



TITLE: Optimal Care of Chronic, Non-Healing, Lower Extremity Wounds: A Review of Clinical Evidence and Guidelines

DATE: 17 December 2013

CONTEXT AND POLICY ISSUES

Chronic wounds are those which do not progress through the healing process in a timely and predicted manner.¹ Chronic leg and foot ulcers occur in many adults with vascular disease or diabetes.² These ulcers last, on average, 12 to 13 months, are recurring in up to 60%³ to 70% of patients, and can lead to loss of function, poor quality of life, and ill-health.² As the population ages, chronic wounds are becoming more prevalent, more difficult to treat,⁴ and care for chronic wounds has been reported to cost 2% to 3% percent of the healthcare budgets in developed countries.²

The goal of chronic wound management is to facilitate healing,¹ which may include optimal moisture balance,¹ restoration of blood flow to the wound,³ compression therapy,^{5,6} prevention of infection,⁵ and debridement.⁴⁻⁶ This variability of treatment options and treatment needs for chronic wounds requires a multidisciplinary team. This team collaboration can allow for earlier diagnosis, better management, and may reduce the cost of treating wounds.⁴ Although nursing and non-specialist care are parts of an optimal multidisciplinary team, there is the need for specialist consultation and specialist-lead advanced care both as a part of and outside of the multidisciplinary teams as well. It is sometimes unclear when the advanced care is needed, at what point in the process specialists should be involved in the care pathway, and which patients should be referred for specialist care, especially with respect to vascular and plastic surgeons.

The objective of this review is to summarize the clinical evidence regarding the need for specialist-lead advanced care, indications for referral to specialist care, and the guidelines regarding the multidisciplinary management, including specialist care, for chronic, non-healing, non-pressure-related lower extremity wounds

RESEARCH QUESTIONS

1. What is the clinical evidence regarding the need for specialist-led advanced care for chronic, non-healing, non-pressure related lower extremity wounds?

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2. What are the evidence-based guidelines regarding the multidisciplinary management of chronic, non-healing, non-pressure related lower extremity wounds?

KEY FINDINGS

Evidence from one uncontrolled non-randomized study suggests that specialist-lead advanced care for chronic, non-healing, non-pressure related wounds may result in positive outcomes such as healing and that mixed arterial and venous ulcerations are a complex wound presentation for which there is little consensus regarding optimal management. Evidence regarding specialist care compared to healing in the absence of specialist-led advanced care is lacking. Evidence-based guidelines highlight the need for multidisciplinary care that includes participation from at-home caregivers and the patient. Indications for specialist-lead advanced care include evidence of ischemia, inability to comply with wound-care regimens, suspected malignancy, and peripheral arterial disease.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including OVID Medline, PubMed, The Cochrane Library (2013, November), University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, and guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1 2009 and Nov 19 2013.

Selection Criteria and Methods

One reviewer screened the titles and abstracts of the retrieved publications and evaluated the full-text publications for the final article selection, according to selection criteria presented in Table 1.

Table 1: Selection Criteria	
Population	Adult patients with compromised lower-extremity (below the knee) chronic wounds that are healing poorly (pressure ulcers were considered out of scope).
Intervention	Consultation with a specialist (e.g. a vascular or plastic surgeon)
Comparator	None/any
Outcomes	Q1- evidence for the need of specialist treatment to ensure optimal wound care, evidence that specialist treatment results in better patient outcomes or better wound management at a certain level of wound complication Q2 – optimal multidisciplinary management, optimal time for specialist involvement, tools, standards to indicate when advanced care is needed
Study Designs	HTA, SR, MA, RCT, NRS, evidence-based guidelines

HTA = health technology assessment; MA = meta-analysis; NRS = non-randomized study; RCT = randomized controlled trial; SR = systematic review

Exclusion Criteria

Studies were excluded if they did not meet the inclusion criteria or were published prior to 2009. Evidence examining pressure ulcers was beyond the scope of this review.

Critical Appraisal of Individual Studies

The critical appraisal of the individual studies was assessed according to study type. The non-randomized study was assessed using the Downs and Black checklist⁷ and the evidence-based guidelines were assessed using the Appraisal of Guidelines for Research Evaluation II tool.⁸ One reviewer performed critical appraisal and a numeric score was not calculated for each study. Instead, the strengths and weaknesses of the individual studies were summarized and described.

SUMMARY OF EVIDENCE

Quantity of Research Available

A total of 239 citations were identified in the database literature search, 231 of which were excluded upon screening titles and abstracts. Eight potentially-relevant articles were retrieved for full-text review and an additional three citations were retrieved from the grey literature. Of the 11 potentially relevant reports, six did not meet the inclusion criteria and were excluded. As a result, five publications, four evidence-based guidelines⁹⁻¹² and one non-randomized cohort study,¹³ were included in this review. Appendix 1 describes the PRISMA flow chart of the included studies. Additional references that may be of interest, including clinical practice guidelines of insufficient rigour to be considered evidence-based, are included in Appendix 2.

Summary of Study Characteristics

What is the clinical evidence regarding the need for specialist-lead advanced care for chronic, non-healing, lower extremity wounds?

One relevant non-randomized cohort study was identified with respect to the evidence regarding the need for specialist-lead advanced care for chronic, non-healing, lower extremity wounds. This study included a population of 152 patients with 177 lower leg ulcers (between the knee and the malleolus) who were referred to a specialist wound clinic. The majority (69%) of patients were women. Fifty-three patients had ulcers that had been present for at least one year and 99 had ulcers that had been present for less than a year. Data was available for at least three months of follow up for 122 ulcers and the median follow-up was 18 months.

Patients received duplex ultrasound scanning upon evaluation at the clinic and received various treatments including compression bandages, sclerotherapy, and revascularization. The main outcomes reported were risk factors for non-healing ulcers, healing time, differences in outcomes between those with long- (≥ 1 year) or shorter-term (< 1 year) wounds, and venous duplex measurements.

Further details regarding the characteristics of the included NRS are available in Appendix 3, Table 2.

What are the evidence-based guidelines regarding the multidisciplinary management of chronic, non-healing, lower extremity wounds?

The four evidence-based guidelines included in this review were developed in Canada,⁹ the United States,¹⁰ Scotland,¹¹ and Ireland.¹² Two were developed to guide the assessment and management of diabetic foot ulcers,^{9,10} one to guide the management and assessment of venous leg ulcers,¹¹ and one to guide the management of all challenging wounds, with the exception of burns and malignant wounds.¹²

Three of the guidelines⁹⁻¹¹ were updates of previous guidelines, all four guidelines⁹⁻¹² were based on systematic reviews of the literature and the evidence and strength of recommendations were graded, and all four were developed by a multidisciplinary panel of wound care and patient care specialists. One of the guidelines – the guideline developed by the Scottish Intercollegiate Guidelines Network (SIGN) – included input from patients.¹¹

Further details regarding the characteristics of the included guidelines are available in Appendix 3, Table 3.

Summary of Critical Appraisal

What is the clinical evidence regarding the need for specialist-lead advanced care for chronic, non-healing, lower extremity wounds?

The key strengths of the non-randomized cohort study¹³ included good reporting of patient characteristics, key confounders, key outcomes, and reporting of actual probability values when they were calculated. The patients in the study likely received a similar standard of care as non-study patients attending a wound clinic would and the statistical test – the Fisher's t-test – used was appropriate for the relatively small sample size. The key limitations of the study stemmed from the study design. There was no control group included in the study – therefore there is no way to know if patients who were not referred to specialist care had similar or different healing rates compared to those included in the study. There was no blinding of study assessors, there was limited information on patients lost to follow-up, and there was no description of the patients for whom 3-month follow-up data was not available. It was also unclear if the study had the power to detect a clinically important effect where the probability value for a difference being due to chance was <5%. It is possible that the patients participating in the study had wounds that were considered more complicated or that had been non-healing for a longer period of time than the average patient with a chronic wound, as they had been referred to specialist care. Further detail regarding the critical appraisal is included in Appendix 4, Table 4.

What are the evidence-based guidelines regarding the multidisciplinary management of chronic, non-healing, lower extremity wounds?

Overall, the four evidence-based guidelines included in the review⁹⁻¹² had similar strengths. All were clear with respect to their scope and purpose, used systematic methods to search for evidence, used a grading scheme to evaluate the level of evidence, included individuals from relevant professional groups (e.g. wound care nurses, physical therapists, chiropodiatrists, and vascular surgeons), they were reviewed by external experts, and auditing criteria were provided. All but one guideline¹² provided guidance regarding the implementation of the recommendations and provided a procedure for updating the guideline.

With respect to limitations, all of the guidelines lacked clarity regarding whether the views of the funding body influenced the content of the guideline. The Canadian guideline lacked clarity with respect to the methods for formulating recommendations, whether side effects and risks were taken into account when formulating recommendations, and the potential resource implications of implementation,⁹ the American guideline only partially described the criteria for selecting evidence,¹⁰ and the Irish guideline lacked information regarding implementation of the guideline (both in methods and resource implications) as well as potential conflicts of interest of the guideline development panel.¹² The SIGN guideline¹¹ was the only one to include the views and preferences of the target population and overall had the fewest limitations.

Further details regarding the critical appraisal are included in Appendix 4, Table 5.

Summary of Findings

What is the clinical evidence regarding the need for specialist-lead advanced care for chronic, non-healing, lower extremity wounds?

The most common risk factor for leg ulcers that was present in the patients referred to specialized wound care in the included cohort study¹³ was a history of deep vein thrombosis (DVT). Twenty-five percent of patients had a history of DVT and this was more common in patients for whom the ulcer had been present for longer than one year (40% vs. 17%, $P = 0.0032$). The majority of patients had abnormal venous duplex results, the majority (53%) of whom had isolated superficial incompetence. Widespread deep venous reflux significantly more common in patients with ulcers that had been present ≥ 1 year (34% vs. 18%, $P = 0.0442$).

With respect to healing, 48% of ulcers healed within the study period, with a median healing time of 361 days, and 54% of ulcers that were treated with superficial venous ablation healed ($P = 0.307$ versus patients who did not receive ablation). For patients with arterial disease, 26 of the 32 ulcerated limbs underwent revascularization and the healing rate was 27%. Though 50% of the ulcerated limbs that did not undergo revascularization in patients with arterial disease healed, this represented a very small number of limbs ($n = 6$). Twenty-one percent of limbs with long-term ulceration underwent superficial venous ablation. Further detail is included in Appendix 5, Table 6.

What are the evidence-based guidelines regarding the multidisciplinary management of chronic, non-healing, lower extremity wounds?

Diabetic Foot Infections and Ulcers:

Three of the included guidelines^{9,10,12} made recommendations regarding optimal timing for specialist involvement and multidisciplinary management of diabetic foot infections and ulcers.

The Canadian guideline⁹ recommended that a multidisciplinary, inter-agency team approach to wound management should be established and supported, that the team should monitor and address quality improvement and management of diabetic foot ulcers, and that the care should follow a client-centred approach (Level IV). Furthermore, they recommended that a formal process for the referral of patients with diabetic foot ulcers to specialist care should be developed (Level IV). They outlined the key members that should be included in the multidisciplinary teams, this included endocrinologists, vascular surgeons, and plastic surgeons. The full list is detailed in Appendix 5, Table 7.

The American guideline¹⁰ also recommended a well-coordinated, multidisciplinary effort (moderate evidence, strong recommendation). Further recommendations included:

- patients may benefit from consultation with an infectious disease or clinical microbiology specialist and a surgeon with experience and interest in managing diabetic foot infections (low evidence, strong recommendation)
- a vascular surgeon should be consulted regarding revascularization if there is imaging or clinical evidence of significant ischemia (moderate evidence, strong recommendation)
- clinicians working in communities without specialist care should consider systems such as telemedicine in order to consult with experts when expert management is needed (low evidence, strong recommendation)
- all patients with severe infections, some patients with moderate infections but complications such as lack of home support, and patients unable to comply with wound care regimens should be hospitalized (low evidence, strong recommendation)
- patients who do not have the risk factors but whose wounds are not improving should be hospitalized (low evidence, strong recommendation).

The Irish guideline¹² also made a recommendation regarding hospitalization. They recommended that ulcers deeper than subcutaneous tissues should be treated intensively and that hospitalization must be considered (level of evidence not reported).

Further details regarding the evidence grading and levels of evidence is included in Appendix 3, Table 3 and further details regarding the specific recommendations are included in Appendix 5, Table 7.

Venous Leg Ulcers

Two of the included guidelines made recommendations regarding optimal timing for specialist involvement and multidisciplinary management of venous leg ulcers.^{11,12}

The Irish guideline recommended that if there was any doubt regarding the etiology of the ulcer, the patient should be referred to specialist care (level 3) and that for ulcers that have been open without signs of healing for three months or that do not demonstrate treatment response for six weeks should be referred to a specialist for biopsy (level 3).¹²

Similar to the Irish guideline, the Scottish guideline also recommended that non-healing or atypical wounds should be referred for biopsy (Grade D).¹¹ The guideline¹¹ outlined the following criteria for specialist referral:

- suspected malignancy
- peripheral arterial disease (with ABPI <0.8)
- diabetes mellitus
- rheumatoid arthritis or vasculitis
- atypical distribution of leg ulcers
- suspected contact dermatitis or dermatitis that is resistant to topical steroids
- non-healing ulcers. (Grade D)

The timeframe for specialist referral was described as if the presentation of the wound is atypical, or if there is either deterioration or failure to heal after 12 weeks of active therapy.

Specialist leg ulcer clinics were recommended as optimal treatment in the community (Grade B).

Arterial Ulcers

One of the included guidelines made recommendations regarding optimal time for specialist involvement for patients with arterial ulcers.¹² This recommendation was that patients with rest pain or gangrene associated with an arterial ulcer should be immediately referred to a vascular surgeon. This was considered a Level 1 recommendation.

The Irish guideline also included examples of wound assessment forms for all types of ulcers for both documenting wound history and using the history in order to determine appropriateness for expert care. This included assessment forms from the various Irish hospitals, as well as the Braden Scale and a wound audit tool. These can be accessed by consulting the full guideline.¹²

Limitations

One of the primary limitations is the lack of clinical evidence regarding the need for specialist treatment to ensure optimal wound care and that specialist treatment results in better wound management or patient outcomes. The included non-randomized study examined patients who had all been referred to specialized treatment for wounds between the knee and ankle. There was no control group of patients who received standard care and it is not known if the study is generalizable to foot wounds. It is also possible that the patients who were included in the study had more severe wounds than the average complicated wound, as entry into the study required failure to heal for longer than six months and one of the included guidelines suggests seeking expert care prior to that timeframe. Furthermore, this study had a small sample size that was primarily comprised of women.

The included guidelines are evidence-based and based on rigorous methods, however, there are few recommendations on specific thresholds, indicators, or test values that indicate the need for specialist intervention. Furthermore, the majority of recommendations were based on limited evidence or were lower-grade recommendations, suggesting that they were likely based primarily on expert opinion due to the lack of high quality evidence.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

The authors of the included non-randomized study¹³ concluded that there was a trend toward greater healing in patients who were referred to a specialist centre and who underwent venous ablation versus those who did not undergo ablation, though the difference was not statistically significant, that there was no consensus regarding optimal management of mixed arterial and venous ulceration and determined these to be a particularly difficult clinical presentations, and that a history of DVT and an ulceration that has been present ≥ 1 year should not be reasons not to refer for surgical intervention, as they were not associated with lower healing rates in this study. They also reinforced the need for vascular assessment and venous imaging in the management of leg ulcers. This finding is in line with evidence that revascularization may be an important treatment option for patients with non-healing leg wounds and thus require specialist care.⁶

Overall, guidelines from Canada,⁹ the United States,¹⁰ Scotland,¹¹ and Ireland¹² highlight the need for multidisciplinary management of diabetic foot ulcers, venous leg ulcers, and arterial leg

ulcers. Recommendations regarding immediate need for specialist referral included doubt regarding etiology,¹² suspected malignancy,¹¹ evidence of ischemia,¹⁰ and wounds with atypical distribution.¹¹ Referral for biopsy is recommended for venous wounds without signs of healing for three months, or that do not demonstrate treatment response for six weeks in one guideline,¹² and if the wound is atypical, or there is deterioration or failure to heal after 12 weeks of active therapy in the SIGN guideline.¹¹

Limited information was identified regarding the clinical evidence pertaining to specialist-lead advanced care for chronic, non-healing, lower extremity wounds, however the need for venous imaging, vascular assessment, and biopsy were identified and these require specialist consultation. Although guidelines recommend specialist treatment for many patients with chronic wounds, and that specialist care can promote evidence-based healing practices, such as venous imaging and vascular assessment,² there is some evidence that access to such care can be difficult.² Furthermore, multidisciplinary care and both family and patient integration into care plans is important;^{3,9} without co-ordination of services, optimal treatment may not occur.

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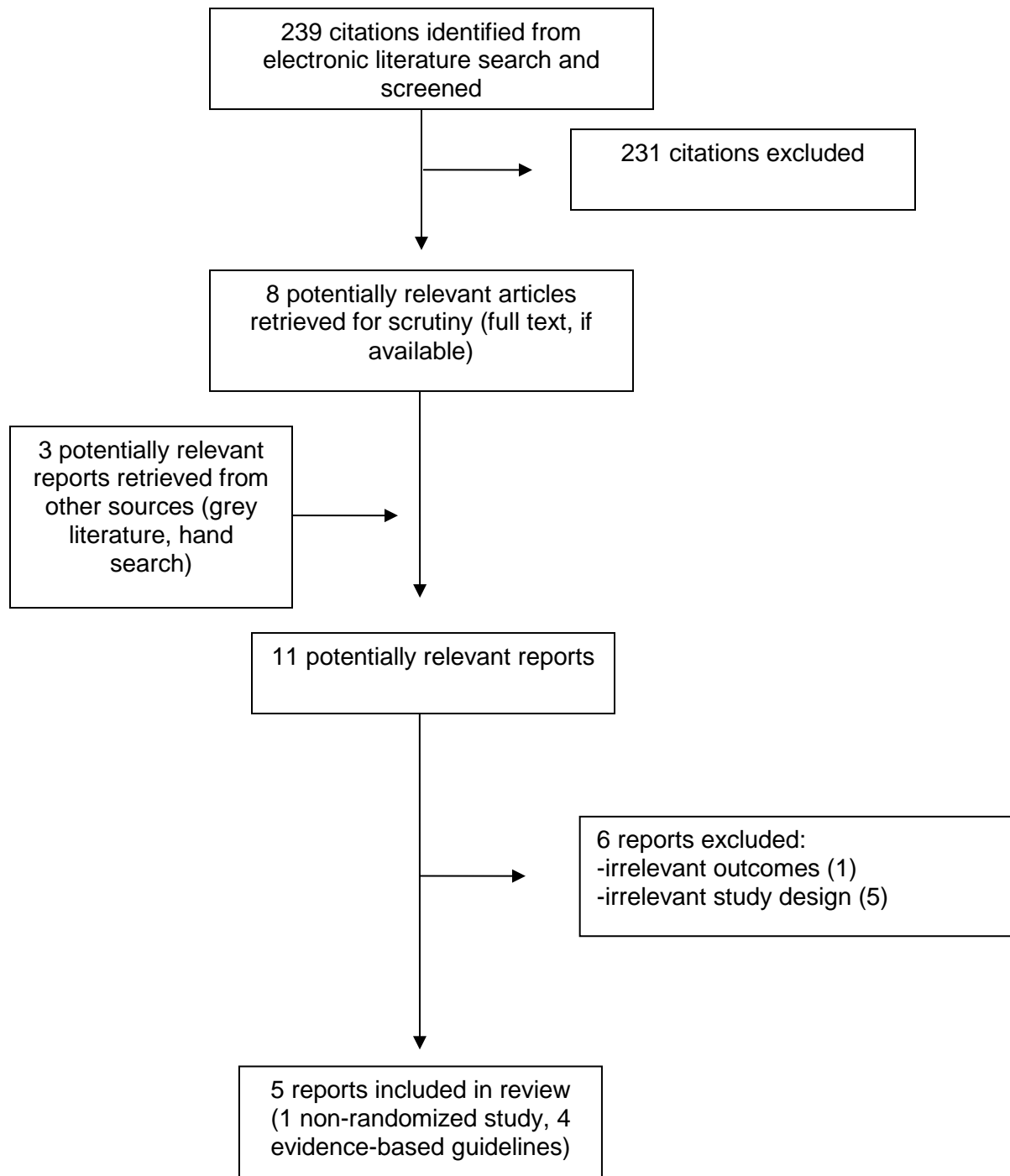
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APPENDIX 1: Selection of Included Studies



APPENDIX 2: References of potential interest

Guidelines of Low Methodological Rigour, Best Practice Statements

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Clinical Study – Implementation of Guidelines and Pathways

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APPENDIX 3: Summary of Study Characteristics

Table 2: Characteristics of the Included Non-Randomized Study		
First Author, Year, Type of Study	Objective, Patient Population	Outcomes Measured
Neequaye, 2009 ¹³ Non-Randomized Case Series	<p>Examine the baseline characteristics and outcomes of a cohort of patients who were referred for vascular surgical assessment following failure management in a community and nurse-led specialist clinic setting.</p> <p>Consecutive patients who had active ulcerations above the malleolus but below the knee and were referred to a dermatology leg ulcer clinic between January 2002 and December 2005. Most common reasons for referral were failure to heal within 6 months and concomitant arterial disease. 152 patients were examined. ≥3-month follow-up data was available for 122 ulcers, median follow-up was 18 months.</p>	<ul style="list-style-type: none"> • Risk factors for leg ulcerations • Differences between outcomes for patients with long-term ulcerations and short term ulcerations • Venous duplex measurements • Type of therapy • Healing time

Table 3: Characteristics of the Included Evidence-Based Guidelines				
Objectives		Methods		
Intended Users/Target Population	Scope, Purpose, Country of Origin	Evidence Collection, Selection, and Synthesis	Evidence Quality and Rating of Strength of Recommendations	Formulation of Recommendations and Validation
<i>IABG Guideline, 2013⁹</i>				
Nursing and other wound team members who provide care in both inpatient and outpatient settings.	<p>Best management and assessment of patients with diabetic foot ulcers.</p> <p>Canada</p>	Systematic review of the literature, grading of level of evidence	<p>Evidence graded using an adapted version of SIGN levels of evidence.</p> <p>Ia: Evidence obtained from meta-analysis or systematic reviews of randomized controlled trials</p> <p>Ib: Evidence obtained from at least one randomized controlled trial.</p> <p>Ila: Evidence obtained from at least one well-designed controlled study without randomization.</p> <p>Ilb: Evidence obtained from at least one other type of well-designed quasi- experimental</p>	Multidisciplinary panel reviewed a previous guideline, systematically searched the literature to identify new information, verify appropriateness of the previous recommendations, updated where needed. No process outlined regarding how the formulation of recommendations occurred, but external panel also reviewed the drafts.

Table 3: Characteristics of the Included Evidence-Based Guidelines

Objectives		Methods		
Intended Users/Target Population	Scope, Purpose, Country of Origin	Evidence Collection, Selection, and Synthesis	Evidence Quality and Rating of Strength of Recommendations	Formulation of Recommendations and Validation
			study, without randomization III: Evidence obtained from well-designed non-experimental descriptive studies, such as comparative studies, correlation studies and case studies. IV: Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.	
<i>IDSA Guideline, 2012¹⁰</i>				
	Outline best practice for the management for diabetic foot infections. United States	Systematic review of the literature, panel used GRADE to assess literature, panel used a process to systematically weigh the evidence, used consensus development based on evidence.	Strong recommendation, high-quality evidence: Desirable effects clearly outweigh undesirable effects, or vice versa. <ul style="list-style-type: none"> Consistent evidence from well-performed RCTs or exceptionally strong evidence from unbiased observational studies Strong recommendation, moderate-quality evidence: Desirable effects clearly outweigh undesirable effects, or vice versa. <ul style="list-style-type: none"> Evidence from RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from unbiased observational studies. Strong recommendation, low-quality evidence: Desirable effects clearly outweigh undesirable effects, or vice versa. <ul style="list-style-type: none"> Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws or indirect 	Multidisciplinary, international panel including specialists in infectious diseases, primary care/general internal medicine, hospital medicine, wound care, podiatry, and orthopedic surgery

Table 3: Characteristics of the Included Evidence-Based Guidelines

Objectives		Methods		
Intended Users/Target Population	Scope, Purpose, Country of Origin	Evidence Collection, Selection, and Synthesis	Evidence Quality and Rating of Strength of Recommendations	Formulation of Recommendations and Validation
			<p>evidence</p> <p>Strong recommendation, very low-quality evidence: Desirable effects clearly outweigh undesirable effects, or vice versa.</p> <ul style="list-style-type: none"> Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence. <p>Weak recommendation, high-quality evidence: Desirable effects closely balanced with undesirable effects.</p> <ul style="list-style-type: none"> Consistent evidence from well performed RCTs or exceptionally strong evidence from unbiased observational studies. <p>Weak recommendation, moderate-quality evidence: Desirable effects closely balanced with undesirable effects.</p> <ul style="list-style-type: none"> Evidence from RCTs with important limitations (inconsistent results, methodological flaws, indirect, or imprecise) or exceptionally strong evidence from unbiased observational studies. <p>Weak recommendation, low-quality evidence: Uncertainty in the estimates of desirable effects, harms, and burden; desirable effects, harms, and burden may be closely balanced.</p> <ul style="list-style-type: none"> Evidence for at least 1 critical outcome from observational studies, RCTs with serious flaws, or indirect evidence. 	

Table 3: Characteristics of the Included Evidence-Based Guidelines

Objectives		Methods		
Intended Users/Target Population	Scope, Purpose, Country of Origin	Evidence Collection, Selection, and Synthesis	Evidence Quality and Rating of Strength of Recommendations	Formulation of Recommendations and Validation
			Weak recommendation, very low quality evidence: Major uncertainty in the estimates of desirable effects, harms, and burden; desirable effects may or may not be balanced with undesirable effects or may be closely balanced. <ul style="list-style-type: none"> Evidence for at least 1 critical outcome from unsystematic clinical observations or very indirect evidence. 	
<i>SIGN Guideline, 2010¹¹</i>				
Patients, general practitioners, nursing staff, dermatologists, vascular surgeons, plastic surgeons, pharmacists, podiatrists, and physiotherapists	To provide guidance regarding the management (assessment, treatment, prevention) of venous leg ulcers. Scotland	Update of previous guideline; systematic review of literature, recommendations formulated, then internal and review cycle occurred.	<i>Levels of evidence</i> 1++: High quality meta-analyses, systematic reviews of RCTs, or RCTs with a very low risk of bias. 1+: Well conducted meta-analyses, systematic reviews, or RCTs with a low risk of bias. 1-: Meta-analyses, systematic reviews, or RCTs with a high risk of bias 2++: High quality systematic reviews of case control or cohort studies. High quality case control or cohort studies with a very low risk of confounding or bias and a high probability that the relationship is causal. 2+: Well conducted case control or cohort studies with a low risk of confounding or bias and a moderate probability that the relationship is causal. 2-: Case control or cohort studies with a high risk of confounding or bias and a significant	Panel formulated recommendations, draft was peer reviewed, then revised, editorial panel reviewed guideline, guideline developers approve document, it is then finalized.

Table 3: Characteristics of the Included Evidence-Based Guidelines

Objectives		Methods		
Intended Users/Target Population	Scope, Purpose, Country of Origin	Evidence Collection, Selection, and Synthesis	Evidence Quality and Rating of Strength of Recommendations	Formulation of Recommendations and Validation
			risk that the relationship is not causal. 3: Non-analytic studies, eg. case reports, case series. 4: Expert opinion. <i>Grades of recommendation</i> A: At least one meta-analysis, systematic review, or RCT rated as 1++, and directly applicable to the target population; or A body of evidence consisting principally of studies rated as 1+, directly applicable to the target population, and demonstrating overall consistency of results. B: A body of evidence including studies rated as 2++, directly applicable to the target population, and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 1++ or 1+. C: A body of evidence including studies rated as 2+, directly applicable to the target population and demonstrating overall consistency of results; or Extrapolated evidence from studies rated as 2++. D: Evidence level 3 or 4; or Extrapolated evidence from studies rated as 2+.	
<i>HSE Guideline, 2009¹²</i>				
All professionals in wound management.	Applies to all wounds (with the exception of	Systematic Review of literature, review of existing	<i>Levels of evidence:</i> 1: The evidence consists of results from studies of strong design for answering the	Multi-disciplinary group, existing guidelines adapted to the Irish setting.

Table 3: Characteristics of the Included Evidence-Based Guidelines

Objectives		Methods		
Intended Users/Target Population	Scope, Purpose, Country of Origin	Evidence Collection, Selection, and Synthesis	Evidence Quality and Rating of Strength of Recommendations	Formulation of Recommendations and Validation
	<p>malignant wounds, burns), focus on wounds commonly seen in clinical practice that present challenges for healthcare professionals.</p> <p>Ireland</p>	<p>guidelines using AGREE</p>	<p>question addressed.</p> <p>2: Either based on a single acceptable study, or a weak or inconsistent finding in multiple, acceptable studies.</p> <p>3: Limited scientific evidence that does not meet all the criteria of acceptable studies or absence of directly applicable studies of good quality. This includes published or unpublished, expert opinion.</p> <p><i>Levels of Recommendation:</i></p> <p>A: Strongly recommended/likely to be of benefit</p> <p>B: Recommended</p> <p>C: Recommended but not essential</p> <p>D: Not recommended</p>	<p>Recommendations drafted and reviewed by the guideline development group, then externally reviewed, re-drafted, then endorsed by national and international professional groups and organizations.</p>

AGREE = Appraisal of Guidelines for Research Evaluation; GRADE = Grades of Recommendation Assessment, Development and Evaluation; HSE = Health Service Executive; IABG = International Affairs and Best Practice Guidelines; IDSA = Infectious Disease Society of America; RCT = randomized controlled trial; SIGN = Scottish Intercollegiate Guidelines Network

APPENDIX 4: Summary of Critical Appraisal

Table 4: Critical Appraisal of the Included Non-Randomized Study¹³ based on the Downs and Black⁷ tool	
Key Strengths	Key Limitations
<p>REPORTING The main outcomes are clearly described The characteristics of the patients are clearly described The distribution of some key confounders – such as length of time the ulcer was present and key risk factors – were reported. The main findings are clearly described. When probability values are reported, the actual values are reported.</p> <p>EXTERNAL VALIDITY The care received by study participants at the specialized wound clinic is likely representative of the type of care and treatment most patients would receive at such a clinic.</p> <p>INTERNAL VALIDITY Unlikely that data dredging occurred. Statistical tests used to assess the outcomes were appropriate – Fisher’s test was used and this is especially appropriate with small sample sizes.</p>	<p>REPORTING The estimates of random variability are not consistently reported. Characteristics of patients without 3-month follow up are not described.</p> <p>EXTERNAL VALIDITY The proportion of women in the study (69%) was higher than the proportion in the population, thus the sample may not be representative of the population.</p> <p>INTERNAL VALIDITY Study subjects and outcome assessors were not blinded. No control group of patients not treated with specialized wound care was examined. There was no randomization to types of treatment received. Losses to follow-up were noted but limited detail was presented</p> <p>POWER The sample size was small and it was unclear if the study had sufficient power to detect a clinically important effect where the probability value for a difference being due to chance was <5%.</p>

Table 5: Critical Appraisal of Included Guidelines using AGREE II⁸	
Strengths	Limitations
<i>IABG Guideline, 2013⁹</i>	
<p>SCOPE AND PURPOSE The overall objectives of the guideline are specifically described – to provide evidence-based guidance for the management of diabetic foot ulcers. The health questions covered by the guideline are described – how best to manage patients with diabetic foot ulcers. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.</p> <p>STAKEHOLDER INVOLVEMENT The guideline development group includes individuals from all relevant professional groups. The target users of the guideline are clearly defined.</p>	<p>STAKEHOLDER INVOLVEMENT Does not appear that the views and preferences of the target population have been sought.</p> <p>RIGOUR OF DEVELOPEMENT The methods for formulating the recommendations are not clearly described. The health benefits, side effects, and risks have been considered in formulating the recommendations.</p> <p>APPLICABILITY The guideline does not describe facilitators and barriers to its application. The potential resource implications of applying the recommendations are not presented.</p>

Table 5: Critical Appraisal of Included Guidelines using AGREE II⁸

Strengths	Limitations
<p>RIGOUR OF DEVELOPMENT Systematic methods were used to search for evidence. The criteria for selecting the evidence are clearly described. The strengths and limitations of the body of evidence are clearly described. There is an explicit link between the recommendations and the supporting evidence. A procedure for updating the guideline is provided. The guideline has been externally reviewed by experts prior to its publication.</p> <p>CLARITY OF PRESENTATION The recommendations are specific and unambiguous. The different options for management of the condition or health issue are clearly presented. Key recommendations are easily identifiable.</p> <p>APPLICABILITY The guideline provides advice and/or tools on how the recommendations can be put into practice. The guideline presents monitoring and/or auditing criteria.</p> <p>EDITORIAL INDEPENDENCE Competing interests of guideline development group members have been recorded and addressed.</p>	<p>EDITORIAL INDEPENDENCE Unclear if the views of the funding body have not influenced the content of the guideline.</p>
<i>IDSA Guideline, 2012¹⁰</i>	
<p>SCOPE AND PURPOSE The overall objectives of the guideline are specifically described. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described – patients with diabetic foot wounds. The health questions covered by the guideline are specifically described. The target users of the guideline are clearly defined.</p> <p>STAKEHOLDER INVOLVEMENT The guideline development group includes individuals from all relevant professional groups.</p> <p>RIGOUR OF DEVELOPEMENT Systematic methods were used to search for evidence. The methods for formulating the recommendations are clearly described. The health benefits, side effects, and risks have been considered in formulating the</p>	<p>STAKEHOLDER INVOLVEMENT The views and preferences of the target population did not appear to have been sought.</p> <p>RIGOUR OF DEVELOPEMENT The criteria for selecting the evidence are partially described.</p> <p>EDITORIAL INDEPENDENCE Unclear if the views of the funding body have not influenced the content of the guideline.</p>

Table 5: Critical Appraisal of Included Guidelines using AGREE II⁸

Strengths	Limitations
<p>recommendations. There is an explicit link between the recommendations and the supporting evidence. The guideline has been externally reviewed by experts prior to its publication. The strengths and limitations of the body of evidence are described. A procedure for updating the guideline is provided.</p> <p>CLARITY OF PRESENTATION The recommendations are specific and unambiguous. The different options for management of the condition or health issue are clearly presented. Key recommendations are easily identifiable.</p> <p>APPLICABILITY The guideline describes facilitators and barriers to its application. The guideline provides advice and/or tools on how the recommendations can be put into practice. The potential resource implications of applying the recommendations have been considered. The guideline presents monitoring and/or auditing criteria.</p> <p>EDITORIAL INDEPENDENCE Competing interests of guideline development group members have been recorded and addressed.</p>	
<i>SIGN Guideline, 2010¹¹</i>	
<p>SCOPE AND PURPOSE The overall objectives of the guideline are specifically described – to provide evidence-based guidance for the treatment of leg ulcers. The health questions covered by the guideline are specifically described. The population to whom the guideline is meant to apply is specifically described – and clear to whom the guideline does not apply.</p> <p>STAKEHOLDER INVOLVEMENT The guideline development group likely includes individuals from all relevant professional groups. The views and preferences of the target population (patients, public, etc.) have been sought. The target users of the guideline are clearly defined.</p> <p>RIGOUR OF DEVELOPEMENT Systematic methods were used to search for evidence. The criteria for selecting the evidence are clearly</p>	<p>EDITORIAL INDEPENDENCE Unclear if the views of the funding body have influenced the content of the guideline.</p>

Table 5: Critical Appraisal of Included Guidelines using AGREE II⁸

Strengths	Limitations
<p>described. The strengths and limitations of the body of evidence are clearly described. The methods for formulating the recommendations are clearly described. There is an explicit link between the recommendations and the supporting evidence. The health benefits, side effects, and risks have been considered in formulating the recommendations. The guideline has been externally reviewed by experts prior to its publication. A procedure for updating the guideline is provided.</p> <p>CLARITY OF PRESENTATION The recommendations are specific and unambiguous. The different options for management of the condition or health issue are clearly presented. Key recommendations are easily identifiable.</p> <p>APPLICABILITY The guideline describes facilitators and barriers to its application. The guideline provides advice and/or tools on how the recommendations can be put into practice. The potential resource implications of applying the recommendations have been considered. The guideline presents monitoring and/or auditing criteria.</p> <p>EDITORIAL INDEPENDENCE Competing interests of guideline development group members have been recorded and addressed.</p>	
<i>HSE Guideline, 2009¹²</i>	
<p>SCOPE AND PURPOSE The objectives are specifically described – to help guide all professionals who deal in wound management through the management of commonly seen in clinical practice that present challenges for healthcare professionals. The health questions covered by the guideline are not listed as questions, but the type of wounds and type of patient covered in the guideline are clearly described. The population to whom the guideline is meant to apply is specifically described – types of wounds are named, type of patient described.</p> <p>STAKEHOLDER INVOLVEMENT Multidisciplinary group was involved in the guideline development process – tissue viability</p>	<p>STAKEHOLDER INVOLVEMENT Unclear if the views and preferences of the target population (patients, public, etc.) have been sought.</p> <p>RIGOUR OF DEVELOPEMENT A procedure for updating the guideline is not provided.</p> <p>APPLICABILITY The guideline does not describe facilitators and barriers to its application. The guideline provides wound management tools and audit tools, but limited information on how to implement the recommendations. The potential resource implications of applying the</p>

Table 5: Critical Appraisal of Included Guidelines using AGREE II⁸

Strengths	Limitations
<p>nurses, wound management organizations, representatives from the National Hospitals Office, and private healthcare providers. The target users of the guideline are clearly defined – all health professionals who deal in wound management.</p> <p>RIGOUR OF DEVELOPEMENT Systematic methods were used to search for evidence (multiple databases, years presented). The criteria for selecting the evidence clearly described – years of guidelines, country of origin specified. The strengths and limitations of the body of evidence are somewhat clearly described – the guideline limitations are explicitly stated and most evidence statements are graded for level of evidence, however not all statements are clear with respect to grading and there is no overall statement regarding limitations. The methods for formulating the recommendations are clearly described – multidisciplinary developers drafted recommendations, these were reviewed internally and externally by other experts and redrafted as-needed. The guideline was externally reviewed by experts prior to its publication.</p> <p>APPLICABILITY The guideline presents auditing criteria.</p> <p>CLARITY OF PRESENTATION The recommendations are specific and unambiguous. The different options for management of the condition or health issue are clearly presented. Key recommendations are easily identifiable.</p>	<p>recommendations have not been outlined in the document.</p> <p>EDITORIAL INDEPENDENCE Unclear if the views of the funding body have not influenced the content of the guideline. Competing interests of guideline development group members have not been included in the publication.</p>

HSE = Health Service Executive; IABG = International Affairs and Best Practice Guidelines; IDSA = Infectious Disease Society of America; SIGN = Scottish Intercollegiate Guidelines Network

APPENDIX 5: Summary of Outcomes and Results

Table 6: Summary of the Results of the Non-Randomized Study ¹³		
Key Patient Characteristics	Key Results	Author Conclusions and Comments
<p>Median age: 78 years (17 to 96) Female: 69% Risk Factor Prevalence:</p> <ul style="list-style-type: none"> Ex-smoker: 16% Current smoker: 13% Rheumatoid arthritis: 10% History of any DVT: 25% History of ipsilateral DVT: 16% Diabetes mellitus: 17% <p>Long term (≥ 1 year) ulcer: 53 patients Shorter term (<1 year) ulcer: 99 patients Site of leg ulcer:</p> <ul style="list-style-type: none"> Medial: 36% Lateral: 22% Anterior: 20% Posterior: 7% Circumferential: 15% 	<ul style="list-style-type: none"> History of DVT was more common in patients who had long term ulcers (40% vs. 17%, P = 0.0032) Widespread deep venous reflux significantly more common in patients with ulcers that had been present ≥1 year (34% vs.18%, P = 0.0442). <p>Majority of patients had abnormal venous duplex results:</p> <ul style="list-style-type: none"> Isolated superficial incompetence: 53% Limited deep incompetence: 11% “Total” deep incompetence: 28% <p>Significant peripheral arterial disease:^a</p> <ul style="list-style-type: none"> Present in 30% of limbs Arterial revascularization occurred in 34 (19%) limbs <p>Healing in ulcers followed longer than 3 months:</p> <ul style="list-style-type: none"> 48% of ulcers healed during the study period Median time to healing was 361 days (25 to 1,599) 54% of ulcers that underwent superficial venous ablation (surgery or foam sclerotherapy) healed. (P = 0.307 vs. those who did not undergo ablation) 26/32 limbs with arterial disease underwent revascularization Healing rate for revascularized limbs with arterial disease was 27%; for non-revascularized was 50% 	<ul style="list-style-type: none"> Widespread deep reflux and DVT were found to be associated with long-term ulceration. The finding that superficial venous ablation (foam or surgery) was used in 21% of long-term ulcerated legs despite superficial venous reflux reflected conservative management that was common prior to the publication of a key treatment study, as well as the reluctance of older adults to undergo the procedure. There was a trend (not statistically significant) toward greater healing in limbs that underwent superficial venous ablation There was no consensus regarding optimal management of mixed arterial and venous ulceration – authors determined these to be a particularly difficult clinical presentation. Authors stated that the study reinforced the need for vascular assessment and venous imaging in the management of leg ulcers. A history of DVT and an ulceration that has been present ≥ 1 year should not be reasons not to refer for surgical intervention as they were not associated with lower healing rates in this study.

DVT = deep vein thrombosis; vs. = versus

^adefined as impalpable foot pulses and an ankle brachial pressure index < 0.8

Table 7: Summary of Key Recommendations of the Included Evidence-Based Guidelines

Wound Type	Recommendations (Level of Evidence)
<i>IABG Guideline, 2013⁹</i>	
Diabetic foot ulcer.	<p>Planning:</p> <ul style="list-style-type: none"> If healing is not occurring, there should be collaboration between the client, the family, and an interprofessional team^a (Level IV) based on client-centred care. <p>Organization and Policy</p> <ul style="list-style-type: none"> Interprofessional, inter-agency team approach to wound management should be established and supported. This team should monitor and address quality improvement and management of diabetic foot ulcers. (Level IV) A process should be developed that facilitates the referral of patients with diabetic foot ulcers to diabetes resources and healthcare professionals. (Level IV) <p>Suggest that key members of the interprofessional team should be:</p> <ul style="list-style-type: none"> Diabetologists Endocrinologists Vascular surgeons Plastic surgeons Dermatologists Chiropodists/podiatrists Infectious disease specialists Family physicians Nurses specializing in diabetes and wound care Occupational therapists Physiotherapists Dietitians
<i>IDSA Guideline, 2012¹⁰</i>	
Diabetic foot infection	<p>Consultation</p> <ul style="list-style-type: none"> For both inpatients and outpatients, there should be a well-coordinated, multidisciplinary effort by a diabetic foot care team. (moderate, strong) Patients may benefit from consultation with infectious disease or clinical microbiology specialist and a surgeon with experience and interest in managing diabetic foot infections. (strong, low) Healthcare professionals without wound debridement experience or expertise should seek aid or consultation from those with experience, especially when extensive debridement is needed. (strong, low)

Table 7: Summary of Key Recommendations of the Included Evidence-Based Guidelines

Wound Type	Recommendations (Level of Evidence)
	<ul style="list-style-type: none"> • A vascular surgeon should be consulted regarding revascularization if there is imaging or clinical evidence of significant ischemia. (strong, moderate) • Clinicians who are not familiar with pressure off-loading or specialized dressings should consult foot or wound care specialists. (strong, low) • Clinicians working in communities without specialist care should consider systems such as telemedicine in order to consult with experts when expert management is needed. (strong, low) <p>Hospitalization</p> <ul style="list-style-type: none"> • All patients with severe infections, some patients with moderate infections but complications such as lack of home support, and patients unable to comply with wound care regimens should be hospitalized OR patients who do not have the aforementioned risk factors but whose wounds are not improving should be hospitalized. (strong, low)
<i>SIGN Guideline, 2010¹¹</i>	
Chronic venous leg ulcers	<p>Specialist leg ulcer clinics recommended as optimal treatment in the community (Grade B)</p> <p>Patients who have non-healing or atypical wounds should be referred for consideration for biopsy (Grade D)</p> <p>Criteria for specialist referral (Grade D)</p> <ul style="list-style-type: none"> • Suspected malignancy • Peripheral arterial disease (with ABPI <0.8) • Diabetes mellitus • Rheumatoid arthritis or vasculitis • Atypical distribution of leg ulcers • Suspected contact dermatitis or dermatitis that is resistant to topical steroids • Non-healing ulcers
<i>HSE Guideline, 2009¹²</i>	
Venous leg ulceration	<p>“Practitioners should record any unusual presentation of the ulcer and if there is any doubt or concern about the aetiology the patient should be referred for specialist medical assessment. (Level 3)”</p> <p>“Venous ulcers that have been open continuously without signs of healing for 3 months or that do not demonstrate any response to treatment after 6 weeks should be reassessed and a biopsy for histological diagnosis considered. (Level 3).”</p>
Arterial ulcers	<p>“Patients presenting with rest pain or gangrene should be promptly referred to a vascular specialist. (Level 1)”</p>
Diabetic foot ulceration	<p>“Comprehensive assessment of the patient including the wound bed should be conducted by persons trained in such assessment. It is recognized that such assessment will require knowledge and skills of more than one professional discipline.” (Level of evidence NR)</p> <p>“Patients with an ulcer deeper than subcutaneous tissues should be treated intensively and depending on</p>

Table 7: Summary of Key Recommendations of the Included Evidence-Based Guidelines

Wound Type	Recommendations (Level of Evidence)
	local resources and infrastructure, hospitalization must be considered.” (Level of evidence NR)

ABPI = ankle brachial pressure index; HSE = Health Service Executive; IABG = International Affairs and Best Practice Guidelines; IDSA = Infectious Disease Society of America; NR = not reported; SIGN = Scottish Intercollegiate Guidelines Network

^adefined in the guideline as “multiple health caregivers who work collaboratively to deliver quality care within and across settings to provide comprehensive health services to clients”