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Review

Points to consider for reporting digital ulcers in systemic sclerosis interventional studies: An initiative from the world Scleroderma Foundation digital ulcer ad hoc committee

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ABSTRACT

Background: Digital ulcers (DUs) are among the most painful and functionally disabling complications of systemic sclerosis (SSc), affecting up to 50% of patients. Despite their clinical relevance, interventional studies on DUs are limited and vary widely in design, definitions, and outcome reporting, hindering comparability and the development of standardized treatment approaches.

Objectives: This initiative, led by an international expert group under the World Scleroderma Foundation (WSF), aims to establish points to consider for the standardized reporting of DUs in interventional studies, improving study quality, interpretability, and clinical relevance.

Methods: A steering committee of SSc experts developed these recommendations based on three systematic literature reviews on local, surgical, and systemic treatments for SSc-DUs. Consensus was achieved through iterative discussion among committee members, without external funding or third-party influence.

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Results: Seven domains were identified as essential for standardization: (1) a uniform definition and classification of DUs; (2) consistent inclusion and exclusion criteria; (3) standardized primary and secondary outcome measures, including clinical and patient-reported outcomes; (4) detailed reporting of background and concomitant therapies; (5) harmonized local wound care protocols; (6) predefined timing and frequency of assessments; and (7) consideration of seasonal and environmental influences.
Conclusion: Adopting these standardized reporting principles in future DU trials will enhance the quality and comparability of data, support more robust meta-analyses, and facilitate the development of effective, patient-centered treatment strategies for SSc-related DUs.

1. Introduction

Systemic sclerosis (SSc) is a complex, chronic rheumatological disorder characterized by vasculopathy, inflammation, and fibrosis [1,2]. Among its various clinical manifestations, digital ulcers (DUs) are particularly debilitating, causing significant pain, functional impairment, and, in severe cases, leading to complications such as infection, gangrene, and sometimes necessitating amputation [3,4]. DUs are reported to affect up to 50% of patients with SSc during the course of their disease, often leading to recurrent and slow-healing digital lesions that exacerbate the overall burden of disease [5].

Despite the substantial clinical impact of DUs, there is a notable lack of standardization in how DUs are managed, which is in part due to the limited number of high-quality studies focusing on DUs in SSc patients [6–8], and the current notable absence of a standardization on how to report these studies in the medical community. This inconsistency significantly hinders the interpretation of study results, complicates performing meta-analyses, and limits the applicability of findings to clinical practice. The diversity in trial designs, outcome measures, and patient populations further complicates efforts to develop a unified approach to DU management [6–10]. Against this background, there is an urgent need to establish standardized reporting criteria for SSc-DUs in interventional studies in an attempt to improve the quality of emergent evidence, and to facilitate the development of effective treatment strategies.

This paper outlines key considerations for the standardized reporting of DUs in interventional studies involving SSc patients. By addressing aspects such as the definition and classification of DUs, inclusion and exclusion criteria, outcome measures, and the reporting of background and concomitant therapies, the aim is to enhance the consistency and comparability of trial outcomes. Additionally, the paper discusses the importance of local wound management protocols and the impact of environmental factors on DU healing.

2. Methods

A project steering committee of internationally recognized experts in the field of SSc (CC, NM, LR, YS, BAP, YA, FDG, CPD, OD, DEF, DK, TK, MK, MMC, JP, MH) was established to determine the points to consider for reporting SSc-DUs in interventional studies. These points were elaborated as part of the tasks of the World Scleroderma Foundation (WSF) digital ulcer ad hoc committee which produced three systematic literature reviews (SLRs) on the local non-surgical and surgical treatments for SSc-DU [6,7] and systemic treatments for SSc-DU [8] and has developed recommendations for DUs [11,12]. There was no external involvement of third parties in the process (including financial support) of developing these points to consider.

2.1. Points to consider

A summary of the points to consider for reporting DUs in SSc interventional studies was developed by CC, BAP and MH. The draft was presented to the other members of the steering committee and discussed via email for final approval, see Table 1.

3. Results

3.1. Key considerations for reporting digital ulcers in RCTs

3.1.1. Standardized definition and classification of digital ulcers

Definition: The establishment of a standardized definition for DUs is a fundamental step in improving the reporting of these lesions in RCTs. In clinical practice, among the different digital lesions that can be observed in SSc patients, DUs are generally considered the ones of (varying) ischemic nature present in the distal (acral) areas of the hands and feet e.g. around the distal phalanx of the digits, which result from the severe vasculopathy characteristic of SSc [4,13,14]. Other aetiopathogenic drivers may also play important roles in the formation of DUs on this anatomical area, or in other parts of the digits. For example, the presence of calcinosis cutis, or skin fibrosis. The latter reducing the skin ability to withstand repetitive microtraumas related to mechanical use of the digits, and producing increase tensile stress on bony prominences particular over the interphalangeal joints (IPJ) (especially when related to significant finger contractures). However, definitions used in previous clinical trials vary considerably, with some studies including a broad range of digital lesions, while others have focussed exclusively on ischemic ulcers [6–8].

The absence of a previous standardized DU definition leads to challenges in comparing results across different studies. For example, some studies have strictly limited their definition to ulcers considered to have an 'ischemic' origin (usually present at the distal phalanx), while others have included under the broader category of DUs, ulcers that might be multifactorial in origin such as those present over the IPJ. In reality, DU overlying the IPJ are ischemic but also suffer from increased skin tension which aggravates and accelerates wound healing; however, in RCT they have tended to be separated from fingertip ulcers. This also applies to the inclusion of ulcers with complications such as actively infected ulcers, or those with presence of gangrene. This lack of uniformity complicates the interpretation of study results and makes it difficult to synthesize data across trials. Furthermore, the lack of a standardized definition may lead to the inclusion of heterogeneous patient populations, which can dilute the observed effects of an intervention and/or reduce the generalizability of findings.

Ultimately, the inclusion of one or multiple types of ulcer in a RCT will depend on the intervention/s studied and the trial aim. However, if more than one type of ulcer is included then the rational for its inclusion and potentially exploratory subgroup analysis (when appropriate) should be provided.

Recommendation: Interventional studies should adopt a uniform definition of DUs, ideally endorsed by recognized organizations such as the WSF [15], the Scleroderma Clinical Trials Consortium (SCTC), or the Outcome Measures in Rheumatology (OMERACT) initiative [9,10]. This definition should clearly specify the (diagnostic) criteria for DUs, emphasizing the rationale for the mechanism/s of action of the proposed intervention, and excluding other types of digital lesions (e.g. fissures and abrasions). The definition should include criteria such as non-traumatic origin and other causes (e.g., calcinosis-related). Moreover, it should be emphasized that DUs are pitting scars are not interchangeable terms as the definition of pitting scars refers to pinhole-sized, concave depressions with hyperkeratosis, reflecting prior

Table 1
Recommendations for points to consider for reporting digital ulcers in interventional studies of systemic sclerosis.

Points to consider for reporting SSc-related digital ulcers in interventional studies		
Key Points to consider	Recommendations	Lessons learnt from clinical trials
Standardized Definition and Classification of Digital Ulcers	Interventional studies should adopt a uniform definition of DUs, ideally endorsed by recognized organizations such as the World Scleroderma Foundation (WSF), the Scleroderma Clinical Trials Consortium (SCTC), or the Outcome Measures in Rheumatology (OMERACT) initiative.	Heterogeneous definitions and inconsistent differentiation between digital ulcers and other lesions (e.g., pitting scars) have been a major source of variability in DU trials, limiting comparability across studies.
Clear Inclusion and Exclusion Criteria	Inclusion criteria should encompass patients with a clearly defined duration of DU and stable background therapy. The intent of the study (i.e., DU healing and/or prevention) should be clearly stated.	Published DU interventional studies show wide variation in enrolment criteria, particularly regarding ulcer chronicity, background therapy stability, and comorbidities, leading to heterogeneous study populations
Standardized Outcome Measures	The primary outcome measure in DU studies should consistently be the healing of the cardinal ulcer or 50% improvement in cardinal ulcer and improvement in function by HIDSS-DU. Secondary outcomes should also include pain and patients' reported outcomes.	Outcome measures differ markedly across DU trials, with inconsistent definitions of healing, variable use of patient-reported outcomes, and limited reporting of time-to-healing, hindering synthesis of results.
Reporting of Background and Concomitant Therapies	A detailed report of all background and concomitant therapies should be included for all trial including the types, doses, and duration of these treatments. In controlled studies, efforts should be made to match the study populations on their background therapies.	Systemic pharmacologic SLRs show that many trials did not adequately report concomitant vasoactive or immunosuppressive therapies, which may confound healing outcomes and reduce interpretability.
Reporting on Local Wound Management Protocols	Interventional studies should include a standardized protocol for local wound management, ensuring uniform care across study sites. This protocol should provide details on debridement, topical therapies and dressing types.	Evidence from the local treatment SLR indicates substantial variation in wound care practices (debridement, dressings, topical agents), which can influence healing and complicate comparisons across studies.
Timing and Frequency of Assessments	Studies should specify the timing of assessments, including the duration of the evaluation period and intervals between assessments. Multiple assessments over an extended period are recommended.	Published trials differ widely in assessment schedules, with many studies using short follow-up periods or infrequent evaluations, limiting the ability to capture the true course of DU healing.
Consideration of Seasonal and Environmental Factors	RCTs should account for seasonal and environmental factors in their design and analysis.	Environmental influences on perfusion and Raynaud's severity are rarely accounted for in trial designs, although these factors may meaningfully affect DU onset and healing.

microinfarcts without active tissue loss [16].

Classification: In addition to a standardized definition, it is essential to *classify* DUs based on their underlying pathophysiology. Distinguishing between ischemic ulcers, which are directly related to SSc-associated vasculopathy, and those with other concomitant aetiologies is critical for tailoring treatment approaches and ensuring homogeneity within study populations [14]. The proposed way to classify DUs relies on their nature and certain features [17]: DU developed on digital pitting scars, pure DU, DU developed on calcinosis and DU derived from gangrene. This classification should be considered in order to include homogeneous group which arise from likely different pathogenic mechanisms and whose response to treatment might be different.

Categorization: Further, the categorization of DUs by severity and chronicity may offer additional insights into the natural history of DUs in SSc and improve the evaluation of therapeutic interventions. A proposed novel categorization of four patient categories (no-DU; episodic, recurrent, chronic) was proposed by Matucci-Cerinic and colleagues based on the pattern of DU recurrence of ulcers during a 2-year observation period of patients enrolled in the prospective, multinational Digital Ulcers Outcome Registry [3]. Practically speaking, more chronic DUs, for instance, may require different management strategies compared to acute DUs, and understanding these differences is crucial for designing effective clinical trials [4]. Moreover, the inclusion of a severity grading scale for DUs could help standardize the assessment of ulcer severity across studies, allowing for more accurate comparisons of treatment outcomes. Measures of DU persistency is also important to be considered for trial enrolment as this might affect the rate of ulcer healing (the chances of a chronic ulcer to heal are lower compared to those of recent onset). We propose to define a chronic DU as being greater than 6 to 12 weeks, depending on the study intended aim and proposed intervention, to help accurately define the included patient population (that is, without intervention, ulcer healing would continue to be very slow or not heal at all).

3.1.2. *Clear inclusion and exclusion criteria*

The inclusion and exclusion criteria in interventional studies must be clearly defined to ensure that study populations are homogeneous and that results are generalizable. Given the variability in DU presentation, it is crucial to standardize these criteria across studies.

Inclusion criteria play a pivotal role in determining the characteristics of the study population. When inclusion criteria are not standardized, studies may enrol patients with a wide range of ulcer types, sizes, and durations, leading to heterogeneous populations that can obscure the true effects of the intervention. For example, a trial that includes both patients with chronic, non-healing ulcers and those with acute, recently developed ulcers may find it challenging to determine whether the observed effects of the intervention are due to differences in ulcer chronicity rather than the treatment itself. Moreover, the intent of the study (i.e., DU healing and/or prevention) should be clearly stated.

Recommendation: Inclusion criteria should encompass patients with a clearly defined duration of DU (e.g., ulcers present for more than two weeks but less than six months) and stable background therapy (e.g., no changes in systemic vasodilators for at least 2 weeks, or immunosuppressive therapy for at least one 12 weeks prior to enrolment). This standardization ensures that any observed effects can be attributed to the intervention under study rather than variations in baseline treatments or ulcer characteristics. Additionally, it is important to ensure that patients have a confirmed diagnosis of SSc based on established criteria according to the most recent American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) criteria [18], to ensure the study population is representative of the intended target patient population. Future studies could also examine ulceration in patient populations with earlier forms of SSc.

Exclusion Criteria: This should include individuals with severe comorbid conditions that could affect ulcer healing including clinically significant peripheral vascular diseases (including diabetes mellitus) or clinically significant atherosclerotic disease, or those receiving therapies that might confound the study results. Patients with active infection at the ulcer site should usually also be excluded to avoid compromising the

interpretation of treatment efficacy, but can be considered again for inclusion only after resolution of the active infection. Furthermore, those that develop infection during the study should be considered as a complication, and the rates of infection developed during the study must be reported in the study results.

3.1.3. Standardized outcome measures

Outcome measures in DU trials have traditionally focused on ulcer healing, typically defined as complete re-epithelialization without discharge or infection [6–8]. While this remains an essential endpoint, it may not be feasible to follow up the participants until healing occurs or fully capture the clinical and patient-relevant effects of an intervention.

In the context of DU trials, primary and secondary outcomes should be selected to provide a comprehensive assessment of treatment effects, including both clinical and patient-reported outcomes.

Primary Outcomes: The primary outcome measure in DU studies should consistently be the proportion of patients achieving complete ulcer healing within a specified timeframe or 50% improvement in cardinal ulcer and improvement in function or pain by HIDSS-DU [19]. The definition of "healing" must be clearly articulated and uniformly applied across studies, potentially defined as 'complete re-epithelialization sustained for at least two weeks without signs of infection'[6–8]. This outcome measure provides a clear and objective endpoint that can be easily assessed by clinical investigators.

However, it is important to recognize that complete ulcer healing may not be achievable in all patients, particularly those with severe or chronic DUs. In such cases, alternative primary outcomes, such as 50% improvement in cardinal ulcer or the improvement in ulcer-related symptoms as measured by the HIDSS-DU [19], may be more appropriate in line with the most recent FDA guidance document [20]. Additionally, the time to ulcer healing should be considered as a key secondary outcome, as it provides valuable information on the speed of the therapeutic response.

Secondary Outcomes: Secondary outcome measures should provide a more comprehensive assessment of treatment efficacy, including:

- **Reduction in Ulcer Size or Depth**: Tracking changes in ulcer size or depth can offer insights into the partial efficacy of an intervention. This measure is particularly important for assessing the effects of therapies that may not lead to complete healing but can still provide significant clinical benefits by reducing the overall burden of the ulcer.
- **Time to Healing**: Measuring the time required for ulcer healing helps differentiate between treatments with similar efficacy but different speeds of action. This outcome is particularly relevant as patients may benefit from faster-acting therapies that can reduce the duration of pain and disability associated with DUs and this might eventually influence the physician's choice of the appropriate treatment
- **Pain Relief**: Pain is a significant symptom of DUs and should be assessed using validated scales such as the Visual Analog Scale (VAS) or Numeric Rating Scale (NRS), reported as a change from baseline [21,22]. Pain relief is a critical component of DU management, as pain can significantly impair patients' quality of life and functional capacity [23].
- **Impact on Physical Function**: Functional outcomes should be assessed using tools like the Scleroderma Health Assessment Questionnaire (SHAQ). However, to specifically evaluate the effects of DUs on hand-related activities the Cochin Hand Function Scale (CHFS) [24] should be included, and if DUs of the toes are also included in the trial, foot specific outcomes measure (incorporating foot functional status), such as the Manchester Foot Pain and Disability Index [25], are recommended. Given that DUs often occur on the fingers, impairing hand function, this outcome measure is particularly relevant for assessing the real-world impact of the intervention.
- **Quality of Life Assessments**: Instrument selection should be carefully considered and clearly reported based on the study aims (multiple instruments may be needed). Disease-specific instruments may be appropriate (e.g., the Scleroderma Quality of Life Questionnaire (SScQoL]); whereas, others may which provide broader insight into QoL (and thereby allowing for comparisons with other diseases) (e.g., SF-36 or EQ5D) [26].

Patient-Reported Outcomes (PROs): PROs are essential for capturing the full impact of DUs on patients' daily lives, including pain, functional impairment, and emotional burden. Incorporating PROs into RCTs provides valuable insights into how patients perceive the benefits and drawbacks of treatments, supporting a more patient-centred approach to care. PROs can also help identify areas where current treatments may be falling short, guiding future research and clinical practice improvements [27].

In addition to these measures, exploratory outcomes, such as biomarkers of vascular function or advanced imaging techniques, could be included to investigate the mechanistic effects of interventions and guide future research. For example, the use of nailfold capillaroscopy or laser Doppler imaging could provide novel insights into the effects of therapies on microvascular structure and function, which is a key factor in the pathogenesis of SSc-DUs [28].

3.1.4. Reporting of background and concomitant therapies

The effectiveness of a new intervention in interventional trials can be significantly influenced by the presence (or absence) of background and concomitant therapies that patients receive. Variability in these treatments can introduce confounding factors that obscure the true effects of the intervention.

In SSc, patients often receive a variety of systemic therapies aimed at managing the underlying vasculopathy and fibrosis that characterize the disease [29]. These therapies may include vasodilator/vasoactive, immunosuppressive, and other disease-modifying agents. The effects of these background therapies on DU outcomes can be substantial, and failure to account for them may lead to misleading conclusions about the efficacy of the intervention under study.

Recommendation: Detailed reporting of all background and concomitant therapies is crucial, including the types, doses, and duration of these treatments. The impact of these therapies on DU healing must be carefully considered, and any changes in therapy during the study should be carefully documented and analysed. Moreover, in controlled studies, efforts should be made to match the study populations on their background therapies so to improve the possibility of correctly evaluating the efficacy of the trial agent.

3.1.5. Reporting on local wound management protocols

Local wound care is a critical component of DU management, yet practices can vary widely between centres, leading to inconsistencies in trial outcomes [30,31]. The choice of debridement methods, topical therapies, and dressings can all influence ulcer healing rates and the patient experience [32].

The variability in local wound management practices can introduce significant confounding factors into interventional studies, making it difficult to attribute observed effects to the intervention under study and generalisability of findings. For example, differences in the frequency or method of debridement across study sites could lead to variability in ulcer healing rates, independent of the effects of the study medication.

Recommendation: interventional studies should include a standardized protocol for local wound management, ensuring uniform care across study sites. This protocol should detail:

- **Debridement**: The method and frequency of debridement, including pain management strategies during the procedure, should be specified. In particular, whether sharp or mechanical debridement is used,

or other forms (e.g., enzymatic), and if methods are used in combination [30].

- **Topical Therapies**: The use of various potential topical (local) agents, such as antibiotic or antiseptic therapy, should be standardized. The type, concentration, and frequency of application should be consistent across study sites. The choice of topical therapy can influence both the rate of ulcer healing and the risk of complications such as infection, making it a critical component of the study protocol [32].
- **Dressing Types**: The choice of dressing, whether hydrogel or hydrocolloid, foam, alginate or any other type of dressings, should be standardized. In particular, the clinician requires a dedicated study dressing regime protocol to be applied throughout the trail for each of the healing stages (e.g., based on the ulcer wound characteristics such as the level of exudate present). Any changes during the study should be clearly documented. Dressings play a key role in maintaining an optimal healing environment, and variations in dressing type can lead to differences in moisture balance, temperature regulation, and protection from external contaminants [32].

Follow-Up Care: The protocol should outline the frequency of wound assessments and interventions in response to complications such as infection or delayed healing. Regular follow-up is essential for monitoring the progress of ulcer healing and identifying any adverse events that may arise during the study, and study rescue (escape) mechanisms (e.g., need for surgical intervention or intravenous vasodilatory therapy) should also be considered in the study design.

By standardizing local wound care protocols, interventional studies can reduce variability in treatment practices, ensuring that differences in outcomes are attributable to the intervention rather than inconsistencies in basic wound care. This standardization is particularly important in multicentre trials, where differences in local wound care practices across sites can introduce significant variability into the study results.

3.1.6. Timing and frequency of assessments

DUs often heal slowly, and therefore assessments that are performed too early may not capture the intervention's full effects, while infrequent assessments may miss important changes. The timing of assessments in interventional studies for DUs is critical for accurately capturing the effects of the intervention on DU healing. For example, the primary outcome for the two international, randomized, double-blind, placebo-controlled trials (DUAL 1 & 2) of macitentan was the cumulative number of new DUs from baseline to week 16 [33]. Whereas the (SEDUCE) randomized, placebo-controlled study of sildenafil including the number of new DUs at weeks 4, 8 and 12 (the primary end time to healing for each DU) [34]. Therefore, if assessments are conducted too early, they may not reflect the full impact of the treatment, particularly for therapies that require longer periods to achieve their maximum effect. Conversely, if assessments are too infrequent, important changes in ulcer status may be missed, leading to an incomplete understanding of the treatment's efficacy. Timing therefore should reflect those studies aiming to assess DU healing and/or DU prevention.

- **Recommendation**: studies should specify the timing of assessments, including the duration of the evaluation period and intervals between assessments. Multiple assessments over an extended period are recommended to accurately capture the healing process (and ideally, performed by the same assessor due to poor inter-rater reliability) [35,36]. For instance, assessments could be scheduled at baseline, every two weeks during the active treatment phase, and monthly during a follow-up phase. This schedule allows for the monitoring of both the short-term and long-term effects of the intervention.

Longitudinal Monitoring for Recurrence: Long-term follow-up, extending at least six months post-treatment, is essential for assessing the durability of ulcer healing and the potential for recurrence. Longitudinal monitoring can provide valuable insights into the long-term benefits of the intervention and help identify factors associated with ulcer recurrence.

3.1.7. Consideration of seasonal and environmental factors

Environmental factors, such as temperature and humidity, likely affect DU healing in SSc patients [37]. Cold temperatures exacerbate vasoconstriction, while high humidity levels may theoretically increase infection risk. Also professional exposure should be recorded as this should be include among the potential exposure factors.

The impact of environmental factors on DU healing is an important consideration in interventional studies (although little studied to date), particularly in studies conducted across multiple geographic regions and/or during different seasons. For example, patients enrolled in a trial during the winter months may potentially experience slower ulcer healing due to the exacerbation of Raynaud's phenomenon, while those enrolled during the summer may benefit from warmer temperatures that promote vasodilation and improved blood flow to the affected areas. Behavioural changes (e.g., cold avoidance) have yet to be specifically explored concerning DUs in patients with SSc. Moreover, smoking habit should be recorded or mentioned among the exclusion criteria as smoking might play a role in impairing ulcer healing [38].

Recommendation: RCTs should account for seasonal and environmental factors in their design and analysis. This could involve stratifying patients based on the season during which the trial is conducted and/or adjusting for these factors statistically. Geographic variation in climate should also be considered, particularly in multicentre trials conducted across different regions. For example, researchers could conduct subgroup analyses to compare outcomes in patients enrolled during different seasons or in different climates, providing a more nuanced understanding of the impact of environmental factors on DU healing [37].

By accounting for environmental factors, interventional studies can improve the generalizability of their findings and ensure that results are applicable to a broader 'real-world' patient population. This approach also highlights the importance of personalized medicine in SSc, where individual patient characteristics, including their environment, must be considered when developing and implementing treatment strategies.

4. Discussion

Standardizing the reporting of DUs in SSc interventional studies is essential for improving the reliability and applicability of research findings and to inform clinical practice. The recommendations outlined in this paper provide a framework for consistent reporting, enhancing the comparability of trial results and facilitating the development of effective treatments for SSc-DUs.

First of all, to support accurate lesion classification, we want to highlight the distinction between pitting scars and DUs. Pitting scars are pinhole-sized, concave depressions with hyperkeratosis, reflecting prior microinfarcts without active tissue loss [16]. In contrast, DUs represent an active loss of epidermal covering with a break of the basement membrane, exposing fibrin, granulation tissue, visible vessels or, upon debridement, deeper structures. Emphasizing this difference is essential to avoid misclassification and to ensure consistency across DU interventional studies.

The management of DUs remains challenging due to variability in clinical practices and a lack of standardized treatment protocols. This variability is reflected in inconsistent reporting across interventional studies, complicating the ability to compare study outcomes and draw meaningful conclusions about treatment efficacy. Indeed, in the most recent EULAR recommendations on the treatment of systemic sclerosis only three classes of systemic drugs have been included [39]. By adopting standardized definitions, inclusion criteria, outcome measures,

and reporting protocols, researchers can ensure that their studies contribute meaningfully to the evidence base on DU management in SSc [36]. Researchers should also be mindful of the comprehensive guidance issued by the FDA on the 'Guidance for Industry Chronic Cutaneous Ulcer and Burn Wounds — Developing Products for Treatment' [40]; which strongly align with our proposed recommendations for SSc-DU reporting.

Another area of improvement could be the use of digital tools that could help to measure DU by analysing clinical pictures (e.g. Wound Genius® or Imito AG®) or smartphone app (e.g. SALVE: Scleroderma App for Lesion Verification) [41] that could be more reliable to assess the evolution of DUs over time. Other non-invasive assessment techniques of DU perfusion (e.g., by laser-based imaging), objective measurements(e.g., ultrasound) of size, and others, should also continue to be explored (and validated) for consideration for inclusion in future clinical trials [10]. Out points to consider directly align with the recent WSF treatment recommendations for SSc-DUs [11,12]. Indeed, the treatment recommendations recently published identified key unmet needs in DU clinical trials: inconsistent DU definitions, heterogeneous inclusion criteria, variable outcomes, and limited reporting of concomitant therapies. Our framework addresses exactly these gaps by providing standardized guidance for study design and reporting, thereby supporting more reliable and comparable evidence in future DU trials.

Future studies should focus on deploying and refining these standards and exploring innovative approaches to the assessment and management of DUs. This includes developing novel outcome measures that capture the full impact of DUs on patients, investigating biomarkers and imaging techniques to assess (and predict) ulcer healing, and evaluating patient-centred care strategies. Additionally, multicentre trials should consider the influence of environmental (including behavioural) factors and geographic variation on DU outcomes, ensuring that findings are broadly applicable. An important area of future research is the development and validation of PROs that reflect the real-world impact of DUs on patients' lives [27]. PROs provide insights into aspects of health and well-being that are not captured by traditional clinical measures, such as the emotional and social effects of living with chronic ulcers [21]. Incorporating PROs into interventional studies will ensure that the outcomes assessed are relevant to patients and will support the development of therapies that address the multifactored broad-ranging impact and severity of DUs on the patient experience, including the activities of daily living.

5. Conclusion

DUs are a significant and challenging complication of SSc, profoundly affecting patients' quality of life and functional ability. The variability in how DUs are presently reported in interventional studies hampers the ability to compare and apply research findings to clinical practice, thereby reducing the discriminatory ability to detect meaningful treatment effects. By standardizing the reporting of DUs in clinical trials, researchers can improve the quality of evidence and ultimately enhance the care of patients with SSc-DU. These recommendations provided from the WSF ad hoc committee in this paper offer a pivotal roadmap and framework for achieving this goal, emphasizing the need for consistent definitions, outcome measures, and reporting protocols that reflect both clinical and patient-reported outcomes. Future research should focus on refining these standards and exploring innovative approaches to the assessment (including incorporation of the patient perspective) and management of DUs in SSc.

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Data availability

The data underlying this article will be shared upon reasonable request to the corresponding author.

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