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The international ‘100 DU’ study

Submission date
23/07/2025

Recruitment status
Recruiting

Registration date
09/02/2026

Overall study status
Ongoing

Last Edited
10/03/2026

Condition category
Musculoskeletal Diseases

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

Plain English summary of protocol

Background and study aims
Digital ulcers (DU) are common in systemic sclerosis (SSc), affecting over half of patients during their disease course, with a point prevalence of approximately 10%. They are a major cause of pain, impaired function and reduced health-related quality of life. To date, clinical trials of SSc-DU have traditionally focused on clinician assessment of DU occurrence and healing, with comparatively little attention having focused on how patients with SSc-DU ‘feel’ and ‘function’, despite the importance placed on these clinically meaningful endpoints by regulators when considering marketing authorisation. The patient experience of SSc-DU has largely been captured using legacy patient-reported outcome (PRO) instruments such as the HAQ-DI (health assessment questionnaire disability index) and validated generic pain scales, which do not fully capture the multi-faceted lived experience of SSc-DU. There is an unmet need to develop a specific PRO instrument for use in clinical practice, observational studies and clinical trials to capture the impact of SSc-DU on how patients feel and function. The Scleroderma Clinical Trials Consortium (SCTC) Vascular Working Group have a strong track record for developing novel PRO instruments, having recently completed a five-year body of work to develop and validate the Assessment of Scleroderma-associated Raynaud’s Phenomenon (ASRAP) questionnaire for assessing SSc-RP. Prior SCTC Vascular Working Group seed-funding has enabled us to complete a comprehensive literature review and multicentre qualitative research study to explore the patient experience of SSc-DU. From this work, a conceptual map has been devised comprising five separate domains that encapsulate the lived patient experience of SSc-DU. The principal objective of this study is to elaborate and validate a novel PRO+ instrument for assessing the severity and impact of SSc-DU. SSc is a rare orphan disease (affecting around 200 people per million). A study of 100 patients will therefore represent a medium-sized study of this condition. The site, burden and aetiopathogenesis of SSc-DU differ between patients. Little is known about the contribution of DU burden (number and site of DU) and relevant aetiopathogenic driver (purely ischaemic versus mixed mechanical/inflammatory aetiology) on the lived patient experience of SSc-DU. The present proposal allows us to comprehensively examine the evolving patient experience of active DU using items from the preliminary SScDU questionnaire. A secondary objective will therefore be to understand the aetiopathogenic drivers of different types of DU (e.g. size, location) and their relationship to the lived patient experience of SSc-DU, and to benchmark DU healing (including impact of complications and treatment) in the modern era.

Who can participate?
Consecutive SSc patients will be enrolled to capture a representative sample of SSc patients for disease stage, organ complications and severity of vascular manifestations.

What does the study involve?
Participants will be consented and complete all self-administered questionnaires using the RedCap electronic data capture software. Clinicians will complete the case report form(s).

What are the possible benefits and risks of participating?
Recruited patients will be on an existing clinical pathway; it is anticipated that there are no additional benefits or risks with participation.

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

When is the study starting and how long is it expected to run for?
July 2025 to December 2026

Who is funding the study?
The study is jointly funded by the Scleroderma Clinical Trials Consortium (SCTC) and the Scleroderma Research Foundation (SRF)

Who is the main contact?
Dr M Hughes, Clinical Senior Lecturer & Honorary Consultant Rheumatologist, Michael.hughes-6@manchester.ac.uk

Contact information

Type(s)
Public, Scientific, Principal investigator

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Dr Michael Hughes

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Additional identifiers

Integrated Research Application System (IRAS)
359781

Central Portfolio Management System (CPMS)
69727

Study information

Scientific Title
Optimising the assessment and novel mechanistic insights into digital ulcers in systemic sclerosis: the international '100 DU' study

Study objectives
The principal objective of this study is to elaborate and validate a novel patient-reported outcome (PRO) instrument for assessing the severity and impact of SSc-DU.

Ethics approval required
Ethics approval required

Ethics approval(s)
1. Not yet submitted

2. Not yet submitted

Primary study design
Observational

Study design
International multicentre longitudinal study

Study type(s)
Quality of life, Treatment

Health condition(s) or problem(s) studied
Systemic sclerosis (SSc) with active digital ulceration (DU)

Interventions
This study is an international multicentre longitudinal study of 100 systemic sclerosis (SSc) patients with active digital ulceration (DU) from a diverse geographic, cultural and ethnic sample of patients enrolled from 15 English-speaking Scleroderma Clinical Trials Consortium (SCTC) sites in the UK, US, Australasia, and Canada.

Observations to be made include questionnaires, clinician assessment, clinical photography and thermal imaging.

To achieve our study aims, we have designed an international multicentre longitudinal study of 100 SSc patients with active DU from a diverse geographic, cultural and ethnic sample of patients enrolled from 15 English-speaking SCTC sites in the UK and US. The '100DU' study will facilitate the comprehensive capture of patient-reported, clinician-assessed and imaging (photography and nailfold capillaroscopy) data from 100 SSc patients with active DU (including ischaemic, extensor and calcinosis-related ulceration) over 20 weeks. Applicable regulatory frameworks shall be adhered to at each participating unit, with local PIs retaining responsibility for local IRB approval and adherence to good practice. Data sharing MTAs shall be established between sites. The pragmatic study design shall include clinician assessments at 4-8 weeks and

18-22 weeks (attempting to mirror clinical practice) and benefit from self-administered PRO questionnaire completion at home. Patients will complete the study when/if their DU have been considered to have healed by their practising clinician.

Participants will be consented and complete all self-administered questionnaires using the REDCap electronic data capture software. Clinicians will complete the case report form(s).

The SSiDU questionnaire is a preliminary item bank comprising 29 items developed with the support of patient insight partners. Each item is grounded in the 5 major themes that encapsulate the patient experience of SSc-DU identified in our earlier literature review and qualitative research. The themes include physical symptoms and signs, psychological impacts, functional impact, aggravating factors and mitigating factors.

At the initial study visit, participants in our planned multicentre study will support a prioritisation study to rank and score domains of activity and impact of SSc-DU important to patients with SSc. Patients will be presented with a list of the 5 major themes and an explanation regarding what is required of them. Participants shall be asked to sensibly rank the domains rather than individual issues. Specifically, they will rank each issue 1 to 9 (1-3 not necessary; 4-6 interesting but not essential; 7-9 essential) and then load questions by their relative mean scores. Domain loading would follow from the item loading. This shall inform the weighting and scoring of the final SSiDU instrument, with mean weightings derived for each domain from which a total SSiDU score can be derived.

Participants will then complete the preliminary SSiDU item bank and a separate ‘pack’ of seven self-administered validated questionnaires (plus some additional details on smoking, ethnicity, work etc) and directly input their data into REDCap.

A clinician CRF shall collect relevant information regarding patient demographics, clinical phenotype, clinician VAS scales and the DUCAS instrument. A limited physical examination of the hands, forearms and face to assess the number and distribution of digital ulcers, telangiectases and calcinosis. Clinicians shall document the site and size of active DU on CRF hand templates. They shall also document the site of calcinosis cutis and undertake a count of telangiectases within the hands and face (as proxy markers of cutaneous vascular severity).

Additional face-to-face study visits will take place at weeks 6 (+/- 14 days) and 20 (+/- 14 days) to mirror typical routine care for active DU. These visits will either correspond to clinic reviews or additional research visits shall be arranged to accommodate. Participants will be given packs and free post envelopes at each study visit for between-study visit assessments at weeks 1 (+7 days) and week 12 (+/- 14 days).

Patients will complete the study early when/if their DU have been considered to have healed by their practicing clinician at week 6 assessment.

Prospective anchor questions (“My digital ulcer disease symptoms over the past week have been: very mild, mild, moderate, moderately severe, severe, very severe or unbearable.”) and retrospective anchor questions (“Consider all the ways that Digital Ulcer symptoms affect you, compared to the period running up to the 1st assessment, ‘how would you rate your overall Digital Ulcer symptoms since the last visit?’ (“much worse, somewhat worse, about the same, somewhat better, or much better”), will be used to establish Patient Acceptable Symptom States and Minimum Clinically Important Differences for the SSiDU questionnaire.

Ancillary microvascular imaging study: Nailfold Capillaroscopy
Nailfold capillaroscopy of four digits (two 1 mm images on either side of the midline of the middle and ring fingers bilaterally) shall be undertaken. Image analysis shall be undertaken centrally (Manchester, UK) and include qualitative: Cutolo grading of 'early', 'active' and 'late', and quantitative (including by planned utilisation of highly novel centralised automated analysis, Manchester, UK): mean number of capillaries per mm, mean inter-capillary distance, mean number of giant capillaries/microhaemorrhages, assessments.

Ancillary microvascular imaging study: Thermal Image
A thermal image of the dorsum of both hands shall be obtained.

Intervention Type
Mixed

Primary outcome(s)
The severity and impact of systemic sclerosis-related digital ulcers (SSc-DU) will be measured using the SSiDU questionnaire and self-administered validated questionnaires administered at baseline, week 1, week 6, week 12 and week 20.

Key secondary outcome(s)
1. The severity and impact of systemic sclerosis-related digital ulcers (SSc-DU) will be measured using physical examination (assessment of site and status of DU (hands), telangiectases count (hands and face), calcinosis assessment (hands, elbow and knees), mRSS) at baseline, week 6 and week 20
2. The severity and impact of systemic sclerosis-related digital ulcers (SSc-DU) will be measured using imaging (clinical photographs of DUs, nailfold capillaroscopy (two digits of each hand), thermography (fingers)) at baseline, week 6 and week 20
3. The severity and impact of systemic sclerosis-related digital ulcers (SSc-DU) will be measured using clinician assessment (DUCAS, clinician PRO VAS of DU severity and healing) at baseline, week 6 and week 20

Completion date
31/12/2026

Eligibility

Key inclusion criteria
1. Participants will fulfil the 2013 European Union League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR) classification criteria for systemic sclerosis
2. The presence of an active DU at study entry. DU shall be defined according to the World Scleroderma Foundation (WSF) as "Loss of epidermal covering with a break in the basement membrane (which separates dermis from epidermis). It appears clinically as visible blood vessels, fibrin, granulation tissue and/or underlying deeper structures (e.g., muscle, ligament, fat) or as it would appear on debridement"
3. Male or female age ≥18 years
4. Patient is able and willing to follow the requirements of the study, including providing informed written consent
5. Good comprehension of written and spoken English

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
100 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Pregnant women
2. Patients with a change in their vasodilator medication within the previous 2 weeks before study entry

Date of first enrolment
01/09/2025

Date of final enrolment
31/12/2026

Locations

Countries of recruitment
United Kingdom

England

Australia

Canada

United States of America

Study participating centre
North Bristol NHS Trust
Southmead Hospital
Southmead Road
Westbury-on-trym
Bristol

England
BS10 5NB

Study participating centre
University College London Hospitals NHS Foundation Trust
250 Euston Road
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Study participating centre
University of Leeds
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Study participating centre
Northern Care Alliance NHS Foundation Trust
Salford Royal
Stott Lane
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M6 8HD

Study participating centre
Liverpool University Hospitals NHS Foundation Trust
Royal Liverpool University Hospital
Prescot Street
Liverpool
England
L7 8XP

Study participating centre
The Dudley Group NHS Foundation Trust
Russells Hall Hospital
Pensnett Road
Dudley
England
DY1 2HQ

Study participating centre
Hospital for Special Surgery
United States of America
NY 10021

Study participating centre
Johns Hopkins University
United States of America
MD 21218

Study participating centre
University of Michigan
United States of America
MI 48109

Study participating centre
New Orleans Scleroderma and Sarcoidosis Patient Care and Research Center
United States of America
LA 70112

Study participating centre
Vanderbilt University Medical Center
United States of America
TN 37232

Study participating centre
Yale University
United States of America
CT 06511

Study participating centre
Central Adelaide Local Health Network Incorporated (CALHN)
Australia
South Australia 5000

Study participating centre
University of Alberta
Canada
T6G 2R3

Sponsor information

Organisation
University of Manchester

ROR
https://ror.org/027m9bs27

Funder(s)

Funder type
Research organisation

Funder Name
Scleroderma Clinical Trials Consortium (SCTC)

Funder Name
Scleroderma Research Foundation (SRF)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not expected to be made available