Management of nonhealable and maintenance wounds: A systematic integrative review and referral pathway

ABSTRACT

Objective This systematic integrative review aims to identify, appraise, analyze, and synthesize evidence regarding nonhealable and maintenance wound management to guide clinical practice. An interprofessional referral pathway for wound management is proposed.

Data sources An electronic search of Scopus, Web of Science, PubMed, Academic Search Ultimate, Africa-Wide Information, Cumulative Index of Nursing and Allied Health Literature database with Full Text, Health Source: Consumer Edition, Health Source: Nursing/Academic Edition, and MEDLINE was conducted for publications from 2011 to 2019. Search terms included (nonhealable/nonhealing, chronic, stalled, recurring, delayed healing, hard-to-heal) and wound types most associated with nonhealable or maintenance wounds. Published studies were hand searched by the authors.

Study selection Studies were appraised using two quality appraisal tools. Thirteen reviews, six best-practice guidelines, three consensus studies, and six original nonexperimental studies were selected.

Data extraction Data were extracted using a coding framework including treatment of underlying causes, patient-centered concerns, local wound care, alternative outcomes, health dialogue needs, challenges within resource restricted contexts, and prevention.

Data synthesis Data were clustered by five wound types and local wound bed factors; further, commonalities were identified and reported as themes and subthemes.

Conclusions Strong evidence on the clinical management of nonhealable wounds is limited. Few studies describe outcomes specific to maintenance care. Patient-centered care, timely intervention by skilled healthcare providers, and involvement of the interprofessional team emerged as the central themes of effective management of maintenance and nonhealable wounds.

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GENERAL PURPOSE

To synthesise the evidence regarding nonhealable and maintenance wound management and propose an interprofessional referral pathway for wound management.

TARGET AUDIENCE

This continuing education activity is intended for physicians, physician assistants, nurse practitioners, and nurses with an interest in skin and wound care.

LEARNING OBJECTIVES/OUTCOMES

After participating in this continuing professional development activity, the participant will apply knowledge gained to:

1. Identify the ideas from the authors' systematic review that could prove useful in understanding nonhealable and maintenance wound management.
2. Select evidence-based management strategies for nonhealable and maintenance wound management.

INTRODUCTION

Acute wounds follow an organised wound healing sequence and often heal between 3 and 4 weeks. When a wound is still present 4 weeks after wounding, it is defined as a chronic wound[1]. Many research studies have been conducted on chronic wound management to address the rising demand for effective and affordable care. The healing trajectory of chronic wounds is expected to take 12 weeks[2,3]. This period may be prolonged if the wound presents with an altered molecular environment, chronic inflammation or fibrosis,[4] or uncorrected preexisting systemic factors[1].

Patients who present with a wound not responding to conventional treatment are the topic of many best-practice guidelines using the umbrella terms "nonhealing" or "hard-to-heal[5,6]." Advanced modalities such as negative-pressure wound therapy (NPWT), ultrasound, laser, platelet-enriched plasma, hyperbaric oxygen (HBO), use of dermal substitutes, and reconstructive surgery are frequently advised as adjunctive intervention. Although appropriate to some wounds, there is a subgroup of patients for whom alternative approaches or endpoints are needed because advanced modalities either failed or are not feasible. This typically is the case when the patient presents with preexisting underlying systemic disease that cannot be controlled, is in need of additional physiologic support (eg, supplementary oxygen, renal dialysis), has difficulty performing activities of daily living without help, experiences financial and/or social difficulties, or lives in a resource-restricted environment without access to advanced care.

The wound bed preparation (WBP) paradigm[2,7] guides wound care practitioners to determine wound healing potential as a vital first step of wound assessment. By accounting for both underlying causes and patient-centered concerns, providers can plan for realistic outcomes. The paradigm includes "problem wound" scenarios. Wounds with underlying cause(s) that cannot be corrected are categorised as nonhealable wounds (often attributable to critical ischemia, malignancy, or an untreatable underlying systemic condition)[2,7].Wounds with correctable underlying cause(s) in the context of health system challenges (ie, lack of resources, skills, or expertise) or nonoptimal patient factors (ie, smoking, obesity, resistance to change) are categorised as maintenance wounds[2,7].

Evidence-based guidance on nonhealable or maintenance wounds is needed. This systematic integrative review aims to identify, appraise, analyse, and synthesise evidence regarding nonhealable and maintenance wound management to guide clinical practice.

METHODS

This study was granted ethical exemption (nr. 2019_19.8-5.3) by the University of South Africa Department of Health Studies Research Ethics Committee (no. REC-012714-039) because it did not involve human participants. The research question was: What is known from scientific literature regarding the management of nonhealable and maintenance wounds?

Data Sources

A subject information specialist and two authors of the study conducted a comprehensive literature search using the electronic databases Scopus, Web of Science, PubMed, Academic Search Ultimate, Africa-Wide Information, Cumulative Index of Nursing and Allied Health Literature with Full Text, Health Source: Consumer Edition, Health Source: Nursing/Academic Edition, and MEDLINE. Studies from January 2011 (when the WBP classification of healable, nonhealable, and maintenance wounds[2] was established) to September 2019 (the month the search was conducted) were included. The search was not restricted by language or study methodology. Key words included (guideline* or framework* or consensus* or "care pathway*" or paradigm*), (manag* or maint* or treat*), (wound* or ulcer* or injur*) in relation to (nonheal* or chronic or stalled or recur* or "delay* healing" or "hard to heal" or "lower

leg*" or "diabetic foot" or pressure or fungating). In addition to the database search, published studies were hand searched by the authors.

Study Selection

Duplicates were removed using the Evidence for Policy and Practice Information Reviewer software (v 4.0; EPPI-Centre, London, England). Titles were screened by one author, followed by independent screening of abstracts by two authors according to selection criteria (Table 1). In addition, a hard-to-heal category was created to facilitate the sorting of studies on stalled nonhealing chronic wounds for wounds that failed to heal but were not yet defined as either a maintenance or nonhealable wound[1,4]. Two authors independently examined the full-text publications for relevance to the study question and consulted with a third author if they could not reach a consensus.

Publications not meeting the selection criteria (Table 1) were excluded. Investigators also excluded editorials, discussions, corporate education papers, expert opinions not validated by a Delphi process, case studies, case series, and retrospective study designs because of methodology concerns. Non-English articles were excluded if not followed by English translation.

Quality Appraisal

Two-author appraisals were done independently for each study using the Joanna Briggs Institute Critical Appraisal Checklist for Systematic Reviews and Research Syntheses[8] and the Crowe Critical Appraisal Tool (v 1.4[9])for best-practice guidelines, consensus documents, and original studies. A user manual guided the correct use of each quality appraisal tool. The minimum threshold for inclusion for each tool was set at 60% average. A third author was involved if the two scores differed by more than 20%, and the two highest scores were used.

Table 1. Selection criteria

Population	Persons of any sex older than 18 y with nonhealable wound(s), maintenance wound(s), and/or hard-to-heal wound(s)
Intervention	Management of nonhealable, maintenance, or hard-to-heal wounds. Management refers to any treatment option/modality (not restricted to local wound care but including treatment of the cause, identification of patient-centered concerns, alternative outcomes, and health dialogue) including prevention (of disease progression, reoccurrence, mitigating risk for malignancy)
Comparator	Not required
Outcome	Not required
Study design	Original empirical studies (quantitative, qualitative, multimethod, and mixed-method designs) and reviews and guidelines (with recommendations based on strength of evidence and a reported search strategy)

Table 2. Coding framework topics

Treat the cause
Patient-centered concerns
Local wound bed preparation
Setting of alternative outcomes
Health dialogue
Challenges in resource restricted contexts
Prevention
Other (an open code)

Data Extraction

The final set of included articles was distributed among groups of two or three authors responsible for a wound type and independently co-coding study data. Coding framework topics (Table 2) were collaboratively developed by the research team from the work of authors in the field of study[2,7,10-15]. Deductive coding focused on extracting relevant content from the results, discussion, and/or conclusion sections of each included article.

Data Synthesis

Coded sections were clustered into a table to provide a comprehensive overview of evidence by topic and wound type. The teams met in November 2019 to provide a summary of the main findings for each wound type to the whole group. A second analysis was conducted by the three senior authors to identify and describe commonalities (themes) by comparing the extracted information.

RESULTS

The literature search yielded 1,714 records, and the hand search, 36 records. There were 233 relevant titles, with 92 abstracts relevant to the research question. After examining the full-text articles, 61 were excluded. In the remaining 31 studies, three scored less than 60% on the quality appraisal tools. The quality appraisal scores and the strengths and weaknesses of each included study (n = 28) are summarised in Supplemental Table 1 (click here); the flow of the selection process is depicted in Figure 1[16].

Researchers analysed 13 reviews, 6 best-practice guidelines, 3 consensus studies (based on Delphi techniques), and 6 original studies (1 multimethod and 5 nonexperimental, descriptive, and/or correlational quantitative designs). No randomised controlled trials were identified. The characteristics of the included studies are outlined in Supplemental Tables 2 (click here), 3 (click here), and 4 (click here).

Data Synthesis and Theme Identification

This section reports a summary of the extracted data from the included studies for five wound types: malignant fungating wounds (MFWs), lower leg ulcers (LLUs), diabetic foot ulcers

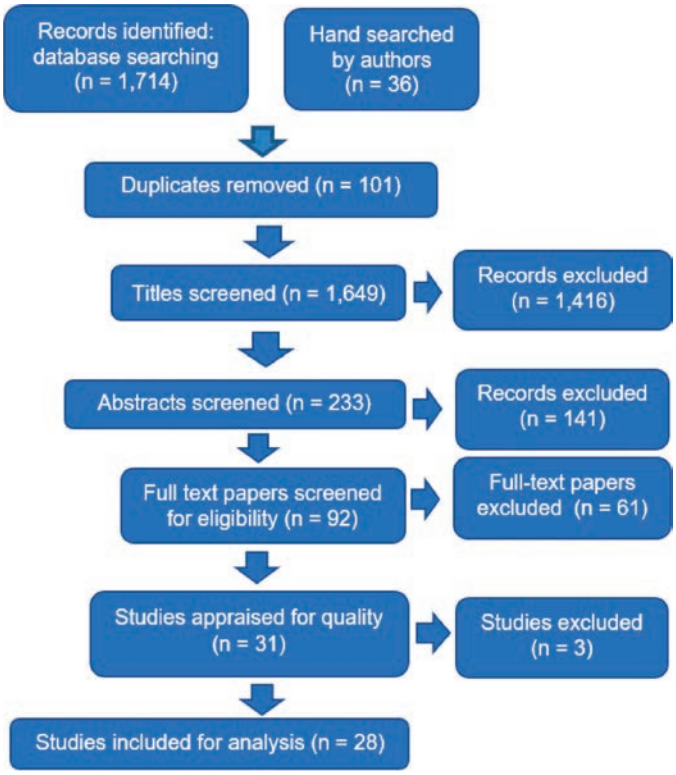

Figure 1. Study selection

(DFUs), pressure injuries (PIs), and atypical wounds. Three articles focused on local wound bed interventions and are summarised separately.

Malignant Fungating Wounds. Two studies on MFWs were included and addressed the effect of topical agents and dressings on quality of life (QoL) for people with MFWs[17] and resilience when living with a wound[18].

Adderley and Holt[17] did not find evidence on the effect of dressings on QoL. Weak evidence suggests the use of 6% miltefosine topical solution or foam dressings with silver on superficial wounds could delay disease progression and reduce malodour[17]. Evidence supporting the use of honey-coated dressings is not sufficient[17].

Ousey and Edwards[18] identified pain and fatigue as barriers to maintaining health-related QoL (HRQoL). Practitioners must acknowledge the emotional needs of patients with MFWs who may experience destructive feelings and feelings of avoidance. Loss of bodily function control also impedes the ability to cope with the disease[18]. Persons living with an MFW want to be informed about physical limitations and psychological consequences (such as sudden hemorrhage), and they appreciate advice on wound management[18].

Lower Leg Ulcers. Venous leg ulcers (VLUs) account for up to 80% of all LLUs[19], which accounts for the eight articles included on VLUs: two reviews[20,21] and one consensus study[22] on compression therapy, one review[3] and one guideline on the holistic management of VLUs[19], one quantitative survey on VLU management[24], and one cohort study on sustained behavior change following a client education program[25], and one review on cost-effectiveness[26]. The ninth article, a review by the Canadian Agency for Drugs and Technologies in Health (CADTH), provided evidence on arterial ulcers and mixed etiology ulcers, reporting the lack of current consensus on optimal wound management for mixed arterial-venous ulcers[27]. All nine studies used the terms *nonhealing chronic wounds* or *wounds with extended time to healing* (>12 weeks).

A consensus-based algorithm recommends that ankle-brachial pressure index (ABPI) should be used for its high specificity in detecting peripheral arterial disease (PAD) as an underlying cause in LLUs[22] and that significant PAD requires immediate referral to a vascular surgeon[19,21,27]. However, a survey among nurses identified a significant knowledge-translation gap regarding ABPIs[24].

All the evidence supports compression therapy as key to VLU management[19-23,27]. However, guidelines advise against compression therapy in the presence of significant PAD or pulmonary edema, but do recommend immediate referral to a vascular assessment service[19,21,27]. The included studies support modified compression carefully monitored by a well-trained clinician for mild PAD (ABPI 0.5-0.8) and standard compression therapy in the absence of PAD[19-22].

The included guideline argues that chronic, hard-to-heal VLUs can be transformed into acute wounds by means of debridement once PAD is excluded, malignancy ruled out, and other inflammatory comorbidities accounted for[19]. All studies supported the WBP paradigm for maintenance wounds[7,22,23]. When LLUs are not healing as expected, providers should reassess the patient at least every 12 weeks for other potential causes and repeat the ABPI measurement[20,22]. Further, NPWT is not indicated for healable VLUs over topical modalities; it is effective for securing a skin graft in hard-to-heal wounds, but not as a modality on its own[23]. There is substantial evidence on the efficacy of electrical stimulation as an adjunctive modality in VLU to achieve healing progress[23].

Venous leg ulcers significantly impact social and physical functioning; pain is particularly prominent in the ulcerative phase or with secondary infection[19]. Only one of the included studies recommends dressings for local pain relief, but concludes that compression therapy remains the key to pain control[19].

Effective VLU management requires sustained behavior change[19,22,25]. Patient education should include leg health, emphasis on regular activity, the role of pharmaceuticals, the importance of compression, optimal positioning of legs during rest, promotion of a healthy diet and adequate hydration, and skin care. Nonadherence to modifying lifestyle factors may lead to extended healing times or nonhealing[22,25]. Positive behavior change was achieved via e-learning in a prospective single sample cohort study[25]. Recurrence of VLU is common, and strong evidence supports use of stockings as primary prevention to improve the aching and itching associated with venous insufficiency[22].

Carter[26] reviewed the cost-effectiveness of new or evidence-based intervention systems versus routine care to guide decision-making. One study in this review (an unblinded randomised controlled trial of moderate evidence strength) concluded that four-layer compression bandages resulted in faster healing versus the control group (standard care) with consequent financial cost savings. However, they also reported compression bandage application skill to be a key factor in achieving positive VLU outcomes[26]. Another key message from this review was that a multidisciplinary team managing VLUs achieved faster healing by 36.5 days in the intervention group with consequent financial cost savings.

Diabetic Foot Ulcers. These ulcers are classified as hard-to-heal wounds; expected healing trajectories are often missed because of patient factors or healthcare resource limitations[28]. One systematic review discussing NPWT for DFUs,[29] one original study[30], and four guidelines[31-34] were included in this portion of the review. The guidelines and original study addressed holistic management of DFUs with one discussing HBO[33].

Two guidelines recommended that PAD should be assessed to establish healability because DFUs can become nonhealable wounds with inadequate perfusion, rendering those patients unsuitable candidates for revascularisation[31,32]. Such nonhealable wounds might result in amputation because of increased infection risk[30].

Glycemic control of and nutrition support for diabetes to enhance wound healing are supported by strong levels of evidence.[31] When addressing the cause of DFUs, plantar pressure redistribution (offloading) is the key to success[32]. The guidelines further recommended that DFUs should be debrided to reduce biologic load and risk of infection when adequate blood supply is present[31,32]. In hard-to-heal wounds with inadequate perfusion, debridement should be conservative[31]. Infection should be treated systemically, especially with a positive probe-to-bone test. When surgery is not an option, systemic antibiotic treatment should be prolonged (6 to 8 weeks)[31]. There is insufficient evidence for topical antibiotics in these wounds, and their use is associated with increased local and systemic microbial resistance[31]. Dressing choice should take into consideration the condition of the wound and surrounding skin[32].

One guideline suggests strong evidence for HBO as adjunctive therapy for the treatment of Wagner stage 3 DFUs[33]. Further, a review by the CADTH concluded that DFUs treated with NPWT showed significantly reduced ulcer areas, healing time, and the need for secondary/major amputation when compared with DFUs not treated with NPWT[29]. These modalities may be indicated in hard-to-heal DFUs but are not recommended for maintenance of nonhealable wounds.

The general review from Ousey and Edwards[18] also included three quantitative studies that reported on the psychological effects of living with a DFU. They found a lower HRQoL with a decline in physical and social functioning among a group of 35 patients living with a DFU compared with a group of 15 persons with diabetes without a wound. Further, depression was related to development of the first DFU among a group of 333 participants and was a persistent risk factor for mortality and presented a 33% increased risk of amputations[18].

Clinicians attending to patients with DFUs must have the necessary skills and equipment to accurately and holistically assess and treat them[31]. All of the guidelines included in this study strongly recommend an interprofessional approach to treating DFUs because of their complex nature[31-34]. These teams should address factors such as patient-centered concerns, access to care, financial limitations, and foot and self-care[31,32].

Pressure Injuries. Four studies were included in this portion of the review: one cross-sectional observational design,[35] two reviews[36,37], and one guideline[38]. Gelis et al[37] stressed that PIs are "not a chronic disease but rather a complication in cases of immobility," suggesting that PI evolution and prognosis correlate with the contexts in which such injuries and wounds occur; that is, PIs may evolve as maintenance or nonhealing wounds according to the underlying pathology. Guihan and Bombardier[35] concluded that the complex underlying comorbidities among persons with slow healing and stage 3 and 4 PIs require an interprofessional approach. Early and aggressive management of acute and chronic PIs may prevent or change the development cycle of hard-to-heal or maintenance wounds over time[35].

Fujiwara et al[38] included studies focusing on diagnosis and treatment of stage 1-4 PIs. They support pressure and shear forces as underlying causes and strongly recommend pressure relief with position changes every 2 hours and the use of appropriate pressure-relieving mattresses (based on strong evidence). Pain control is an important aspect of patient-centered concerns to improve the HRQoL of patients with PIs. Some evidence in the review suggests pressure-relieving mattresses and specific wound dressings (eg, soft silicone, alginate, and hydrogels). Evidence for the use of nonsteroidal anti-inflammatory and/or psychotropic drugs exists, but is weak.[38] Their recommendation to debride devitalised tissue was for healable wounds where the cause could be corrected. For hard-to-heal, maintenance, or nonhealable PIs, no recommendation on debridement could be drawn from the evidence. Surgery may remain as an option once the underlying cause can be corrected and the condition of the patient improved.

In the presence of deep infection, a systemic antibiotic is suggested using a positive bacterial culture from the wound bed to guide treatment[38]. In addition, signs of persistent inflammation in the periwound area, pyrexia, an increased white blood cell count, or worsening of the inflammatory reaction should be addressed[38]. A comprehensive assessment of the patient, the wound bed, and periwound area should be conducted to diagnose wound infection. The CADTH did not find evidence to support specific wound dressings and stated: "one dressing will be as good as the other[36]."

Gelis et al[37] reviewed evidence on patients with chronic neurologic impairment at risk of PI and suggested continuing therapeutic education for older adults, persons with spinal cord injuries, and others at risk[37]. They also recommend several pedagogic models for use based on the learning style of the specific patient and involving the circle of care in prevention. Providers should support patient self-management of multiple chronic conditions, because several comorbidities often occur simultaneously in persons with slow-healing PIs[35].

Atypical Wounds. Four articles were included in this part of the review. These referred to Buruli ulcer, hidradenitis suppurativa, epidermolysis bullosa, and vasculitis- and autoimmune-associated wounds. These wounds present with unusual signs and symptoms and/or locations and do not heal within 4 to 12 weeks, and often the underlying conditions are difficult to manage in clinical practice.

In a Ghanaian Buruli ulcer prospective observational study, the authors found that earlier wound closure (less than 12 weeks) was more likely in primary healthcare settings compared with secondary settings despite a lack of resources, staff incompetency, and high patient loads[39]. This was attributed to earlier presentation, smaller wounds, better nutrition status, better patient adherence to treatment, and intact social support. Wound closure failure occurred in primary healthcare in the presence of underlying complications, such as osteomyelitis, squamous cell carcinoma, chronic lymphedema, and infection. In the secondary healthcare setting, nutrition deficiency, venous and arterial insufficiency, lymphedema, and malignant deterioration were associated with impaired wound healing. This was mostly attributable to poor hygiene and deficient skills and resources leading to recurrent wound infection. Failure to heal became predictable between weeks 2 and 4.

Alavi et al[40] explored hidradenitis suppurativa patient-centered concerns related to sexuality. This observational two-legged cross-sectional study found both men and women with HS experience negative impacts on their QoL. Men experienced sexual performance issues and women experienced sexual distress because of the location of these painful exuding lesions.

The epidermolysis bullosa study reports an expert consensus of recommendations for practice[41]. The main recommendations included active interventions to control persistent inflammation leading to malignancy; an interprofessional team approach to assessment, identification, and management of underlying factors; delicate management of blisters; optimisation of nutrition status with attention to albumin and hemoglobin levels; use of healing trajectory indicators to predict healing potential; and the importance of a skin edge biopsy in recalcitrant wounds to rule out squamous cell carcinoma.

Shanmugam et al[42] review the evaluation and management of hard-to-heal wounds associated with vasculitis and autoimmune etiologies. Wounds not responding to local care and appropriate vascular intervention may have an underlying vasculitis or autoimmune disorder present. An interprofessional team can facilitate the required underlying systemic disease investigation. Skin graft failure should prompt high provider suspicion of vasculitis; an edge biopsy may be helpful to confirm diagnosis[42].

Local Wound Bed Factors. Three articles addressed local wound bed issues prevalent in problem wounds regardless of type and addressed malodour, the nonhealing spiral, and maggot debridement therapy (MDT).

Akhmetova et al[43] aimed to summarise studies focusing on odour control in chronic wound management. Five control measures with substantial evidence were identified. Metronidazole gel was most extensively studied; five studies reported it reduced odour, exudate, and pain. Topical silver (and silver sulfadiazine use) was included because it is not deemed an antibiotic but rather an antimicrobial agent. Four studies supported its use because of its antimicrobial and anti-inflammatory effect on the wound bed. Charcoal is known to absorb gases, bacteria, and liquids; one study supported its use. Medical-grade honey for odour control was mentioned in three studies, and research on topical cadexomer iodine use in VLUs reported odour reduction as a secondary outcome[43].

Schultz et al[44] published a guideline for the identification and treatment of chronic nonhealing wounds. "Nonhealing" is not defined in the article in terms of a time frame or underlying cause, but in general as chronic wounds not healing in a timely fashion despite optimal intervention. A key recommendation is the initial use of aggressive debridement in combination with topical antiseptics and systemic antibiotics followed by a step-down approach until healing[44]. A consensus statement indicates that this recommendation is relevant for aggressive management of wounds that might have some potential for healing[44]. Further research is required to evaluate the effectiveness, validity, reliability, and reproducibility of the algorithms available to diagnose and treat biofilm. Further exploration into different wound types will be necessary to provide a clear guide on definite signs and symptoms associated with biofilm in the wound bed; for example, ischemic ulcers may not manifest the same signs and symptoms of biofilm because of the lack of blood flow[44].

Sherman[45] provided a summary of MDT and recommendations on when to initiate it as modality. The author concluded that MDT has three broad actions: debridement, disinfection, and tissue growth stimulation, although the focus was on debridement. The chemical debridement occurs via alimentary secretions and excretions containing digestive enzymes, inhibiting microbial growth and biofilm formation. Further, this action induces maturation of monocytes and neutrophils from proinflammatory cells into their angiogenic phenotype, which could lift the wound out of the inflammatory phase[45]. Therefore, MDT is of value as an adjunctive modality in addressing local wound bed factors in hard-to-heal wounds to counteract stalled wound growth, but it is contraindicated in dry wounds because maggots need moisture to survive.

DISCUSSION

Despite the proposed definition/classification of wounds into healable, maintenance, and nonhealable by Sibbald et al[2], very few authors used those terms in publications, a concern also voiced by Olsson et al[46]. Common terms were "chronic," "nonhealing," "slow healing," or "atypical," all with limited reference to wound duration, healing time, or alternative outcomes. This led to authors' extraction of available data elements into an additional "hard-to-heal" category, allowing for inclusion where healing time or the influence of underlying

Table 3. Main themes and subthemes identified

Main Themes	Subthemes
Accurate and appropriate assessment	Initial assessment by skilled clinicians
	Assessment with valid and reliable tools and equipment
	Early establishment of healability potential
	Regular reassessment
	Consistent attention to presence of arterial blood supply
Focused, evidence-based cause intervention	Intervention prioritized by underlying holistic management plan including patient preferences
	Risk mitigation
	Timely interventions and referral
Improvement of health-related quality of life	Pain management (systemic and local)
	Address depression, patient coping skills and emotional needs
	Consider impact of social isolation factors
	Intervene to optimize functionality
	Awareness of financial implications/limitations
Adapted local wound care	Conservative debridement if sufficient arterial flow is present
	Aggressive systemic and local infection control
	Address local inflammation
	Odor control
	Moisture control to protect surrounding skin
	Prevention of wound bed bleeding
	Edge biopsy if wound has gone 12 wk without progress
	Selection of appropriate dressings (guided by wound condition and surrounding skin)
Health dialogue priorities determined	Information on coping with limitations (altered body image, activities of daily living)
	Information to nonadherence to treatment protocols (consequences)
	Guidance on sustained behavioral change
	Tailored to patient learning styles and methods
	Incorporation of self-care skills (foot, wound, and physical body)
	Involvement of the immediate circle of care
Health system challenges identified	Resource availability
	Clinicians with (in)sufficient skills, qualifications, knowledge
	High patient loads
	Access to care issues
	Access to devices and equipment issues
	Hygiene issues on lower levels of care
Rational use of adjunctive modalities	Dependent on healability potential/expected outcome
	Accounted for in a risk/benefit ratio
	Contraindicated in nonhealable and maintenance wounds
	For hard-to-heal wounds in an interprofessional team context
Interprofessional team intervention significance	Early involvement to prevent/mitigate wound chronicity
	Management of complex patient needs
	Advanced skill intervention as needed per wound phase
	Cost-effectiveness with a timely and focused care approach

causes was not described. However, despite the lack of clear definitions, this study identified similarities in management across the different hard-to-heal wound types, and these commonalities encompass the following themes (Table 3).

Accurate and Appropriate Assessment. Early identification of underlying conditions and skillful attention to existing patient and system factors are essential to promote healing at an optimal rate (decreasing 30% in size within 4 weeks)[10]. Providers must determine healability (within the first 12 weeks) and use valid assessment tools. A systematic and comprehensive approach to history taking, physical examination, and laboratory investigations to reach a clear diagnosis improves outcomes[39]. Lack of adequate blood supply remains a major underlying cause present in most nonhealing or maintenance wounds and should be assessed regularly[19,21,24,27]. Depression is strongly associated with the onset of DFUs, and if left untreated, increases subsequent amputation and mortality risk[18]. Providers should actively screen and prioritise intervention and appropriate treatment for depression in patients with long-duration wounds[18].

Focused, Evidence-Based Cause Intervention. Adequate cause identification and initiating corrective interventions to mitigate underlying causes early in the wound healing sequence could prevent wound conversion. The substantial list of direct deficits that add to local wound deterioration and chronicity includes osteomyelitis, squamous cell carcinoma, chronic lymphedema, and wound infection[39], and these conditions require intervention or aggressive control to recreate and establish wound bed progression or stability. A hard-to-heal, stalled, or atypical wound should prompt an edge biopsy including the reticular dermis and subcutaneous tissue to assess pathology[41]. Providers should strive for early classification of nonhealable wounds when underlying causes cannot be effectively treated or are deemed uncorrectable[47], with an accompanying shift in focus toward palliation and HRQoL.

Improve HRQoL. Chronic wounds lead to personal, financial, social, psychosocial, and sexual adaptations beyond simply coping with the effects of the wound. Critically, depression is associated with increased morbidity and mortality in patients with diabetes[18]. The benefits of consistent attention to pain management are a key finding in most of the evidence reviewed[18], and multiple pain types may require polypharmacy interventions. It is vital to recognise and manage patient-centered concerns with a focus on improving HRQoL by maintaining activities of daily living and addressing ambulation[48], self-reliance[18], knowledge translation, and self-esteem[17,18]. Patient-centered concerns should be prioritised as highly as underlying causes because the impact of wound healing on HRQoL may be hidden or dormant, which in turn negatively impacts healing.

Adapted Local Wound Care. Appropriate interventions regarding tissue, infection and inflammation, moisture, and edge management remain a cornerstone of local wound care. Different debridement approaches may range from careful and conservative removal of devitalised tissue[31,32], puncturing blisters and not deroofing[41], to surgical debridement to remove biofilm or advance edges[39,44]. These authors recommend careful conservative debridement, which should be performed only by skilled practitioners if adequate arterial blood supply is present to support the wound bed and surrounding tissue.

Aggressive infection control should include actions to treat and prevent recurring superficial and deep wound infection[44,45,48], including assessment of the patient's vital and metabolic status, wound bed, and periwound area. The topical application of any antibiotic preparation such as ointments or creams (eg, gentamicin, fusidic acid, mupirocin) is not recommended by the International Wound Infection Institute because of global concern about antibiotic resistance and the subsequent systemic resistance[49]. Addressing malodour with appropriate dressings is recommended[43] and may be included after a risk analysis on the additional moisture added to a wound bed. Providers and patients should keep nonhealing and maintenance wound beds as dry as possible[23] to preserve tissue[22]; to protect the edges against trauma[41], bacterial invasion[44], and moisture-related skin breakdown[18,26]; and prevent further tissue loss or wound expansion. These results provided clear guidance on the edge effect; wound area reductions less than 20% to 40% in 2 to 4 weeks could be a reliable predictor of nonhealing[39]. That is, providers should not wait 12 weeks without wound edge progress to intervene.

Health Dialogue Priorities. Patients need to understand their situation fully and be guided to self-reliance[18]. Education should accommodate different learning styles with attention to modifiable risk factors (smoking, poor glycemic control, and resistance to lower limb compression). Health dialogue is strongly associated with financial cost savings[26]. eLearning platforms (mobile phone, social media) are powerful patient education tools and facilitate health dialogue that incorporates the patient's care circle in a culturally and patient-appropriate manner. Online learning strategies that include pressure redistribution, nutrition supplementation, skincare, and incontinence care could effectively incorporate the family into the care circle with cost containment as an additional outcome[26]. The value of targeted patient learning may be further enhanced via the financial benefits of DFU prevention[26].

Health System Challenges. This review identified sets of professional skills, or the lack thereof, which impact wound-related outcomes and healing times. These include assessment (ABPI in LLUs[22],DFU grading[33]) and correct clinical management (application of compression bandages[20-22], initial foot pressure redistribution[32]). Lack of provider expertise is an often-overlooked iatrogenic factor in hard-to-heal or stalled wounds[24] that leads to loss of valuable time, additional wound complications, and late referral to an interprofessional team for advanced intervention. Recognizing limitations is vital in early referral to a skilled practitioner/interprofessional team.

However, in resource-restricted or rural settings, interprofessional teams may not be feasible, emphasizing the importance of wound care knowledge for all providers. In fact, limited resources leading to delayed healing is a factor often overlooked in the literature. The review by Carter[26] supports the cost-effectiveness of guideline-driven versus standard care for chronic wounds. Early identification of maintenance wounds may prevent the prolonged use of resources despite the lack of progress[22,26], which could in turn positively impact treatment-associated costs for both the patient and healthcare system.

In the future, the prevention of skin breakdown regardless of wound etiology may be the highest priority of any healthcare professional because of the direct cost saving associated with skin-protective strategies[7,22,26]. This is evident in PI and DFU prevention, where early intervention and prevention are frequently measured by key performance indicators (incidence and prevalence data[50])to save skin from repetitive breakdown and prevent amputations[51].

Rational Use of Adjunctive Modalities. In the hands of the interprofessional team, last-resort adjunctive wound therapies (NPWT, HBO, flap/graft surgery, electrostimulation, MDT)[23,27,33,45] have the best potential to promote healing when patient issues, wound history, and resource limitations are accounted for in hard-to-heal wounds. However, most advanced modalities are not a viable adjunctive option for maintenance and nonhealable wounds with dry[23] or bleeding wound beds[18] and may not represent the most optimal use of resources[22,26].

Interprofessional Team Approach Significance. The most important finding (present in the majority of the included studies) was that an early interprofessional approach can facilitate correct interventions and wound management options[19,21,26,27,31,32,35,41,42]. This timely and accurate intervention may prevent downward spirals into chronicity.[18,31-33,35,41,42] Assessment, diagnosis, and appropriate interventions for slow healing or stalled wounds often require advanced wound care skills[19-22,27] more readily available in an interprofessional team. Evidence supports this intervention as cost-effective compared with standard routine care over prolonged periods of time[26].

Despite this strong recommendation, the interprofessional team is often a last resort and utilised too late to break the cycle of slow healing and chronicity. Patients are vital members of the interprofessional team because they dictate the potential of the team to achieve set outcomes, especially if faced with prolonged healing[22]. However, clinicians may still struggle to determine when it is appropriate to consult with an interprofessional team. For this reason, the authors developed an interprofessional referral pathway using time- and wound-related markers that may indicate the appropriate time to involve the interprofessional team (Figure 2).

Interprofessional Referral Pathway

In doing this review, the research team realised that hard-to-heal wounds follow a typical sequence of events attributable to provider, patient, payer, policy, or persistent uncorrected underlying factors[52,53] rather than being a wound type per se. Essentially, hard-to-heal wounds have specific needs and are an additional category in the process of determining healability:

1. healable: where healing occurs predictably according to expected time frames;
2. hard-to-heal: where slow, stalled, or nonhealing wounds are in need of additional assessment or care modalities;
3. maintenance: where health dialogue for lifestyle modification becomes more important than achieving a wound healing outcome;
4. nonhealable: where aggressive attention to local infection prevention and preservation against further tissue loss is needed and no wound healing outcome can be achieved.

It became clear from compiling data elements into themes that prompt identification of wound healing failure is a priority. The complex factors affecting wound healing should be routinely reassessed, and providers should maintain a flexible perspective on the healing trajectory. In current literature, the exact expected time to healing (ie, a defined cutoff point when wounds are classified as maintenance wounds) remains elusive. With this in mind, the research team proposes a referral pathway with specific time frames to help health professionals in decision-making (Figure 2). Timely referral could lead to optimal intervention in the vital early period of wounding and promote available adjunctive interventions when positive outcomes can still be attained.

The pathway proposes that hard-to-heal wounds be granted another 12 weeks of optimal wound care to achieve healing (30% decrease rate within 4 weeks). If the wound does not progress despite advanced team intervention, it can then be classified as a maintenance wound (where patient or system issues prevent cause correction)[2]. Reassessment and management by wound care specialists fully trained to apply current best evidence and well-positioned on an interprofessional wound care team are critical. The proposed additional 12 weeks of aggressive interprofessional management should be further explored and tested in future research. These studies could consider interventions with or without advanced wound care modalities because such modalities may not be available in resource-restricted contexts.

Limitations

This review was limited to studies from 2011 to 2019 and only considered evidence prior to 2011 if it was included in the selected studies. Guidelines not identified through the search could be of value if the guidelines clearly and transparently report the identification and appraisal of the evidence. Further, key words for specific atypical wounds were not included in the search. This was done to extract studies focused on maintenance and nonhealable wound interventions as well as to limit the yield. However, studies on atypical wounds were hand searched by the research team but had small sample sizes and paucity of evidence.

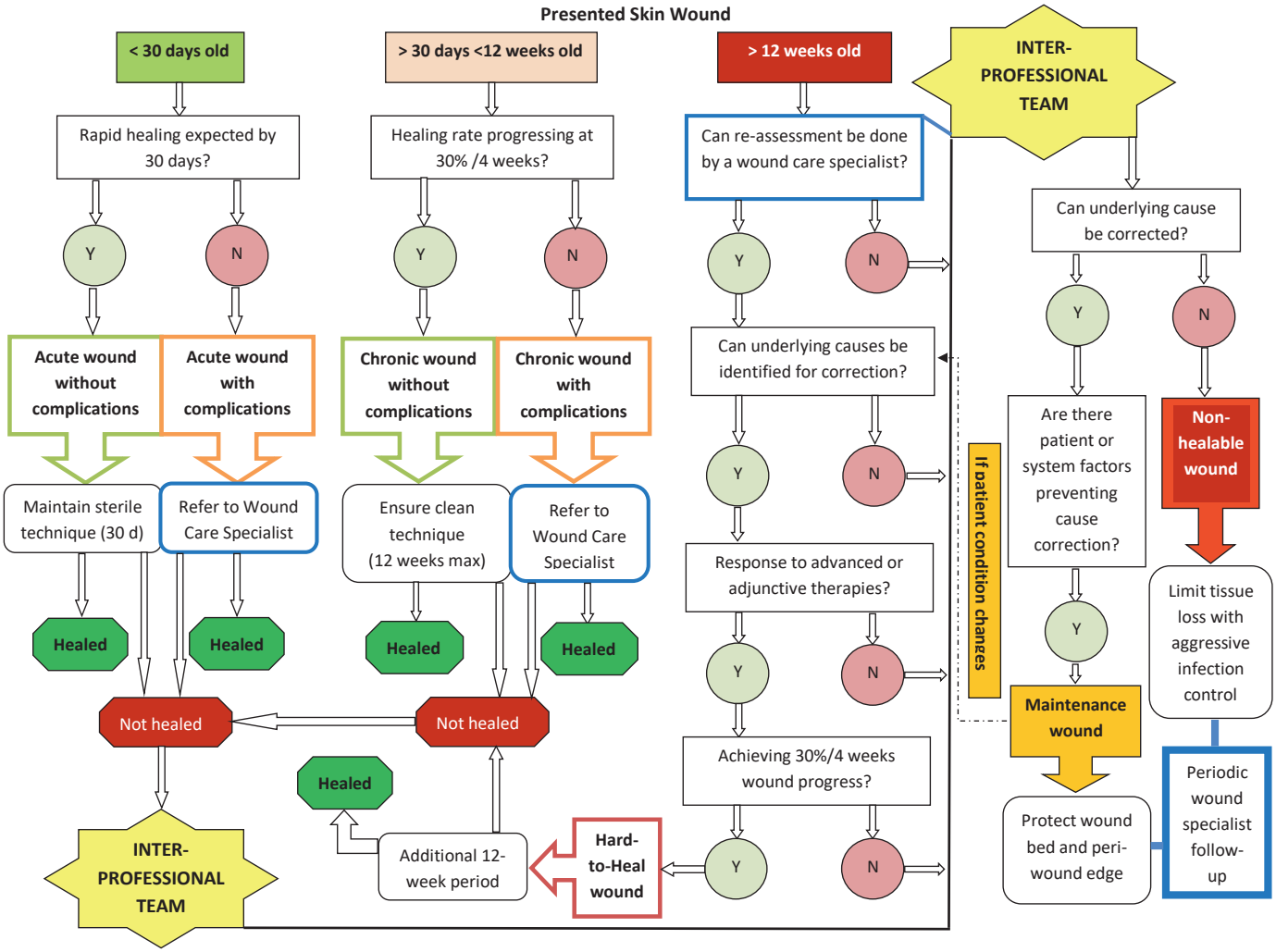

Figure 2. Interprofessional team referral pathway for patients with wounds
The clinician should enter the pathway according to the relevant "time since wounding" in the top horizontal line. Once that box is identified, the decision-making process follows a vertical line downward to an outcome and time frame for that outcome to be achieved. Note that the interprofessional team takes responsibility for diagnosis of maintenance and nonhealable wounds to ensure that no wound lands or remains in those categories unnecessarily.

Definitions: Wound care specialist: a healthcare professional (doctor/nurse/allied health) with additional training and specialization in wound care, part of a functioning interprofessional team. Sterile technique: prevention of bacterial contamination and infection spread by adherence to strict sterile procedural protocol when performing wound-related procedures. Sterile-to-sterile rules apply. Clean technique: also known as nonsterile technique: involves hand washing, a clean environment with a clean field set, clean gloves, and sterile instruments aiming to prevent direct contamination of supplies or material. Acute and chronic wound risk factors: impaired vascular supply, underlying systemic disease, trauma, immune compromise, extensive tissue loss, exposed bone or tendon, patient adherence to treatment issues, patient in need of additional intervention(s), lack of appropriate resources/skills. Advanced/adjunctive therapies: maggot debridement, negative pressure, and hyperbaric oxygen therapies; electrostimulation; ultrasound; laser; platelet-enriched plasma; surgical closure; interventional radiology, etc. Healed outcome—acute wound healed within 30 days; chronic wound healed within 12 weeks (followed 30%/4 weeks' edge advancement); allowance for additional 12-week period(s) for hard-to-heal wounds as determined by the interprofessional team.
Note: Nonhealable wound could also be a first entry point without any flow through the rest of the pathway, with confirmation from the interprofessional team.

This study did not include case studies or case series, but the investigators acknowledge that multiple case studies could be the highest level of evidence available in challenging cases or environments. A future review of existing case studies/case series could prove of value to identify current practicalities when dealing with this subgroup of wounds. Studies on the efficacy and cost-effectiveness of local wound bed innovations in resource-restricted contexts would be a valuable contribution and more so if conducted in real-life clinical settings and in collaboration with academics and practitioners.

CONCLUSIONS

Active patient involvement in the care process is critical to manage a maintenance or nonhealable wound and achieve acceptable outcomes. Once a nonhealable, maintenance, or hard-to-heal wound is identified, not only should a full reassessment be made by a skilled team of healthcare professionals, but focused clinical interventions such as an edge biopsy or advanced vascular assessment should confirm the wound classification and guide patient and provider decision-making.

Evidence on the exact clinical management of maintenance and nonhealable wounds is insufficient to guide practice. The most common findings were the need for early diagnosis and prompt treatment within the first 12 weeks, comprehensive identification of underlying factors delaying healing, and early involvement of the interprofessional team. An interprofessional referral pathway was developed to incorporate an additional 12-week intervention period in hard-to-heal or late-referral wounds.

If wound assessment reveals a maintenance or nonhealable wound, it is important to realise that this diagnosis will impact the patient on physical, personal, interpersonal, social, and financial levels. The main priority should be to preserve patient integrity in these arenas with a focused patient-centered intervention. Long-term pain management should be prioritised. Further, patient preparation with focused health dialogue is vital to identify and facilitate life adaptations needed and cope with this diagnosis. The incorporation of newly learned or adapted skills into the patient's own activities of daily living will positively impact QoL. Patients with maintenance, nonhealing, and hard-to-heal wounds should take responsibility for their own self-care where possible and for as long as possible.

PRACTICE PEARLS

- A wound that does not heal at a rate of 30% per week should be reassessed by an interprofessional team sooner rather than later; do not wait 12 weeks before referral.
- Hard-to-heal wounds, or those that stall over time, may benefit from an interprofessional team's intervention that may include reassessment and a change of treatment strategy to address the underlying cause of the wound.
- Once diagnosed with a maintenance wound, patients need to be empowered with sufficient knowledge and social/family support to maintain activities of daily living and self-care as long as possible.
- The holistic management of both maintenance and nonhealable wounds involves shifting focus away from achieving wound outcomes and toward addressing patient-centered concerns such as pain management and odour control.
- The clinical focus for nonhealable wounds should include aggressive topical infection control to achieve tissue stability, preservation of existing stable dry tissue, and prevention of wound edge expansion.

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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