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# Can the use of decellularised dermis allograft (DCD) help improve ulcer healing in patients with chronic venous leg ulceration?

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|---|---|---|
| **Submission date** | **Recruitment status** | [X] Prospectively registered |
| 12/08/2019 | No longer recruiting | [X] Protocol |
| **Registration date** | **Overall study status** | [ ] Statistical analysis plan |
| 13/08/2019 | Stopped | [ ] Results |
| **Last Edited** | **Condition category** | [ ] Individual participant data |
| 23/02/2024 | Circulatory System | [ ] Record updated in last year |

## Plain English summary of protocol

Background and study aims

A large number of patients (around 1% of the adult population) suffer from an ulcer (break in the skin surface) near the ankle. In most people, such an injury should heal up within a week or two. However, many ulcers do not heal and may result in longstanding (chronic), painful, smelly and embarrassing wounds. Compression bandaging is the main standard of care for these patients, which corrects the underlying venous hypertension and helps the ulcer to heal. Skin grafting can act as an additional therapy to compression bandaging to aid healing. Skin grafts can be taken from the patient's own skin, from a donor or from tissue-engineered skin. Graft from the patient's own skin is often taken from the thigh but can result in scarring in the area from which it is taken and the procedure needs to performed in a surgical theatre. Grafts from donor and animal skin have been used successfully employed, but have the risk of being rejected and disease transmission. The DCD graft is made from human skin from deceased donors which has been processed to remove the human cells and leave a matrix behind. DCD contains no human cells, unlike other donated skin grafts, which means that it is unlikely to be rejected by the body. The graft is placed over the ulcer and secured into place with glue, staples or stitches and then covered with a dressing so that compression bandaging can be placed on top. The DCD acts as a scaffold into which the body's own cells can grow and generate new skin and therefore does not need to be removed. The aim of this study is to see if using DCD grafts in addition to compression bandaging can help leg ulcers to heal quicker.

Who can participate?

Patients aged 18 or over who have had a venous leg ulcer for longer than 6 months

What does the study involve?

Participants are randomly allocated to one of two treatments: either compression bandaging alone, or compression bandaging and a DCD graft. Participants are followed-up for 1 year and undergo routine leg ulcer care in community or hospital (or both) settings, in accordance with the local standard care. Participants attend clinic visits (in person until the ulcer has healed or by telephone once the ulcer has healed) at 1 week, 3 weeks, 6 weeks, 12 weeks, 6 months, 9 months and 12 months. Patients are contacted by telephone in between visits to check for ulcer

healing, and are invited for a visit to confirm healing if the patient reports that it has healed. Once healing has been confirmed, patients are contacted monthly by telephone to ask if the ulcer has returned. The researchers will look at the number of ulcers healed in both patient groups and the speed at which the ulcers healed and whether they came back. They also ask the patients to complete health questionnaires at the first visit, 12 weeks, 6 months and 12 months to see if there were any changes in their quality of life following treatment. Furthermore, they look at the costs of the two treatments.

What are the possible benefits and risks of participating?
The advantage of DCD allograft is that it can be applied to the wound without an admission for a procedure under general anaesthetic, and does not have a risk of scarring at the graft site. The decellularisation process removes the cells that could contain intracellular viruses and prions, and the graft undergoes a sterilisation process which means the graft is in the lowest risk category for disease transmission. It is possible that patients could have an allergic reaction to the graft, although to date there have been no documented cases of disease transmission or allergic reaction. In addition, the wound or graft could get infected or suffer from fluid buildup which could dislodge the DCD graft, although this can be minimized by making cuts into the graft prior to application.

Where is the study run from?
The study is sponsored by Imperial College London, where the trial manager is based. The data management and statistical support is provided by Edinburgh Clinical Trials Unit

When is the study starting and how long is it expected to run for?
April 2019 to March 2023 (updated 30/07/2021, previously: March 2022)

Who is funding the study?
The Jon Moulton Charitable Trust

Who is the main contact?
Valeria Balan, valeria.balan22@imperial.ac.uk

# Contact information

### Type(s)
Scientific

### Contact name
Ms Valeria Balan

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# Additional identifiers

### Clinical Trials Information System (CTIS)
Nil known

### ClinicalTrials.gov (NCT)
NCT04021316

### Protocol serial number
42168

# Study information

### Scientific Title
Decellularised dermis allograft for the treatment of chronic venous leg ulceration

### Acronym
DAVE

### Study objectives
Chronic venous ulceration are open wounds on the lower limbs which have been present for at least six months and are caused by a poorly functioning venous system. The affect about 1% of the general population and about 4% of those over 65. The wounds cause pain, reduced movement, and can smell - greatly affecting the quality of life of leg ulcer patients. The standard care for these patients is compression bandaging, which requires changing several times a week by community or district nurses; this drives the high cost of leg ulcer care, which can amount to £2.5 billion per annum.

Skin grafting can be used alongside compression bandaging and can help the ulcers heal faster than compression alone. Grafts can be taken from the patient’s own skin, from a donor or from tissue engineered skin. An autograft (using own skin) can cause scarring and the need for a formal surgical procedure in theatre so are not suitable for all ulcer patients. Allografts (donor skin) and xenografts (animal skin) have been used successfully, but present similar drawbacks to autografts, plus the potential for the body to reject the graft and disease transmission. Tissue engineered skin has several advantages as it has been processed to remove the cells, and therefore won't be rejected via the immune response. Human decellularised dermis (DCD) is generated from donated skin from deceased people and processed to remove the cells. It can be glued or sewn onto the skin under local anesthetic, in an outpatient setting. DCD has mainly been studied in patients with diabetic foot ulceration and has shown improved healing rates and quality of life.

This study will investigate the use of DCD in addition to compression therapy versus compression therapy alone in patients with chronic venous leg ulceration.

### Ethics approval required
Old ethics approval format

### Ethics approval(s)

Approved 15/08/2019, London - Bloomsbury Research Ethics Committee (HRA RES Centre Manchester, Barlow House 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, UK; Tel: +44 (0) 2071048127; Email: nrescommittee.london-bloomsbury@nhs.net), REC ref: 19/LO/1271

## Study design
Randomised; Interventional; Design type: Treatment, Surgery, Other

## Primary study design
Interventional

## Study type(s)
Treatment

## Health condition(s) or problem(s) studied
Chronic venous leg ulceration

## Interventions
Patients will be randomly allocated to one of two treatments: either compression bandaging alone, or compression bandaging and a DCD graft. Participants will be followed-up for 1 year and will undergo routine leg ulcer care in community or hospital (or both) settings, in accordance with the local standard care. Participants will attend clinic visits (in person until the ulcer has healed or by telephone once the ulcer has healed) at 1 week, 3 weeks, 6 weeks, 12 weeks, 6 months, 9 months and 12 months. Patients will be contacted by telephone in between visits to check for ulcer healing, and will be invited for a visit to confirm healing if the patient reports that it has healed. Once healing has been confirmed, patients will be contacted monthly by telephone to ask if the ulcer has returned. The researchers will look at the number of ulcers healed in both patient groups and the speed at which the ulcers healed and whether they came back. They will also ask the patients to complete health questionnaires at the first visit, 6 weeks, 6 months and 12 months to see if there were any changes in their quality of life following treatment. Furthermore, they will look at the costs of the two treatments.

Added 18/12/2020:
A qualitative sub-study has been embedded into the current study and will utilise the Theoretical Framework of Acceptability (TFA) to explore both participant and healthcare provider (HCP) attitudes towards the acceptability of the intervention, as well as general experiences. Semi-structured, one-to-one interviews will be held with patients assigned to the intervention arm and HCPs involved in applying the DCD graft. All the interviews will be audio-recorded (with consent) and transcribed verbatim. Two members of the team will participate in data analysis to ensure transparency and credibility of the themes that are identified and their interpretation. Data will be analysed using thematic analysis. The qualitative study will be conducted in line with and written up in accordance with the COREQ guidelines.

## Intervention Type
Procedure/Surgery

## Primary outcome(s)
Proportion with a healed index ulcer assessed with ulcer photography at 12 weeks after randomisation

## Key secondary outcome(s))

Current secondary outcome measures as of 16/04/2020:
1. Time to index ulcer healing from randomisation, assessed with ulcer photography at 12 months
2. The percentage change in index ulcer area in cm2 measured with ulcer planimetry at 12 weeks from randomisation
3. The proportion of participants with a healed index ulcer assessed with ulcer photography at 12 months from randomisation
4. The proportion of participants whose index ulcer healed for whom an ulcer recurred at the index site assessed with telephone self-report within 12 months from randomisation
5. Generic quality of life measured using the EuroQol-5D (EQ-5D) questionnaire at 12 weeks, 6 months and 12 months from randomisation
6. Disease-specific quality of life measured using the Charing Cross Venous Ulcer Questionnaire (CCVUQ) at 12 weeks, 6 months and 12 months from randomisation
7. The cost for each patient, calculated from the healthcare resources used at 12 months
8. Incremental cost-effectiveness ratio (ICER) from the EQ-5D questionnaire with appropriate sensitivity analysis at 12 months

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7. The cost for each patient, calculated from the healthcare resources used at 12 months
8. Incremental cost-effectiveness ratio (ICER) from the EQ-5D questionnaire with appropriate sensitivity analysis at 12 months

### Completion date
31/03/2023

### Reason abandoned (if study stopped)
Objectives no longer viable

## Eligibility

### Key inclusion criteria
Current inclusion criteria as of 16/04/2020:
1. > = 18 years or older (no upper age limit)
2. The ability to consent to participation
3. A diagnosis of venous leg ulceration* (defined as ‘colour duplex confirmation of superficial and or deep venous reflux with any break in the skin that has either: a) been present for more than 2 weeks, or b) occurred in a person with a history of venous leg ulceration)
4. A wound duration of at least 6 months
5. Documented venous incompetence on duplex ultrasound

6. Ulcer wound size > 2 cm2.
7. ABPI> = 0.8, or if the ABPI is incompressible, other forms of clinical assessment must exclude peripheral arterial disease (peripheral pulse examination, toe pressure, duplex ultrasound, clinical judgment)

*if more than one ulcer is present, the largest ulcer will be chosen as the reference ulcer for the purposes of the trial

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1. > = 18 years or older (no upper age limit)
2. The ability to consent to participation
3. A diagnosis of venous leg ulceration* (defined as 'colour duplex confirmation of superficial and or deep venous reflux with any break in the skin that has either: a) been present for more than 2 weeks, or b) occurred in a person with a history of venous leg ulceration)
4. A wound duration of 6 to 24 months inclusive
5. Documented venous incompetence on duplex ultrasound
6. Ulcer wound size > 2 cm2.
7. ABPI> = 0.8, or if the ABPI is incompressible, other forms of clinical assessment must exclude peripheral arterial disease (peripheral pulse examination, toe pressure, duplex ultrasound, clinical judgment)

*if more than one ulcer is present, the largest ulcer will be chosen as the reference ulcer for the purposes of the trial

## Participant type(s)
Patient

## Healthy volunteers allowed
No

## Age group
Adult

## Lower age limit
18 years

## Sex
All

## Total final enrolment
71

## Key exclusion criteria
Current exclusion criteria as of 16/04/2020:
1. A diagnosis of sickle cell
2. Unable to receive one or more of the randomised treatment strategies for any reason at the discretion of the attending clinical team (e.g. known allergies to dCELL dermis preparation components)
3. A clinically infected ulcer defined as evidence of erythema, cellulitis or systemically unwell

4. Treatment with biomedical/topical growth factors within previous 30 days
5. Previous history of an inability to tolerate compression therapy
6. Foot ulcer (i.e. below the ankle)

Previous exclusion criteria:
1. A diagnosis of sickle cell
2. Known sensitivities to any of the reagents/antibiotics listed on the DCD package insert
3. A clinically infected ulcer defined as evidence of erythema, cellulitis or systemically unwell
4. Treatment with biomedical/topical growth factors within previous 30 days
5. Previous history of an inability to tolerate compression therapy
6. Foot ulcer (i.e. below the ankle)

### Date of first enrolment
01/10/2019

### Date of final enrolment
30/09/2022

## Locations

### Countries of recruitment
United Kingdom

England

### Study participating centre
**Imperial College Healthcare NHS Trust**
St Mary's Hospital
Praed Street
London
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W2 1NY

### Study participating centre
**Worcestershire Acute Hospitals NHS Trust**
Worcestershire Royal Hospital
Charles Hastings Way
Worcester
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WR5 1DD

### Study participating centre
**Cambridge University Hospitals NHS Foundation Trust**
Addenbrookes Hospital
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**Study participating centre**
**London North West University Healthcare NHS Trust**
Northwick Park Hospital
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HA1 3UJ

**Study participating centre**
**Gloucestershire Hospitals NHS Foundation Trust**
Trust HQ
Alexandra House
Cheltenham
United Kingdom
GL53 7AN

**Study participating centre**
**North Cumbria University Hospitals NHS Trust**
West Cumberland Hospital
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CA28 8JG

**Study participating centre**
**University Hospitals Plymouth NHS Trust**
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PL6 8DH

**Study participating centre**
**Taunton and Somerset NHS Foundation Trust**
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**Study participating centre**
**Guy's and St Thomas' NHS Foundation Trust**
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**Study participating centre**
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**Study participating centre**
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# Sponsor information

**Organisation**
Imperial College of Science, Technology and Medicine

**ROR**
https://ror.org/041kmwe10

# Funder(s)

### Funder type
Charity

### Funder Name
J P Moulton Charitable Foundation; Grant Codes: P79954

# Results and Publications

### Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Sarrah Peerbux (s.peerbux@imperial.ac.uk). Raw anonymised data can be requested after publication. Available for 10 years after end of trial. Requests will be approved by the Chief Investigator on a case by case basis.

### IPD sharing plan summary
Available on request

### Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Protocol article | | 02/04/2021 | 06/04/2021 | Yes | No |
| HRA research summary | | | 28/06/2023 | No | No |
| Participant information sheet | Participant information sheet | 11/11/2025 | 11/11/2025 | No | Yes |