how best to organise and deliver care

in order to improve heart health and reduce the risk of future heart problems. This is important as there has not been much research in this area. The results could lead to improved medical treatments and care in the future.
Although there are many benefits of physical activity, it can pose some risks, however it is anticipated that these will be minimal. For example, you may experience delayed onset muscle soreness. Physical activity carried out as part of the MiFoot programme will be light-moderate, which can equate to walking upstairs or completing housework; therefore, your risk would not be increased over and above their usual day to day activities.

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

When is the study starting and how long is it expected to run for?
August 2023 to December 2026

Who is funding the study?
National Institute for Health and Care Research (NIHR) (UK).

Who is the main contact?
Agnieszka Glab, agnieszka.glab@uhl-tr.nhs.uk

Study website
https://mifoot.org.uk

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
322098

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 55056, NIHR202021, IRAS 322098, sponsor ref number 0922

Study information

Scientific Title
A Multifactorial intervention to improve cardiovascular outcomes in adults with type 2 diabetes and current or previous diabetes-related Foot ulcers - randomised controlled trial (MiFoot RCT)

Acronym
MiFoot RCT

Study hypothesis
The MiFoot intervention will elicit a 20% improvement in the survival rate for the primary outcome Extended MACE (Major Adverse Cardiovascular Event – comprising myocardial infarction, stroke, cardiovascular death, peripheral arterial bypass, coronary angioplasty, or peripheral artery angioplasty) at 2 years from 65.6% (i.e. 34.4% experience an Extended MACE event) to 78.7% (i.e. 21.3% experience an Extended MACE event) in the intervention group.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 04/08/2023, North East - York Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 207 104 8143; york.rec@hra.nhs.uk), ref: 23/NE/0136

Study design
Interventional randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
See study outputs table

Condition
Diabetes

Interventions
Visit Schedule and Assessments
Remote, telephone screening
• Explain study in more detail and answer any questions
• Check eligibility for the study
• Confirm baseline visit date

Visit 0 – Face to face Baseline visit
Meet with health care professional, sign consent, have baseline measures taken such as

• Height, weight
• Blood pressure
• ECG (Intervention group only)
• Physical activity screening
• Questionnaires completion
• Demonstration of an activity monitor (wristwatch) which would be posted to their home address to wear for 8 days
• Data collection from relevant routine existing healthcare records (including test results, medication and other factors that may affect diabetes and DFUD). This does not require a visit or completion of any assessments

Usual care or Intervention MiFoot programme
If allocated to usual care, participant will continue with that. If allocated to MiFoot programme they will continue with usual care and MiFoot programme.
The MiFoot programme will include:
• One to one session with a health care professional
• Group-based education and physical activity sessions
o Weekly sessions - week 2-7
o Monthly boosters up to month 12
o Follow up booster month 18-24
• An online platform designed to support participant to live a healthy lifestyle

As a part of the study, we will ask participants permission to observe some of the sessions/ appointments (optional) and gain their feedback on the MiFoot programme.

Remote Follow up Visit at month 12
• Questionnaire booklet completed online or posted to home address
An activity monitor (wristwatch) posted to home address to wear for 8 days

Remote Follow up Visit at month 24
• Questionnaire booklet completed online or posted to home address
An activity monitor (wristwatch) posted to home address to wear for 8 days

(added 04/07/2024): Some of the study data will be entered into Dacima (Electronic Data Capture System) by site staff

Post month 24 Interview (optional for intervention group only)
If participants consent to this, they might be selected to take part in the interview over the phone or video call at a time that is convenient to talk to about their experience.

Internal feasibility assessment
The feasibility of the trial will be assessed against pre-specified targets with analysis based on the first 3 months of recruitment data, when recruitment should be 25% complete (i.e., 98 participants). Information from the internal feasibility assessment will be used to inform subsequent action planning to ensure the trial meets key milestones. To allow for a slower start, feasibility criteria will be set as 20% of the total recruitment target (i.e., 78 participants).

Health economics
Two health economic analyses will be conducted. An analysis of resource use data collected within the trial and a long-term economic modelling analysis will be completed. It is envisaged that the primary analysis will be long-term health economic model, as it is expected that MiFoot will have an effect on patient outcomes beyond the trial period.

Process evaluation
To investigate individual experiences with the intervention, potential barriers and facilitators to intervention delivery, attendance (including delineation of these factors based on each different element of the intervention) and intervention fidelity. A mixed-methods process evaluation will be completed, using both qualitative and quantitative data collection methodologies. This is based on using the RE-AIM framework.

Intervention Type
Behavioural

Primary outcome measure
Extended MACE (myocardial infarction, stroke, cardiovascular death, peripheral arterial bypass, coronary artery bypass, coronary angioplasty, or peripheral artery angioplasty) by 2 years, measured at 0, 12 and 24 months via data extraction from routine healthcare records

Secondary outcome measures
1. Composite renal endpoints: end-stage kidney disease (defined as dialysis, transplantation, or a sustained (>3 months) eGFR of <15 ml/minute/1.73m2), doubling of the serum creatinine level, or death from renal causes, measured at 0, 12 and 24 months via data extraction from routine healthcare records
2. 3P-MACE (non-fatal myocardial infarction, non-fatal stroke, cardiovascular death) and individual components of the Extended MACE composite: non-fatal myocardial infarction, non-fatal stroke, cardiovascular death, peripheral arterial bypass, coronary artery bypass, coronary bypass, coronary angioplasty, peripheral artery angioplasty, measured at 0, 12 and 24 months via data extraction from routine healthcare records
3. All-cause mortality, measured at 0, 12 and 24 months via data extraction from routine healthcare records
4. Lower-limb major amputation, measured at 0, 12 and 24 months via data extraction from routine healthcare records
5. Re-ulceration, measured at 0, 12 and 24 months using via data extraction from routine healthcare records
6. Distress, measured at 0, 12 and 24 months using the PAID-20 questionnaire
7. Self-efficacy, measured at 0, 12 and 24 months using the DMSES-15 questionnaire
8. Quality of life DFUD-specific, measured at 0, 12 and 24 months using the DFS-SF questionnaire, and generic, measured at 0, 12 and 24 months using the EQ-5D-5L questionnaire
9. Depression and anxiety, measured at 0, 12 and 24 months using the HADS questionnaire
10. Health resource use, such as primary care visits, emergency department visits, hospitalisations and medication use, measured at 0, 12 and 24 months using the ModRUM questionnaire
11. Medication adherence, measured at 0, 12 and 24 months using the Moriskey MMAS-8 questionnaire
12. Diet, measured at 0, 12 and 24 months using the short-form food frequency questionnaire
13. Physical activity volume/intensity measured at 0, 12 and 24 months using wrist worn accelerometers
14. Biomedical markers: Blood pressure (systolic, diastolic, heart rate) (mmHg, BPM); Low-density lipoprotein-cholesterol (LDL-C) (mmol/L); High-density lipoprotein-cholesterol (HDL-C) (mmol/L); Total cholesterol (TC) (mmol/L); Triglycerides (TG) (mmol/L); Glycated haemoglobin (HbA1c) (% and mmol/mol); Estimated Glomerular Filtration Rate (eGFR) (ml/min/1.73m2); Urine albumin: creatinine ratio (AUCR), measured at 0, 12 and 24 months via data extraction from routine healthcare records
15. Anthropometric measures (weight and body mass index) measured directly at 0 months and

measured at 0, 12 and 24 months via data extraction from routine healthcare records
16. Safety measures (Myocardial infarction, Stroke, Cardiovascular death, Peripheral arterial bypass, Coronary artery bypass, Coronary angioplasty, Peripheral artery angioplasty, Hypoglycaemic events) measured at 0, 12 and 24 months via data extraction from routine healthcare records
17. Demographic variables (collected for exploratory stratified analyses): Age; Sex; Ethnicity; T2DM duration; DFUD duration; Socio-economic score (Index of Multiple Deprivation (IMD); a postcode-based measure of socio-economic score), measured at baseline (0) months via data extraction from routine healthcare records
18. Medications (glucose-lowering, lipid-lowering, blood pressure-lowering, anti-platelet, anti-depressants) measured at 0, 12 and 24 months via data extraction from routine healthcare records and using MODRUM questionnaire

Overall study start date
01/08/2023

Overall study end date
31/12/2026

Eligibility

Participant inclusion criteria
1. Males and Females aged >= 18 years
2. Diagnosed with T2D
3. Current or previous DFUD (defined as diagnosed with DFUD in the previous 5 years)
4. Ability to speak and read English
5. Participant is able (in the Investigators opinion) and willing to fulfil all the study requirements
6. Currently not taking part in a CTIMP or any other disease management or lifestyle-related intervention trial

At the baseline visit, physical activity screening will be undertaken to assess safety considerations as a precaution prior to physical activity as part of the intervention. The participant may be excluded from the physical activity part of the intervention, but not the remaining intervention elements. Participants with both vascular and neuropathic ulcers will be eligible.

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 392; UK Sample Size: 392

Participant exclusion criteria
1. Diagnosed with other forms of diabetes (e.g., type 1 diabetes, monogenic diabetes (MODY), gestational diabetes or latent autoimmune diabetes in adults (LADA)
2. Other, non-diabetic forms of ulceration (e.g., venous)
3. Serious illness or event with life-expectancy < 1 year or other significant illness which, in the opinion of a study clinician, precludes involvement
4. Planned major surgery
5. Requirement for renal replacement therapy
6. Current pregnancy, or actively trying to conceive
7. Unwilling or unable to give informed consent to participate in the study
8. Current participation in a CTIMP or any other disease management or lifestyle-related intervention study (as determined by study investigator)
9. Unable to understand or read English

Inability to participate in physical activity part of the intervention will not preclude inclusion in the study or the rest of the intervention, in order to represent the real-world situation. We will collect data concerning this as part of the process evaluation (section 5.2.2). The intervention will be delivered in English language and as such any participants who do not speak or read English to a sufficient standard will be excluded from the study. Every effort will be made to support participants with minimal English proficiency to participate.

Recruitment start date
01/11/2023

Recruitment end date
31/03/2024

Locations

Countries of recruitment
England

Scotland

United Kingdom

Study participating centre
Leicester Royal Infirmary
Infirmary Square
Leicester
United Kingdom
LE1 5WW

Study participating centre
Royal Derby Hospital
University Hospitals of Derby and Burton NHS Foundation Trust
Uttoxeter Road

Derby
United Kingdom
DE22 3NE

Study participating centre
Imperial College Healthcare NHS Trust
The Bays
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Study participating centre
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Sheffield Teaching Hospitals NHS Foundation Trust
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S5 7AU

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Study participating centre
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Sponsor type
University/education

Website
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ROR
https://ror.org/04h699437

Funder(s)

Funder type
Government

Funder Name

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
31/12/2027

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be available upon reasonable request submitted in writing to the study Chief Investigator: Professor Kamlesh Khunti, kk22@le.ac.uk.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	version 1.0	30/05/2023	25/09/2023	No	Yes
Protocol file	version 2.0	19/07/2024	11/09/2024	No	No