ISRCTN64926597 https://doi.org/10.1186/ISRCTN64926597

Comparing treatments for diabetic foot ulcers

Submission date
22/05/2017

Recruitment status
No longer recruiting

Registration date
06/06/2017

Overall study status
Completed

Last Edited
20/01/2025

Condition category
Nutritional, Metabolic, Endocrine

[X] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
Diabetic foot ulcers (DFU) are a complication of diabetes mellitus, a lifelong condition that causes high or uncontrolled blood sugar. In the UK, DFUs affect about 2.5% of people with diabetes. If a DFU takes a long time to heal there is more chance of developing other complications such as infection. This can mean more hospital visits and can impact daily life. These are called 'chronic' or 'hard to heal' diabetic foot ulcers. The NHS has different treatment choices for hard-to-heal diabetic foot ulcers. The usual treatment involves wearing special footwear to reduce pressure on the ulcer, removing hard skin, and bandaging the ulcer. Some of the other treatment options include: hydrosurgical debridement (HD) which uses a stream of water to help take away the dead skin, decellularised dermal allograft (DCD) which is a skin graft from donated human skin applied to the ulcer and negative pressure wound therapy (NPWT) that uses dressing on the ulcer that is attached a pump to suck away any fluid. The aim of this study is to find out the best combination of treatments to use to help DFUs heal more quickly by measuring the size of the ulcer and comparing the healing to the different treatment options.

Who can participate?
Adults aged 18 years and older who have diabetes mellitus and a DFU.

What does the study involve?
Participants are randomly allocated to one of four groups, which may contain one, all, or a combination of the treatments. Those in the first group receive the treatment as usual (TAU). Those in the second group receive TAU plus HD. Those in the third group receive TAU, HD, DCD. Finally, those in the last group receive all four treatments (TAU, HD, DCD, NPWT). The wounds are checked in the clinic one week after the treatment has been given. Participants also attend visits at 2, 4, 8, 12, 20 and 52 weeks after the treatment has been given. At some of these visits ulcers are measured again by tracing it onto a clear sheet. Photographs are taken of the foot and participants are asked to fill out some short questionnaires. If the ulcer heals in between these visits, the research team checks the ulcer in the diabetic foot clinic. The treatment options that show the greatest improvement in the DFUs will be continued in another phase of this study and are again compared to the TAU group.

What are the possible benefits and risks of participating?
Participants may benefit from improvements in healing their foot ulcers. Participants may experience pain during the treatments and dressing changes, as well as infection and skin

irritation. There is a small risk of increased bleeding with the HD treatment, as well as a small risk of allergic reaction and fluid build-up with DCD.

Where is the study run from?
This study is being run by the University of Leeds (UK) and takes place in hospitals with diabetic foot ulcer clinics across the UK

When is the study starting and how long is it expected to run for?
April 2017 to February 2025

Who is funding the study?
National Institute for Health Research (UK)

Who is the main contact?
Miss Rachael Gilberts
r.m.gilberts@leeds.ac.uk or midfut@leeds.ac.uk

Contact information

Type(s)
Public

Contact name
Miss Rachael Gilberts

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Type(s)
Scientific

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Additional identifiers

Protocol serial number
CPMS 33945

Study information

Scientific Title
Multiple Interventions of Diabetic Foot Ulcer Treatment trial

Acronym
MIDFUT

Study objectives
The aim of this study is to assess the use of hydrosurgical debridement alone or in combination with negative pressure would therapy and/or decellularised dermal allograft in the treatment of hard to heal diabetic foot ulcers. These health technologies and their use will be compared in combination to treatment as usual.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Yorkshire and The Humber Bradford Leeds Research Ethics Committee, 26/04/2017, ref: 17/YH/0055

Study design
Randomized; Interventional; Design type: Treatment, Device

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Diabetes mellitus

Interventions
Current interventions as of 10/12/2019:
Phase II:
Participants are randomly allocated to one of five four groups, which may contain one, all, or a combination of the treatments. The treatments include:

Treatment as usual (TAU): Everyone receives TAU. This involves checking the ulcer often in the diabetic foot ulcer clinic and with the community team and helping to reduce pressure on the

ulcer. This may include using special footwear to help reduce pressure when standing or walking. Any hard skin is removed and appropriate bandages or dressings are applied in the clinic and at home. Advice about how to look after the ulcer and diabetes management is also given.

Hydrosurgical debridement (HD): This uses a machine called 'VERSAJET'. VERSAJET uses a stream of water to help take away dead skin. It is used once on the ulcer in the diabetic foot ulcer clinic.

Decellularised dermal allograft (DCD): This is a type of skin graft. It is made from donated human skin with all human cells removed. It is applied once to the ulcer at the diabetic foot ulcer clinic.

Negative pressure wound therapy (NPWT): This uses a dressing on the ulcer covered with a waterproof layer. The dressing is attached to a pump which sucks fluid away from the ulcer. This is left in place for 2 weeks (but the dressing is changed during this time).

Participants are randomly allocated on a 2:1:1:1:1 basis to receive the following treatment strategies;

Group 1: Treatment as usual (TAU)
Group 2: TAU + hydrosurgical debridement (HD)
Group 3: TAU + HD + decellularised dermal allograft (DCD)
Group 4: TAU + HD + DCD + NPWT

The randomised treatment strategy is applied once at the baseline visit on the day of randomisation, however the NPWT remains in place for two weeks. The wounds are checked in the clinic one week after the treatment has been given. Follow up assessments takes place at 1, 2, 4, 8, 12, 20 and 52 weeks. At some of these visits ulcers are measured again by tracing it onto a clear sheet. Photographs are taken of the foot and participants are asked to fill out some short questionnaires. If the ulcer heals in between these visits, the research team checks the ulcer in the diabetic foot clinic.

Phase 3:
The intervention arms showing greatest evidence of efficiency in Phase II as well as the comparison arm (TAU) continue into Phase III. Participants are randomised on a 1:1:1 basis to one of the groups. The same processes are repeated as the second phase.

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Previous interventions:
Phase II:
Participants are randomly allocated to one of five groups, which may contain one, all, or a combination of the treatments. The treatments include:

Treatment as usual (TAU): Everyone receives TAU. This involves checking the ulcer often in the diabetic foot ulcer clinic and with the community team and helping to reduce pressure on the ulcer. This may include using special footwear to help reduce pressure when standing or walking. Any hard skin is removed and appropriate bandages or dressings are applied in the clinic and at home. Advice about how to look after the ulcer and diabetes management is also given.

Hydrosurgical debridement (HD): This uses a machine called 'VERSAJET'. VERSAJET uses a stream of water to help take away dead skin. It is used once on the ulcer in the diabetic foot ulcer clinic.

Decellularised dermal allograft (DCD): This is a type of skin graft. It is made from donated human skin with all human cells removed. It is applied once to the ulcer at the diabetic foot ulcer clinic.

Negative pressure wound therapy (NPWT): This uses a dressing on the ulcer covered with a waterproof layer. The dressing is attached to a pump which sucks fluid away from the ulcer. This is left in place for 2 weeks (but the dressing is changed during this time).

Participants are randomly allocated on a 2:1:1:1:1 basis to receive the following treatment strategies;

Group 1: Treatment as usual (TAU)
Group 2: TAU + hydrosurgical debridement (HD)
Group 3: TAU + HD + negative pressure wound therapy (NPWT)
Group 4: TAU + HD + decellularised dermal allograft (DCD)
Group 5: TAU + HD + DCD + NPWT

The randomised treatment strategy is applied once at the baseline visit on the day of randomisation, however the NPWT remains in place for two weeks. The wounds are checked in the clinic one week after the treatment has been given. Follow up assessments takes place at 1, 2, 4, 8, 12, 20 and 52 weeks. At some of these visits ulcers are measured again by tracing it onto a clear sheet. Photographs are taken of the foot and participants are asked to fill out some short questionnaires. If the ulcer heals in between these visits, the research team checks the ulcer in the diabetic foot clinic.

Phase 3:
The two intervention arms showing greatest evidence of efficiency in Phase II as well as the comparison arm (TAU) continue into Phase III. Participants are randomised on a 1:1:1 basis to one of the groups. The same processes are repeated as the second phase.

Intervention Type
Procedure/Surgery

Primary outcome(s)
Phase II:
Reduction in index ulcer area size is calculated using wound tracing grid and image J software measurements at baseline and week four.

Phase III:
Time to healing is the length of time from randomisation to the date the index ulcer is confirmed as healed by the blinded assessor.

Key secondary outcome(s))
Phase II:
There are no secondary outcome measures:

Phase III:
1. Healing status of the index ulcer is measured by clinical assessment at week two, four, 12, 20 and 52
2. Incidence of infection according to IDSA criteria will be recorded at week two, four, 12, 20 and 52
3. Time to re-ulceration following healing will be measured as the date the index ulcer is confirmed as healed by a blinded assessor to the date re-ulceration is confirmed by a blinded

assessor
4. Quality of life is measured using the DFS-SF and the EQ-5D-5L questionnaires at week four, 12, 20, and 52 weeks post randomisation
5. Hospital admissions and amputations are measured using patient records at week four, 12, 20, 52 post randomisation
6. Cost effectiveness is measured using a health resource utilisation questionnaire at week four, 12, 20 and 52 post randomisation

Completion date
28/02/2025

Eligibility

Key inclusion criteria
Current inclusion criteria as of 15/02/2022:

1. Aged ≥18 years
2. Diagnosis of Diabetes Mellitus (according to WHO criteria)
3. Has a chronic DFU or surgical debridement wound or open minor amputation and in the opinion of the attending clinical team is not on a healing trajectory despite usual best care for a minimum of 4 weeks since initial presentation at the MDT DFU service*
4.1 Ankle brachial index for the leg of the index ulcer ≥0.7 or non-compressible (measurements available in the participants notes taken within 3 months of randomisation can be used if no change in intervention or vascular events have occurred), OR
4.2 Toe brachial index ≥0.5 or opening toe pressure ≥50mmHg or non-compressible
5. Expected to comply with the treatment strategies and follow up schedule
6. Consent to foot and wound photography
7. Consent to participate (written/witnessed verbal informed consent)
*Defined as failure to achieve >50% reduction in index ulcer area over a minimum of 4 weeks using local wound measurement policies

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Previous inclusion criteria as of 10/12/2019:
1. Aged ≥18 years
2. Diagnosis of Diabetes Mellitus (according to WHO criteria)
3. Has a chronic DFU or surgical debridement wound or open minor amputation and in the opinion of the attending clinical team is not on a healing trajectory despite usual best care for a minimum of 4 weeks since initial presentation at the MDT DFU service*
4. Ankle brachial index for the leg of the index ulcer ≥0.7 or non-compressible (measurements available in the participants notes taken within 3 months of randomisation can be used if no change in intervention or vascular events have occurred)
5. Expected to comply with the treatment strategies and follow up schedule
6. Consent to foot and wound photography
7. Consent to participate (written/witnessed verbal informed consent)
*Defined as failure to achieve >50% reduction in index ulcer area over a minimum of 4 weeks using local wound measurement policies

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Previous inclusion criteria as of 22/11/2018:
1. Aged ≥18 years
2. Diagnosis of Diabetes Mellitus (according to WHO criteria)
3. Has a chronic DFU or surgical debridement wound or open minor amputation defined by either (a) OR (b) below:
3(a). Duration of ≥ 12 weeks since initial presentation at the MDT DFU clinic and in the opinion of the attending clinical team is considered not to be on a healing trajectory despite usual best care†
3(b). Having <50% reduction in index ulcer area during a minimum period of 4 weeks prior to randomisation*
4. The index DFU has an area ≥0.8cm2
5. Ankle brachial index for the leg of the index ulcer ≥0.7 or non-compressible (measurements available in the participants notes taken within 3 months of randomisation can be used if no change in intervention or vascular events have occurred)
6. Expected to comply with the treatment strategies and follow up schedule
7. Consent to foot and wound photography
8. Consent to participate (written/witnessed verbal informed consent)
† Participants who are eligible for randomisation under inclusion criteria 3(a) can be registered and randomised on the same day
* Participants who are eligible for randomisation under inclusion criteria 3(b) will be randomised after a minimum 4 week suitability assessment period

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Previous inclusion criteria from 07/09/2018 to 22/11/2018:
1. Aged ≥18 years
2. Diagnosis of Diabetes Mellitus (according to WHO criteria)
3. Has a chronic DFU or surgical debridement wound or open minor amputation defined as having <50% reduction in index ulcer area during a minimum period of 4 weeks prior to randomisation
4. The index DFU has an area ≥0.8cm2
5. Ankle brachial index ≥0.7 or non-compressible (measurements available in the participants notes taken within 3 months of randomisation can be used if no change in intervention or vascular events have occurred)
6. Expected to comply with the treatment strategies and follow up schedule
7. Consent to foot and wound photography
8. Consent to participate (written/witnessed verbal informed consent)

Original inclusion criteria:
1. Aged ≥18 years
2. Diagnosis of Diabetes Mellitus (according to WHO criteria)
3. Has a chronic DFU or surgical debridement wound or open minor amputation defined as having <40% reduction in index ulcer area in the preceding ≥ 4 weeks prior to randomisation
4. The index DFU has an area ≥1cm2
5. Ankle brachial index ≥0.7 or non-compressible (measurements available in the participants notes taken within 3 months of randomisation can be used if no change in intervention or vascular events have occurred)
6. Expected to comply with the treatment strategies and follow up schedule
7. Consent to foot and wound photography
8. Consent to participate (written/witnessed verbal informed consent)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
213

Key exclusion criteria
Current exclusion criteria as of 15/09/2017:
1. Has any current clinically infected DFU on the foot of the index ulcer (as per IDSA guidelines)
2. HbA1C> 110mmol/mol (measurements available in the participants notes taken within 3 months of randomisation can be used if no change in intervention or vascular events have occurred)
3. Estimated glomerular filtration rate (eGFR) < 20mL/min/1.73m2
4. Index ulcer duration > 2 years (measurements taken within 3 months of randomisation can be used if no change in intervention or vascular events have occurred)
5. Planned or previous treatment with corticosteroids to an equivalent dose of prednisolone > 10mg per day or other immunosuppressive/immunomodulating therapy within 4 weeks prior to randomisation
6. Has evidence of connective tissue disorders as a cause of ulceration (e.g. vasculitis or rheumatoid arthritis)
7. Has evidence of dermatological disorders as a cause of ulceration (e.g. pyoderma gangrenosum or epidermolysis bullosa)
8. Planned or previous growth factor treatment within 4 weeks prior to randomisation
9. Planned or previous revascularisation or foot surgery affecting healing within the 4 weeks prior to randomisation
10. Index ulcer base has bone or joint involvement
11. Previously received DCD for the index ulcer within 4 weeks prior to randomisation
12. Previously received NPWT for the index ulcer within 4 weeks prior to randomisation
13. Previously received hydrosurgical or surgical debridement for the index ulcer within 4 weeks prior to randomisation
14. Has previously been randomised to the MIDFUT study
15. Unable to receive one or more of the randomised treatment strategies for any reason at the discretion of the attending clinical team (e.g. risk of excessive bleeding, serious falls risk, known allergies to NPWT dressings or dCELL dermis preparation components)

Previous exclusion criteria:
1. Has any current clinically infected DFU (as per IDSA guidelines)
2. HbA1C> 110mmol/mol
3. Estimated glomerular filtration rate (eGFR) < 20mL/min/1.73m2
4. Index ulcer duration > 2 years
5. Planned or previous treatment with corticosteroids to an equivalent dose of prednisolone > 10mg per day or other immunosuppressive therapy within 4 weeks prior to randomisation

6. Has evidence of connective tissue disorders (e.g. vasculitis or rheumatoid arthritis) and has planned or is under active treatment
7. Has evidence of dermatological disorders as a cause of ulceration (e.g. pyoderma gangrenosum or epidermolysis bullosa)
8. Planned or previous growth factor treatment within 4 weeks prior to randomisation
9. Planned or previous revascularisation or foot surgery affecting healing within the 4 weeks prior to randomisation
10. Index ulcer base has bone or joint involvement
11. Previously received DCD for the index ulcer within 4 weeks prior to randomisation
12. Previously received NPWT for the index ulcer within 4 weeks prior to randomisation
13. Previously received hydrosurgical or surgical debridement for the index ulcer within 4 weeks prior to randomisation
14. Has previously been randomised to the MIDFUT study
15. Lacks mental capacity and is unable to provide informed consent

Date of first enrolment
01/10/2017

Date of final enrolment
31/08/2023

Locations

Countries of recruitment
United Kingdom

England

Scotland

Study participating centre
St James's University Hospital
Beckett Street
Leeds Teaching Hospitals NHS Trust
Leeds
United Kingdom
LS9 7TF

Study participating centre
Sunderland Royal Hospital
City Hospitals Sunderland NHS Foundation Trust
Kayll Road
Sunderland
United Kingdom
SR4 7TP

Study participating centre
Russells Hall Hospital
The Dudley Group of Hospitals NHS Foundation Trust
Pensnett Road
Dudley
United Kingdom
DY1 2HQ

Study participating centre
Royal Cornwall Hospital
Royal Cornwall Hospitals NHS Trust
Truro
United Kingdom
TR1 3HD

Study participating centre
St George's University Hospital
St George's University Hospitals NHS Foundation Trust
Blackshaw Road
London
United Kingdom
SW17 0QT

Study participating centre
Royal United Hospital Bath NHS Foundation Trust
Combe Park
Bath
United Kingdom
BA1 3NG

Study participating centre
Royal Berkshire Hospital
London Road
Reading
United Kingdom
RG1 5AN

Study participating centre
The Royal Free Hospital
Royal Free London NHS Foundation Trust

Pond Street
London
United Kingdom
NW3 2QG

Study participating centre
Salford Royal NHS Foundation Trust
Stott Lane
Salford
United Kingdom
M6 8HD

Study participating centre
East Kent Hospitals University NHS Foundation Trust
Kent and Canterbury Hospital
Ethelbert Road
Canterbury
United Kingdom
CT1 3NG

Study participating centre
Hull and East Yorkshire Hospitals NHS Trust
Hull Royal Infirmary
Anlaby Road
Hull
United Kingdom
HU3 2JZ

Study participating centre
Norfolk and Norwich University Hospitals NHS Foundation Trust
Colney Lane
Norwich
United Kingdom
NR4 7UY

Study participating centre
Oxford University Hospitals NHS Foundation Trust
OCDEM
Churchill Hospital
Old Road
Headington

Oxford
United Kingdom
OX3 7LE

Study participating centre
Lancashire Care NHS Foundation Trust
Lantern Centre
Vicarage Lane
Fulwood
Preston
United Kingdom
PR2 8DW

Study participating centre
York Teaching Hospital NHS Foundation Trust
Wigginton Road
York
United Kingdom
YO31 8HE

Study participating centre
University Hospital Coventry and Warwickshire NHS Trust
Clifford Bridge Road
Coventry
United Kingdom
CV2 2DX

Study participating centre
NHS Greater Glasgow & Clyde
Queen Elizabeth University Hospital
Govan Road
Glasgow
United Kingdom
G51 4TF

Study participating centre
London North West Healthcare
Northwick Park Hospital
Watford Road

Harrow
United Kingdom
HA1 3UJ

Study participating centre
Stockport NHS Foundation Trust
Stockport
United Kingdom
SK2 7JE

Study participating centre
Royal Bournemouth Hospital NHS Trust
Bournemouth
United Kingdom
BH7 7DW

Study participating centre
Midlands Partnership NHS Foundation Trust
Trust Headquarters
Mellor House
Corporation St
Stafford
United Kingdom
ST16 3SR

Study participating centre
Kent Community NHS Foundation Trust
Trinity House
110-120 Upper Pemberton
Kennington
Ashford
United Kingdom
TN25 4AZ

Study participating centre
Provide CIC
Braintree Community Hospital
Chadwick Drive
Braintree
United Kingdom
CM7 2AL

Study participating centre
Guy's & St Thomas NHS Foundation Trust
St Thomas' Hospital
Westminster Bridge Road
London
United Kingdom
SE1 7EH

Study participating centre
Blackpool Teaching Hospitals NHS Foundation Trust
Blackpool Victoria Hospital
Whinney Heys Road
Blackpool
United Kingdom
FY3 8NR

Study participating centre
NHS Grampian
Aberdeen Health and Social Care Partnership
50 Frederick Street
Aberdeen
United Kingdom
AB24 5HY

Study participating centre
Gloucestershire Hospitals NHS Foundation Trust
Cheltenham General Hospital
Sandford Road
Cheltenham
United Kingdom
GL53 7AN

Study participating centre
North Tees and Hartlepool NHS Foundation Trust
University Hospital of Hartlepool
Holdforth Road
Hartlepool
United Kingdom
TS24 9AH

Study participating centre
Derbyshire Community Health Services NHS Foundation Trust
Buxton Hospital
London Road
Buxton
United Kingdom
SK17 9NJ

Study participating centre
Manchester University NHS Foundation Trust
Manchester Royal Infirmary
Oxford Road
Manchester
United Kingdom
M13 9WL

Sponsor information

Organisation
The Leeds Teaching Hospitals NHS Trust

ROR
https://ror.org/00v4dac24

Funder(s)

Funder type
Government

Funder Name
National Institute for Health 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

Individual participant data (IPD) sharing plan
De-identified individual participant data datasets generated and/or analysed during the current study will be available upon request from the Clinical Trials Research Unit, University of Leeds (contact CTRU-DataAccess@leeds.ac.uk in the first instance). Data will be made available at the end of the trial, i.e. usually when all primary and secondary endpoints have been met and all key analyses are complete. Data will remain available from then on for as long as CTRU retains the data.

CTRU makes data available by a 'controlled access' approach. Data will only be released for legitimate secondary research purposes, where the Chief Investigator, Sponsor and CTRU agree that the proposed use has scientific value and will be carried out to a high standard (in terms of scientific rigour and information governance and security), and that there are resources available to satisfy the request. Data will only be released in line with participants' consent, all applicable laws relating to data protection and confidentiality, and any contractual obligations to which the CTRU is subject. No individual participant data will be released before an appropriate agreement is in place setting out the conditions of release. The agreement will govern data retention, usually stipulating that data recipients must delete their copy of the released data at the end of the planned project.

The CTRU encourages a collaborative approach to data sharing, and believe it is best practice for researchers who generated datasets to be involved in subsequent uses of those datasets. Recipients of trial data for secondary research will also receive data dictionaries, copies of key trial documents and any other information required to understand and reuse the released datasets.

The conditions of release for aggregate data may differ from those applying to individual participant data. Requests for aggregate data should also be sent to the above email address to discuss and agree suitable requirements for release.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		19/04/2020	19/10/2022	Yes	No
HRA research summary			28/06/2023	No	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes

Protocol (other)	Diabetic foot ulcer photography study: a study within a trial to assess the reliability of two-dimensional (2D) photography for the assessment of ulcer healing in patients with diabetes-related foot ulcers-protocol paper	09/01/2025	20/01/2025	No	No
Study website	Study website	11/11/2025	11/11/2025	No	Yes