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CHRONIC WOUNDS : RISK FACTORS AND EVIDENCE-BASED INTERVENTION

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ABSTRACT

Introduction: Chronic wounds are a pervasive and escalating public health issue, characterized by their inability to progress through the typical phases of healing, resulting in prolonged tissue damage and patient morbidity. Common types include diabetic, pressure, arterial, and venous ulcers. Factors like comorbidities, infection, poor circulation, and inadequate care delay healing. This review aims to explore the risk factors for chronic wounds and evaluate evidence-based interventions to optimize treatment outcomes, thereby improving patient care and reducing healthcare costs.
Methods: A thorough literature review was performed using peer-reviewed journals and reliable medical databases, focusing on articles from the past 10 years for relevance. The search used keywords like "chronic wounds," "risk factors," "management," and "evidence-based interventions," selecting studies that addressed the epidemiology, causes, and treatment of chronic wounds.
Results: The review identified major risk factors for chronic wounds, such as diabetes, poor circulation, neuropathy, infection, and aging. Effective treatments discussed include advanced dressings, debridement, negative pressure wound therapy, and skin grafts. A multidisciplinary, patient-focused approach was found to improve healing outcomes.
Conclusion: Understanding the risk factors of chronic wounds and applying evidence-based, personalized treatments can significantly improve healing outcomes. Ongoing research and innovation are essential to address gaps in care and enhance patient management.

Highlights:

1. Identifies key risk factors for chronic wounds and the underexplored role of genetics and immune dysregulation in healing.
2. Explores advanced interventions like smart bandages and bioengineered skin, while addressing accessibility challenges.
3. Highlights the potential of personalized medicine and digital health in improving patient-centered wound care.

INTRODUCTION

Chronic wounds are a pervasive and escalating public health issue, defined by their inability to proceed through the typical phases of healing, leading to prolonged tissue damage and patient morbidity.[1] Chronic wounds are associated with significant morbidity, a profound decline in quality of life, and considerable economic and societal burden, globally.[2] Conditions such as diabetic foot ulcers, venous ulcers, and pressure ulcers are among the most common types, with diabetes and vascular diseases identified as primary risk factors.[3-5] These wounds not only diminish the quality of life for affected individuals but also impose an enormous financial burden, with billions spent annually on wound management and related complications.[4,5]

The global prevalence of chronic wounds continues to rise, affecting approximately 1-2% of the population in developed countries.[6] In the United States alone, around 8.2 million Medicare beneficiaries suffer from chronic wounds, contributing to an annual cost estimated between $28.1 billion and $31.[7] billion.[8] Similarly, in Europe, the economic burden is substantial, with wound care expenses accounting for 2-4% of total healthcare costs.[8] Diabetic foot ulcers (DFUs), one of the most common chronic wound types, affect 6.3% of individuals with diabetes worldwide, translating to an estimated 33 million people globally.[9] These figures underscore the urgent need for improved wound management strategies to alleviate the clinical and financial burden on healthcare systems.

The pathophysiology of chronic wounds is multifaceted, involving prolonged inflammation, impaired angiogenesis, and delayed epithelialization.[7] Key contributors include poor blood circulation, neuropathy, and infections,which significantly disrupt the tightly regulated healing process.[3,8] The pathophysiology of chronic wounds involves disruptions in the classical healing pathway, including hemostasis, inflammation, cellular proliferation, and remodeling, leading to prolonged or impaired wound healing.[10] Emerging evidence also highlights the role of genetic factors and immune dysregulation, such as altered expression of key proteins like FOXM1, which are critical for the recruitment of immune cells necessary for tissue repair. [7,8]

Despite advancements in healthcare, a significant gap persists in effective treatment options for chronic wounds.[3] Standard approaches, including debridement and conventional dressings, often fail to address the underlying mechanisms of delayed healing.[4,7] Despite promising clinical results, therapies such as biomaterials and smart bandages remain underutilized. This underuse can be attributed to limited cost-effectiveness studies and regulatory barriers, which hinder widespread adoption. Consequently, addressing gaps in wound care practices and restricted access to specialty care further exacerbate these challenges, especially in low-resource settings.[6,8] This review seeks to analyze the multifactorial risk factors contributing to chronic wounds and evaluate contemporary, evidence-based interventions aimed at improving healing outcomes.[1,3] By addressing gaps in current knowledge, this review highlights the potential for multidisciplinary and innovative approaches to transform chronic wound care.[8] The findings are intended to support clinicians in optimizing therapeutic strategies and guiding future research for more effective interventions.[4,7]

METHODS

A comprehensive literature review was conducted to explore the risk factors and evidence-based interventions for chronic wounds through a systematic search of literature using Google Scholar, a widely used platform for accessing scholarly articles, journals, and books. The search employed thematic keywords such as “chronic wounds, risk factors, interventions,” along with targeted phrases

like "management of diabetic ulcers," "treatment for pressure ulcers," and "techniques in skin grafting" to gather comprehensive and specific insights. Publications from 2014 to 2024 were included to ensure relevance to current practices. The search produced a variety of sources, ranging from general overviews to focused studies on individual aspects of chronic wound care. By analyzing and synthesizing these studies, this review aims to present a thorough understanding of the risk factors and modern therapeutic approaches for chronic wounds. Figure 1 below shows the PRISMA flowchart.

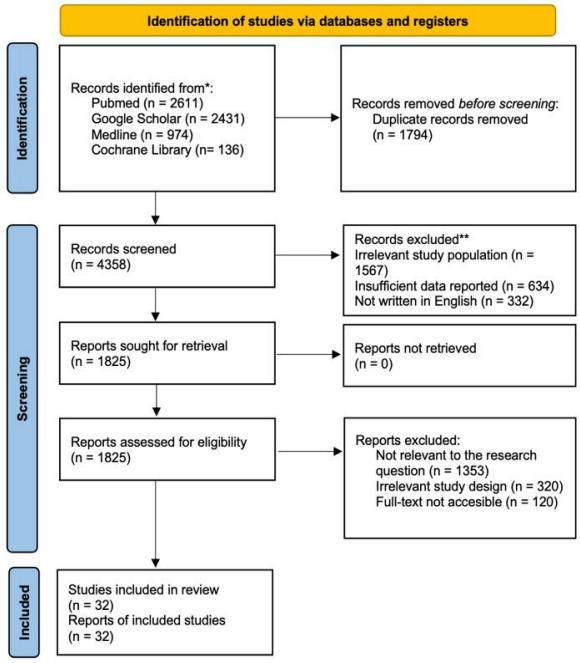

Figure 1. PRISMA Flowchart in This Study

RESULTS

The systematic search conducted across multiple databases, including Medline, Embase, CINAHL, and the Cochrane Library, resulted in a total of 6,152 articles on chronic wound risk factors and evidence-based interventions. Of these, 4,358 articles were published between 2014 and 2024, aligning with the review's criteria. After screening for relevance and removing duplicates, 1,825 articles were further reviewed based on their titles and abstracts. A total of 112 full-text articles were assessed for eligibility.

Ultimately, 32 articles were selected for inclusion in this literature review based on the predefined criteria, including studies on diabetic foot ulcers, pressure ulcers, and venous ulcers. These studies focused on a variety of interventions, such as advanced dressings, negative pressure wound therapy, and skin grafting, as well as key risk factors like diabetes, poor circulation, neuropathy, infection, and aging. Additionally, some studies explored the role of genetic factors and immune dysregulation in wound healing, particularly the impact of proteins like FOXM1 on immune cell recruitment.

The included studies were conducted in various countries, including the United States, the United Kingdom, Australia, and several European nations. The findings from these studies revealed that the most effective interventions for chronic wounds included advanced wound dressings like silver-based dressings and sucrose octasulfate, negative pressure wound therapy, and surgical approaches, such as skin grafting. However, challenges in accessibility and high costs limited the widespread use of some of these treatments, particularly in low-resource settings.

The synthesis of the results suggests that a combination of clinical interventions, patient education, and multidisciplinary care approaches significantly improves chronic wound healing outcomes. Furthermore, the review emphasizes the need for further research into the genetic and immunological factors that contribute to chronic wound development.

DISCUSSION

Risk Factors in Chronic Wound Development

The complexity of the wound healing process makes wounds susceptible to many levels of disruption due to many factors. The most common risk factors identified in the

literature include diabetes, poor circulation, neuropathy, infection, and aging.[9,11] Among these, diabetes mellitus is one of the primary contributors to delayed wound healing. Diabetic foot ulcers are particularly difficult to treat due to impaired immune function and poor blood flow associated with the disease.[12] The elevated blood glucose levels in diabetic patients inhibit the normal inflammatory response necessary for healing, which can delay wound closure and lead to complications such as infections or amputations.[9,13]

In addition to diabetes, vascular insufficiency plays a crucial role in the development of chronic wounds. Impaired blood circulation reduces the delivery of oxygen and nutrients to the affected area, which is essential for tissue repair. Vascular disease is particularly relevant in conditions like venous leg ulcers, where poor venous return causes blood to pool in the lower extremities, further impeding wound healing.[11,12] This impaired venous function occurs because in patients with obesity, intra-abdominal pressure increases, leading to increased reflux, as well as venous diameter and pressure.[14]

Another significant risk factor is neuropathy, which is most common in patients with diabetes but can also occur due to other conditions such as alcoholism and chronic kidney disease. Neuropathy leads to a loss of sensation in the affected areas, which prevents individuals from detecting early signs of wounds, such as cuts or blisters, resulting in untreated injuries that may develop into chronic wounds.[9] Neuropeptides such as nerve growth factor, substance P, and calcitonin gene-related peptide are relevant for wound healing because they cause cell chemotaxis, induce growth factor production, and stimulate cell proliferation.[15]

Infection plays a critical role in the development and persistence of chronic wounds. often delaying healing by prolonging inflammation and disrupting tissue repair. Microorganisms like *Staphylococcus aureus* and *Pseudomonas aeruginosa* commonly form biofilms, which resist antibiotics and immune defenses, leading to persistent inflammation and tissue damage.[16] Chronic wound infections can escalate to systemic complications, especially in immunocompromised patients or those with diabetes.[17]

Approximately 1% to 2% of the population over 60 years of age in developing countries experience chronic wounds during their lifetime.[18] In older people, there are many changes in both physiological and neurological functions in the body that decline and make it difficult for wounds to heal. Younger skin is able to regulate the response to change by producing ECM that adapts to mechanical injury, while older skin atrophies and has a prolonged healing response that often results in inflammation and delays in signal transduction resulting in a lack of ECM production. In addition, in old age there is a decline in the circulatory system which inhibits the wound from achieving angiogenic repair. [19]

Current Evidence-Based Interventions

A significant body of research has focused on identifying evidence-based interventions to improve chronic wound healing. Among the most effective interventions are advanced wound dressings, negative pressure wound therapy (NPWT), and surgical techniques such as skin grafting.[20-22] Advanced dressings, including silver-based dressings, sucrose octasulfate, and hydrocolloids, are designed to provide an optimal wound environment by maintaining moisture, reducing infection, and promoting tissue growth.[20] These dressings have been found to significantly enhance healing rates, particularly for diabetic and venous ulcers, by preventing bacterial colonization and providing a barrier against external contaminants.[21]

Negative pressure wound therapy (NPWT) has also been shown to be effective in managing chronic wounds. NPWT works

by applying controlled negative pressure to the wound, which accelerates healing by improving blood flow, reducing edema, and promoting the formation of granulation tissue.[21] Despite its efficacy, the high cost of NPWT devices and the need for skilled application limit their widespread use, particularly in resource-limited settings.[22]

Skin grafting, often used for larger or deeper wounds, remains a critical surgical intervention. It involves transplanting healthy skin from another area of the body to cover the wound. Recent advancements in grafting techniques, including the use of bioengineered skin, have further improved the success rates of this procedure.[21] However, the challenge remains in ensuring that patients have access to these treatments, which may not be available in all healthcare settings.[22]

Furthermore, innovations such as spray-on skin cells, 3D-printed skin constructs, and stem-cell-enhanced grafts are being explored to enhance healing outcomes and minimize donor site morbidity. These techniques have the potential to accelerate recovery, reduce scarring, and improve the overall functionality of grafted skin. However, factors such as cost, regulatory approval, and the need for specialized equipment limit widespread adoption.

In addition, patient-specific factors, including age, comorbidities such as diabetes or vascular disease, and nutritional status, play a crucial role in graft survival and integration. Optimizing preoperative care, ensuring adequate post-operative wound management, and incorporating multidisciplinary approaches can significantly enhance the effectiveness of skin grafting procedures.

A comparative analysis of different wound therapies reveals significant variations in effectiveness, healing time, and cost. Table 1 summarizes these findings, highlighting key differences between NPWT, advanced dressings, and skin grafting.

Table 1. Comparison of Effectiveness between Wound Therapy Methods

	NPWT	**Advanced Dressings**	**Skin Grafting**
Healing Rate Improvement	40-60% faster healing than standard care[1]	30-50% improvement in wound healing[6]	70-90% wound closure success for full-thickness wounds[11]
Time to Wound Closure	4-6 weeks for moderate wounds[2]	6-8 weeks for moderate wounds[7]	3-6 weeks for full healing[12]
Cost Effectiveness	High initial cost but cost-effective in long-term care[4]	Lower cost, widely accessible[9]	Expensive and requires surgical expertise [14]

NPWT is ideal for accelerating healing in complex wounds despite its higher initial cost. Advanced dressings offer a balance of affordability and effectiveness, suitable for less severe wounds. Skin grafting provides the highest success rates but is resource-intensive, making it best suited for severe wounds requiring complete tissue restoration.

Barriers to Effective Chronic Wound Management

Effective management of chronic wounds is often hindered by various barriers. One key challenge is the lack of adequate knowledge and training among healthcare providers, which can lead to suboptimal care. Many professionals report insufficient wound care education, contributing to delayed healing and complications.[23] Additionally, resource constraints, such as limited access to specialized products and equipment, particularly in rural or low-income areas, exacerbate treatment challenges.[24] Patient-

related factors, including non-compliance with treatment and underlying comorbidities like diabetes, further complicate wound healing, as these conditions impair circulation and immune function.[25] Delayed diagnosis and referral to wound care specialists also contribute to poor outcomes, with many patients presenting too late for effective intervention.[26] Financial barriers, such as the high cost of care and inadequate insurance coverage, can prevent patients from adhering to prescribed therapies.[27] Finally, psychosocial and cultural factors, including mental health issues and stigma, discourage patients from seeking care or following through with treatment plans.[28,29] Overcoming these barriers is essential for improving chronic wound management and ensuring better patient outcomes.

Future Directions in Chronic Wound Research

Looking ahead, several promising areas of research could transform the management of chronic wounds. One such area is the development of "smart" wound care technologies, such as bioengineered skin and intelligent bandages that can monitor wound conditions and release therapeutic agents in real-time. These advancements could greatly enhance wound healing by providing continuous monitoring and targeted treatment.[30] Moreover, advancements in diagnostic tools, such as imaging technologies and biomarkers, could enable earlier detection of chronic wounds and more precise monitoring of healing progress, facilitating timely interventions.[31]

Another exciting direction is the use of stem cell therapy and regenerative medicine to promote wound healing. Stem cells have the potential to accelerate tissue regeneration by stimulating the growth of new blood vessels, skin cells, and other tissue components essential for wound healing.[22,25] Although this field is still in its early stages, ongoing studies are exploring the use of stem cells to treat hard-to-heal chronic wounds, with early results showing promising outcomes.[18]

Furthermore, personalized medicine approaches, which take into account individual genetic profiles and wound characteristics, could significantly improve chronic wound care by tailoring treatments to the specific needs of each patient.[20,21]

The integration of digital health technologies, such as telemedicine and wound care apps, is also an exciting area for research. These technologies can enhance remote monitoring and provide better access to specialist care, particularly in underserved.[32]

Despite promising clinical results, innovative therapies such as biomaterials and smart bandages remain underutilized due to limited cost-effectiveness studies and regulatory barriers.[33-35] The lack of long-term economic evaluations makes it difficult for healthcare providers and policymakers to justify the high initial costs of these technologies.[36] Furthermore, regulatory approval processes for novel wound care products vary across regions, creating additional obstacles to widespread adoption. Addressing these gaps through robust health economic research and streamlined regulatory frameworks is essential to facilitate the integration of innovative wound therapies into standard clinical practice.

Understanding the role of the microbiome in wound healing is another emerging area. The gut and wound microbiomes play a significant role in inflammatory processes, and future research may focus on how modifying these microbiomes can improve healing outcomes.[28]

Lastly, development of health policy strategies to increase access to chronic wound care as one of the most urgent research areas in chronic wound management. Despite advancements in treatment, many patients—especially those in low-resource settings—face significant barriers to receiving timely and appropriate

wound care. Limited availability of specialized wound care centers, high treatment costs, and disparities in insurance coverage contribute to delayed interventions and poor outcomes. Current research should focus on identifying cost-effective healthcare models, such as integrating chronic wound care into primary healthcare services and expanding telemedicine programs for remote monitoring. By integrating chronic wound management protocols into primary healthcare settings, physicians can identify high-risk patients earlier and initiate timely interventions, reducing complications. By addressing systemic gaps through targeted policies, the burden of chronic wounds on healthcare systems could be significantly reduced, improving patient quality of life and decreasing overall healthcare expenditures.

Managing chronic wound infections requires a multidisciplinary approach. Differentiating between infected and uninfected chronic wounds can be challenging, and routine wound culturing is not always appropriate. Debridement is essential to facilitate the healing process. Additionally, proper wound bed preparation and antisepsis must be combined to prevent delayed healing and complications. Systemic antibiotics should be used judiciously, as inappropriate use can lead to multidrug resistance and adverse effects. Therefore, an expert multidisciplinary team is crucial for optimal chronic wound infection management.[37]

This review offers significant strengths, including a synthesis of high-quality evidence from diverse sources and ensuring a comprehensive understanding of chronic wound management. It examines both well-established interventions and emerging innovations, like bioengineered skin and smart bandages, while addressing the role of multidisciplinary, patient-centered care in improving outcomes. The inclusion of global perspectives further strengthens the study by considering variations in healthcare systems and accessibility to advanced chronic wound treatments.

However, this review has several limitations. First, the reliance on secondary data introduces the risk of publication bias, as studies with negative or inconclusive results may be underrepresented. This could lead to an overestimation of the effectiveness of certain interventions. Second, while the review integrates findings from various healthcare settings, its applicability to low-resource environments remains limited due to differences in infrastructure, availability of advanced wound care products, and trained healthcare personnel. Future research should address these disparities by evaluating cost-effective and scalable interventions suitable for diverse socioeconomic contexts.

From a clinical perspective, these limitations highlight the need for further real-world studies that assess the long-term efficacy of novel interventions in different patient populations. Additionally, the findings underscore the necessity of developing standardized treatment protocols that consider genetic and immune-related factors contributing to chronic wounds. On a policy level, this review advocates for increased investment in research and healthcare infrastructure to improve access to innovative wound care solutions, ensuring that transformative technologies are both affordable and widely implemented.

The novelty of this review lies in its exploration of underrecognized genetic and immune factors in chronic wounds and its focus on transformative technologies, such as personalized medicine and digital health. By addressing barriers to accessibility and affordability, it highlights the need for equitable innovations to enhance wound care globally. In addition, this study emphasizes the importance of integrating interdisciplinary approaches that combine molecular biology, immunology, and health technology. It also outlines potential

pathways for translating basic research findings into scalable clinical applications. By bridging gaps between scientific innovation and practical implementation, this review aims to support the development of more effective and inclusive wound care strategies.

CONCLUSION

Chronic wounds remain a major challenge in healthcare, with complex underlying risk factors and limited treatment options. While significant progress has been made in understanding the pathophysiology of chronic wounds, further research is needed to fully unravel the genetic, immunological, and environmental factors that contribute to their development. Evidence-based interventions such as advanced dressings, negative pressure wound therapy, and skin grafting have shown effectiveness, but barriers to accessibility and high treatment costs continue to limit their widespread use.

As chronic wounds become increasingly prevalent worldwide, their management demands a multifaceted, evidence-based approach. Advancements in biomaterials, stem cell therapies, and telemedicine offer promising solutions, but accessibility remains a major barrier, particularly in low-resource settings. Addressing these disparities through policy-driven healthcare reforms and cost-effective treatment strategies is crucial to reducing the health and economic burden of chronic wounds. Moving forward, bridging the gap between technological innovation and clinical application will be key to improving patient outcomes and optimizing wound care on a global scale.

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CONFLICT OF INTEREST

No conflict of interest to be disclosed.

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AUTHOR CONTRIBUTION

VABP contributed to manuscript writing, critical revision, data analysis, and literature review. DSP reviewed, provided expert insights, and approved the final version of the manuscript. EE contributed to manuscript structuring and reviewing relevant literature. MGT was responsible for grammar editing, critical revision, and ensuring coherence in the discussion. HAAT contributed to grammar editing, critical revision, and verification of references for accuracy and relevance. All of the authors approval of this paper for the publishing stages of the research.

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