

# Haemoglobin application to wounds study: A research trial of Granulox haemoglobin spray in addition to standard treatment for healing of diabetic foot ulcers

<b>Submission date</b> 31/07/2017	<b>Recruitment status</b> No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 03/08/2017	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
<b>Last Edited</b> 21/10/2022	<b>Condition category</b> Nutritional, Metabolic, Endocrine	<input type="checkbox"/> Individual participant data

## Plain English Summary

### Background and study aims

Diabetes can lead to various complications in affected people, including diabetic foot ulcer (DFU). This causes a broken area in the foot that is unable to heal due to uncontrolled blood sugar levels. If a DFU develops, it is important to treat it appropriately in order to increase the chance of the DFU healing and minimise the risk of infection. Putting on dressings could reduce the strain on the wound area and keeps it clean. To allow the best healing of the wound, it is essential to have sufficiently high oxygen levels. Hypoxia (oxygen deficiency), can lead to necrosis (a death of cells or tissues) and make the wound worse. Oxygen promotes the formation of new blood vessels and subsequently the growth of new skin. New treatment types have been introduced to increase oxygen levels in wounds, including hyperbaric oxygen (HBO) treatment. However, such treatments tend to be cumbersome, time-intensive and costly. In the UK, InFirst Ltd has brought to market a new medical device for oxygen treatment, which is designed to be more straightforward to apply than HBO. The product, Granulox, contains porcine haemoglobin (made from the part of blood that carries oxygen) contained in a spray canister. It is applied twice weekly to a DFU wound during redressing, and can be used in a clinic or patient's home setting. Initial case series and retrospective comparative studies have shown that Granulox reduces the time for a DFU to heal. The aim of this study seeks to assess if Granulox has a significant positive impact on the rate of wound healing in DFUs.

### Who can participate?

Adults aged 18 and older who have a DFU.

### What does the study involve?

There are two stages of the study: the screening phase and the intervention phase. In the screening stage participants provide information about their wound and other health-related questions. Participants also have an ankle-brachial pressure measurement and a blood sample taken to measure their HbA1c levels. They have the size of the DFU measured. Participants attend a second appointment where they have their DFU measured again. If the wound has

healed less than 30% in the last two weeks, then the participant is eligible for the next phase of the study. Participants are then randomly allocated to one of two groups. Those in the first group receive treatment as usual. Those in the second group receive the usual treatment as well as the Granulox treatment, which is sprayed on the DFU wound twice per week for 12 weeks. Participants attend appointments at week three, six, nine and 12 to have their DFU measurement. Participants also complete four pain and quality of life questionnaires. Participants receive telephone calls after the study to see if the DFU has healed.

What are the possible benefits and risks of participating?

Participants may benefit from improvements in DFU wound healing. There are no notable risks however there is a risk of allergic reactions to the Granulox spray, however only a small amount is sprayed on the wound. Granulox is a licensed medical device with a CE mark so there should be no risk of infection from the medical device itself.

Where is the study run from?

1. Flatt Walks Community Health Centre (UK)
2. Workington Community Hospital (UK)

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

July 2017 to November 2018

Who is funding the study?

Infirst Healthcare Limited (UK)

Who is the main contact?

Dr Leon Jonker

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## Contact information

**Type(s)**

Public

**Contact name**

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# Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

35097

# Study information

## Scientific Title

Haemoglobin Application to Wounds Study, a single-centre, controlled, prospective, randomized trial of Granulox haemoglobin spray for adjuvant treatment of diabetic foot ulcers

## Acronym

HAWS

## Study hypothesis

The aim of this randomised, controlled, prospective clinical trial is to determine the efficacy of the Granulox haemoglobin spray device as an adjuvant therapy for DFU, with a primary outcome measure of DFU healing at 12 weeks of treatment.

## Ethics approval required

Old ethics approval format

## Ethics approval(s)

East Midlands - Leicester South Research Ethics Committee, 17/07/2017, 17/WM/0244

## Study design

Randomised; Interventional; Design type: Treatment, Device

## Primary study design

Interventional

## Secondary study design

Randomised controlled trial

## Study setting(s)

Hospital

## Study type(s)

Treatment

## Participant information sheet

Not available in web format, please use the contact details below to request a patient information sheet

## Condition

Specialty: Diabetes, Primary sub-specialty: Both; UKCRC code/ Disease: Metabolic and Endocrine/ Diabetes mellitus

## Interventions

Following written consent, participants are observed for two weeks to establish healing rate. At the end of two weeks, patients are only eligible for the intervention phase if their wound has healed <30% in the preceding two weeks. This point is deemed as the the baseline and participants are allocated at random to the control or Granulox intervention group, using a randomised sequence from the freeware randomisation programme. The randomisation is stratified for ulcer size, with an ulcer size of below and above 3cm<sup>2</sup> as the cut-off. This size is has been determined as the average size of a presenting DFU previously.

Sequential envelopes with each next randomisation allocation are used to achieve concealment and these are kept in the research department. The researcher then informs the regular healthcare professional for the participant in question, and the participant themselves, which treatment they've been allocated to. As the study involves administration of a spray it is not possible to achieve blinding for the participants nor the researchers – it is recognised that this increases the risk of bias.

Treatment as usual arm: Patients are in the study for a period of 18 weeks, once they've qualified after the 2 week screening phase (ie their wound has insufficiently healed). Thereafter, the patient is followed up as they would be in normal clinical practice. In practice this means that for almost all patients this involves dressing of the DFU, and advice on off-loading of the affected area. For the latter, specialist footwear may be prescribed, or a foot/leg brace. During and after the trial, clinical staff redress the DFU as per routine care, and during the trial they conduct the measurement of the DFU (grid measurement tool and PUSH score). The researcher is in attendance at the beginning of the observation two weeks, baseline, and weeks three, six, nine, and 12 of study participation to randomise the patient, and conduct/collect the study participant questionnaires. The researcher phones the participant at week 18 to check on wound status and any adverse event reporting.

Granulox arm: Participants undergo the same steps as the treatment as usual arm. The only additional intervention is that Granulox is sprayed on the wound twice weekly. Where possible, this is fitted in with standard clinic appointments that the patient may have, and when dressings are changed anyway so that the wound is accessible. The Granulox treatment is done twice week for 12 weeks maximum, for around 24 applications. If the wound heals before 12 weeks have passed, then Granulox treatment will cease.

## Intervention Type

Other

## Primary outcome measure

Efficacy of the Granulox spray in terms of wound healing is assessed using the DFU size, measured with Convatec grid tool at -2 weeks (two weeks observation), baseline, week three, six nine and 12.

## Secondary outcome measures

1. Size and characteristics of DFU is measured using the PUSH score at -2 weeks (two weeks observation), baseline, week three, six nine and 12
2. Grading of DFU is assessed using Texas Univ grading score at -2 weeks (two weeks

observation), baseline, week three, six nine and 12

3. Wound closure status is assessed as either open or closed by clinician at baseline, week three, six, nine and 12

4. Patient mobility score is measured using the LifeSpace questionnaire at baseline, week six and 12

5. Pain related to DFU is measured using the Visual Analogue Pain score at -2 weeks (two weeks observation), baseline, week three, six nine and 12

6. General Quality of life score is measured using the EQ5D-5L and wound-related quality of life score as measured by Charing Cross Venous Ulcer Questionnaire at baseline, week six and 12

7. Wound status check [healed, not healed, recurrence] and any incidences of adverse events at week 18

8. Patient withdrawal rates due to change in management (e.g. need for surgery)

### **Overall study start date**

24/07/2017

### **Overall study end date**

31/01/2019

## **Eligibility**

### **Participant inclusion criteria**

1. Clinical diagnosis of Diabetic Foot Ulcer (DFU), present on plantar or calcaneus area

2. DFU present for at least 2 weeks.

3. Adult patients aged > 18 years

4. Patients with recurrent wounds, including multiple wounds, are eligible. The largest of the wounds, in plantar or calcaneus area, will be selected for the trial.

5. Patients who have undergone an episode of infection prior to the enrolment but are not currently receiving antibiotic therapy or antimicrobial dressings for the DFU in question are eligible – i.e. where a previous infection has resolved.

6. Mental capacity to give consent

### **Participant type(s)**

Patient

### **Age group**

Adult

### **Lower age limit**

18 Years

### **Sex**

Both

### **Target number of participants**

Planned Sample Size: 40; UK Sample Size: 40

### **Total final enrolment**

79

## **Participant exclusion criteria**

1. Under the age of 18 years
2. Unable to fully understand the consent process and provide informed consent due to either language barriers or mental capacity
3. Limited life expectancy, i.e. undergoing palliative care
4. Active infection in DFU
5. Systemic antibiotic treatment
6. Any personal objection to being administered a product containing porcine material.
7. Patients who are participating in another research study involving an investigational product.
8. The patient has concurrent (medical) conditions that in the opinion of the investigator may compromise patient safety or study objectives, including alcohol or drug dependency.
9. DFU in other area of the foot (e.g. in between toes, which would make exact ulcer size measurement impossible)
10. Patient pregnant or lactating
11. Ankle brachial index < 0.5, measured within 3 months of baseline visit

## **Recruitment start date**

07/08/2017

## **Recruitment end date**

30/09/2018

## **Locations**

### **Countries of recruitment**

England

United Kingdom

### **Study participating centre**

#### **Flatt Walks Community Health Centre**

Podiatry Service  
3 Castle Meadows  
Cumbria  
Whitehaven  
United Kingdom  
CA28 7QE

### **Study participating centre**

#### **Workington Community Hospital**

Podiatry Service  
Park Lane  
Workington  
United Kingdom  
CA14 2RW

# Sponsor information

## Organisation

Cumbria Partnership NHS Foundation Trust

## Sponsor details

Carleton Clinic  
Cumwhinton Road  
Carlisle  
England  
United Kingdom  
CA1 3SX

## Sponsor type

Hospital/treatment centre

# Funder(s)

## Funder type

Industry

## Funder Name

Infirst Healthcare Limited

# Results and Publications

## Publication and dissemination plan

The results of this study will be disseminated through publication of a peer-reviewed manuscript in an international scientific journal, planned for late 2018/early 2019 once the trial is completed.

## Intention to publish date

01/03/2019

## Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study during this study will be included in the subsequent 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?
<a href="#">Protocol file</a>	version 6	10/07/2018	14/10/2022	No	No

[Results article](#)

01/09/2021

21/10/2022

Yes

No