

The Impact of Psychosocial Influences on Chronic Wound Healing

Kelly Frasier^{1*}, Vivian Li¹, Sara Christoforides², Kathleen Daly³, Alexandra Loperfito⁴, Karina Stech⁵, Milena Dragovic⁶

¹Nuvance Health/Vassar Brothers Medical Center, Poughkeepsie, NY, USA

²Lake Erie College of Osteopathic Medicine, New York, NY, USA

³Medical College of Georgia, Augusta University, Augusta, GA, USA

⁴Edward Via College of Osteopathic Medicine, Blacksburg, VA, USA

⁵Lewis Katz School of Medicine, Temple University, Philadelphia, PA, USA

⁶College of Osteopathic Medicine, California Health Sciences University, Clovis, CA, USA

Email: *kellymariefrazier@gmail.com

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Abstract

This comprehensive review explores the intricate dynamics between psychosocial factors and chronic wound healing processes, specifically focusing on prevalent conditions such as pressure ulcers, diabetic foot ulcers, and venous leg ulcers. By examining the roles of psychiatric conditions, including depression, anxiety, and post-traumatic stress disorder (PTSD), this paper illuminates how these factors intricately influence wound healing dynamics, including mechanisms of pain perception and inflammatory responses. Furthermore, we evaluate the effectiveness of integrated biopsychosocial interventions, which encompass a holistic approach to wound care, thereby enhancing healing outcomes for dermatology patients. Future studies should focus on investigating the specific psychosocial determinants that significantly influence wound healing, exploring novel therapeutic strategies, and implementing personalized interventions to meet the unique needs of each patient. Such endeavors hold promise in advancing the fields of psychodermatology and wound management, fostering a deeper understanding and application of psychosocial considerations in dermatological care.

Keywords

Psychosocial Factors, Chronic Wound Healing, Biopsychosocial Interventions, Psychiatric Conditions, Dermatology Patients

1. Introduction

Wound healing is divided into four stages: homeostasis, inflammation, prolifera-

tion, and remodeling, all of which are controlled by cytokines and growth factors. Chronic wounds are commonly defined as those that do not heal within four weeks, while other guidelines extend the term to six weeks or three months [1]-[4]. Chronic wounds are commonly classified as burns, diabetic ulcers, malignant ulcers, venous ulcers, pressure ulcers, and pyoderma gangrenosum. Chronic wounds such as diabetic ulcers, venous ulcers, and pressure ulcers typically last for more than six weeks to three months without significant healing, while burns, malignant ulcers, and pyoderma gangrenosum can persist for months or even years. The exact duration can vary based on the type of wound and underlying health conditions, but they all share a resistance to normal healing processes, leading to prolonged inflammation and other complications. Each group is defined by particular clinical features such as granulation, slough, and necrotic tissue [3]. Chronic wounds are resistant to normal healing and demonstrate persistent inflammation, which results in raised levels of proinflammatory cytokines, reactive oxygen species, proteolytic imbalance, decreased growth factors, and increased matrix metalloproteinases. This affects the extracellular matrix and inhibits keratinocyte development [1] [3] [5].

A cross-sectional study in Singapore found global prevalence of chronic wounds is between 1.51 and 2.21 per 1000 individuals and rising, with the incidence projected to grow as global populations age [3] [4]. Chronic wounds affect around 8.2 million adults in the United States [6]. Venous ulcers affect 1% of the population of the United States, while pressure sores afflict 0.75% of the population. With over 30 million diabetic individuals in the United States, roughly 1 million will get a foot ulcer each year and 6 - 7 million will develop one during their lifetime [2]. Chronic wounds place a considerable financial strain on healthcare systems in the United States, with treatment expenditures ranging from 28 to 31 billion dollars per year [1] [6]. Chronic wounds place a heavy healthcare-related financial burden on patients as well, with the cost of hospitalizations ranging from \$12,851 to \$16,267 [7].

Chronic wounds exacerbate the negative influence of psychological factors on dermatological patients' quality of life [3] [6]. Those with defective wound healing frequently have several comorbidities, such as anxiety, depression, and post-traumatic stress disorder (PTSD), which further reduces their quality of life [6]. Psychiatric conditions in chronic wound patients are associated with extended infection [6] [8]. Patients frequently feel a lack of control, which affects daily activities and concerns for the future [6]. Undetected psychological strain can severely reduce a patient's quality of life and worsen their skin illness [9]. Chronic wounds therefore inflict significant physical, emotional, and economic costs on individuals and society as a whole [4]. Adopting a psychosocial approach to treating chronic wound patients can improve outcomes by approaching wound treatment holistically. This means considering not only the physical aspects of wound care but also addressing the psychological and social factors that can impact a patient's healing process. By integrating mental health support and social resources into the treatment plan, healthcare providers can better support the overall well-being of

patients, leading to more effective and sustainable recovery.

2. Discussion

2.1. Psychiatric Factors Influencing Chronic Wound Healing

Depression is a prevalent psychiatric comorbidity amongst individuals with chronic wounds [10]. The pathophysiology of depression impacts wound healing by altering immune function, increasing inflammatory responses, and elevating stress hormone levels, which collectively impede the body's natural ability to repair tissue effectively. A study of 216 patients with chronic wounds found depressive symptoms in 37% of the subjects [11]. More specifically, a meta-analysis revealed a 47% incidence of depression in patients with diabetic foot ulcers [12]. The occurrence of depression in people with chronic wounds complicates the healing process due to its effects on the physiological mechanisms of wound healing, adversely affecting outcomes. Thus, patients with depression have stronger associations with chronic, non-healing wounds. For instance, a study utilizing a Hospital Anxiety and Depression Scale found that higher depression scores (>14) were significantly linked to non-healing wounds at a one-month follow-up [13]. Depression impairs crucial physiological processes involved in wound healing, including immune function and inflammation, by dysregulating the hypothalamic-pituitary-adrenal (HPA) axis and sympathetic nervous system [14]. Increased stress hormones like glucocorticoids hinder cell-mediated immunity at wound sites, resulting in delayed healing. Glucocorticoids also diminish levels of pro-inflammatory cytokines and essential chemoattractants at wound sites, disrupting the crucial initial healing phase [15].

Beyond its direct pathophysiological consequences, depression can lead to behavioral patterns that further impede wound healing. Unhealthy behaviors such as reduced nutrition and decreased exercise are associated with depression and can negatively affect healing [15]. Nutritional deficiencies decrease fibroblast proliferation, collagen formation and tensile strength, and angiogenesis, delaying wound healing. Diminished immune function due to decreased T-cell function in nutritional deficiency also increases the risk of infection [16]. Sleep disturbances are common in depression and delay wound healing. Disrupted sleep alters key lymphocytes and macrophages involved in the healing process [13]. Effective wound care is a critical component of healing, and loss of motivation associated with depression may diminish a patient's ability to properly care for themselves. Moreover, chronic wounds often cause pain, functional limitations, and social isolation, exacerbating depressive symptoms and perpetuating the cycle of poor healing [17] [18]. The multifaceted interplay between the physiological impairments and behavioral patterns associated with depression underscores the complex relationship between depression and wound healing.

Though not as prevalent as depression, anxiety disorders may co-occur with chronic wounds, worsening wound severity and healing. Anxiety impacts wound healing by heightening the body's stress response, leading to increased levels of

cortisol and other stress hormones that can suppress immune function and delay the healing process. In terms of chronic care, wound severity refers to the extent of tissue damage and the complexity of the wound, while wound healing pertains to the progress and effectiveness of the recovery process over time, influenced by both medical treatment and the patient's overall health condition. Research shows a variable presence of anxiety in chronic wound patients. Individuals with leg ulcers demonstrated higher rates of anxiety compared to those without such ulcers [19]. In a multidisciplinary foot clinic, 35% of the 60 patients with diabetic foot ulcers reported anxiety symptoms [20]. In a study involving 293 diabetic foot ulcer patients, 7.58% were diagnosed with generalized anxiety disorder [21]. Comorbid anxiety, like depression, has negative implications for wound care and healing. The detrimental physiological effects of psychological stress on wound healing are well-documented and involve various mechanisms [22] [23]. Heightened anxiety levels contribute to increased pain perception, amplification of wound-related distress, and impaired immune responses, all of which hinder the healing process [24]. Anxiety-related symptoms, such as excessive worry and fear of exacerbating wounds, often undermine treatment adherence in chronic wound patients. Notably, wound-related pain during dressing changes is positively correlated with anxiety levels [24]. Non-compliance with prescribed wound care regimens further compromises healing outcomes and prolongs recovery times.

Post-traumatic stress disorder (PTSD) has also been associated with poor wound healing. PTSD impacts wound healing by causing chronic stress and hyperarousal, which elevate cortisol levels and inflammatory cytokines, thereby impairing immune function and prolonging the inflammatory phase of wound healing. Patients with PTSD exhibit a higher likelihood of experiencing delayed wound healing compared to those without the disorder [22]. PTSD is especially common in patients with burn wounds, impacting up to 30% of burn patients [25]. The chronic hyperarousal and hypervigilance characteristics of PTSD contribute to sustained activation of the body's stress response systems, leading to impaired immune function and dysregulated inflammation, which hinder the wound healing process [8]. Neurobiological pathways linking PTSD and impaired wound healing involve dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis and sympathetic nervous system (SNS), resulting in altered cytokine profiles, increased oxidative stress, and reduced angiogenesis [8]. The psychological distress of PTSD may interfere with self-care, impairing the ability of patients to adhere to wound care regimens. Additionally, PTSD is associated with comorbidities such as major depressive disorder, generalized anxiety disorder, and substance use disorder which may exacerbate wound healing complications in tandem [26].

Generally, stress and coping mechanisms emerge as determinants of healing outcomes in patients with chronic wounds. The pathophysiology of stress impacts wound healing by triggering the release of stress hormones like cortisol, which can suppress immune function and delay the inflammatory response necessary for effective wound healing. Additionally, chronic stress can impair tissue repair processes by disrupting cellular signaling pathways involved in wound

closure and tissue regeneration. The impact of stress on wound outcomes is multifaceted, involving both physiological and psychological mechanisms [22] [23]. Stress triggers the release of cortisol and other stress hormones, which can impair immune function and delay wound healing processes. Chronic stress induces lasting changes in biological mechanisms that enhance or inhibit the immune system that may exacerbate inflammation or cause immunosuppression. These changes lead to decreased wound healing capacity, prolonged healing times, and increased susceptibility to infection [11] [22].

Conversely, coping strategies and adaptation techniques may wield significant influence over wound healing trajectories. Improving quality of life can positively impact wound healing outcomes. A qualitative study found that individuals who employ effective coping mechanisms, such as problem-solving, social support seeking, distraction, and maintaining positive affect, experience improved quality of life and wound healing outcomes [27]. Specific stress-reduction techniques can also improve healing. A randomized control trial suggested that engagement in activities such as relaxation techniques and mindfulness meditation, is associated with benefits in the early stages of wound healing [28]. Pharmacological interventions for psychological comorbidities can reduce stress and improve wound healing. For example, pharmacological treatment of depression demonstrates improved wound healing in animal models [29], though further investigation is needed in humans. Overall, understanding the intricate interplay between stress and coping mechanisms is crucial for developing holistic interventions aimed at optimizing chronic wound outcomes.

2.2. Mechanisms Underlying the Influence of Psychosocial Factors on Wound Healing

The mechanisms through which psychological states impact wound recovery are anchored in neuroendocrine pathways, immune function, inflammation, and the perception and modulation of pain. The neuroendocrine system plays a pivotal role in mediating the effects of psychological stress on wound healing. The release of stress hormones, such as cortisol and catecholamines, in response to psychological stress, can significantly impede the healing process. Cortisol, for instance, has been shown to delay wound healing by inhibiting the inflammatory response essential for the initial phase of wound repair [22]. Similarly, catecholamines compromise healing by diminishing blood flow to the wound site. Notably, a study monitoring the healing of punch biopsies revealed that individuals with slower healing rates exhibited significantly higher stress and cortisol levels upon waking compared to their faster-healing counterparts, indicating a direct link between stress and wound healing, independent of health behaviors [30].

The bidirectional communication between the nervous system and immune system, known as neuroimmune interactions, further examines the impact of psychosocial factors on wound healing. Stress activates the sympathetic-adrenal-medullary axis and the hypothalamic-pituitary-adrenal (HPA) axis, leading to the release of neuroendocrine hormones that can dysregulate immune function [31].

This dysregulation manifests as altered cytokine production, including interferons and tumor necrosis factor (TNF), impairing the immune response and, by extension, wound repair. The disruption in cytokine profiles can shift the balance towards a pro-inflammatory state, which, paradoxically, may delay healing by prolonging inflammation [32]. Proinflammatory cytokines play an integral role in the bidirectional communication between the central nervous system and immune system. Proinflammatory cytokines can stimulate the release of stress hormones via the release of corticotropin releasing hormone which stimulates the HPA axis. Additionally, the downregulation of receptors that bind neuroendocrine hormones in response to chronically elevated levels of stress hormones reduces sensitivity to cortisol and contributes to prolonged inflammation and risk of tissue damage from proinflammatory cytokines [33].

The impact of psychological stress extends to the immune system's capability to effectively respond to wounds. Stress can suppress the activity of key immune cells, such as lymphocytes and macrophages, essential for wound cleaning, infection prevention, and tissue repair [32] [34]. The role of inflammatory mediators in wound healing is intricate, with stress-induced shifts in pro-inflammatory and anti-inflammatory mediators complicating tissue regeneration and potentially promoting chronic inflammation, detrimental to the healing process [35].

Pain perception is significantly influenced by psychological factors, such as stress, anxiety, and depression. These psychological factors can exacerbate pain sensation and sensitivity through central sensitization, which refers to the heightened response of the central nervous system to stimulation [36]. This phenomenon not only results in increased pain in individuals with chronic wounds but also negatively affects their quality of life and treatment adherence. Chronic wound pain is further complicated by neuroplastic changes in the brain and spinal cord, influenced by psychological states and leading to an intensified pain response, which presents additional challenges in pain management [37]. Understanding the psychological factors contributing to pain perception and central sensitization is crucial for the development of effective pain management strategies in patients with chronic wounds.

2.3. Impact of Psychosocial Factors on Chronic Wound Outcomes

It is important to consider the physiology behind psychosocial factors involved in healing when studying predictors of delayed wound healing. Patients with depression demonstrate slower wound healing rates [29]. Stress and depression also impact the immune system, leading to increased wound severity and slower recovery [38] [39]. Psychological stress stimulates stress response systems, such as the HPA and sympathetic-adrenal-medullary axes, which increase glucocorticoid and catecholamine production and can have a direct impact on recovery [40] [41]. PTSD has distinct biological characteristics, including increased inflammation, oxidative stress, metabolic imbalance, and impaired angiogenesis, that contribute to slowed wound healing. PTSD severity is linked to chronic wound severity [8].

Psychosocial factors play an important role in the outcomes of chronic wounds. Lower educational attainment is frequently associated with worse health outcomes and may be linked to factors such as low health literacy and socioeconomic status. Contrastingly, higher education levels are associated with faster recovery times. Increased stress, depression, and poor perceptions of illness are linked to slower wound healing [38]. Individuals with higher stress levels are more likely to consume alcohol and tobacco, exercise less, have sleep disruptions, and make poorer nutritional choices than individuals with lower stress levels. Heavy alcohol consumption slows cell migration and collagen deposition at wound sites, impeding the healing process. Smoking is also associated with decreased wound healing in both naturally occurring and surgical wounds. Sleep deprivation delays skin barrier regeneration and lowers growth hormone synthesis. Insufficient physical activity can also slow wound healing. Furthermore, insufficient intake of glucose, polyunsaturated proteins, and certain vitamins can delay the healing process [40]. Patients may be unaware of the harmful effects of behaviors on health outcomes without proper education or health literacy.

Living with a wound can result in the loss of freedom, mobility, and employment, which may negatively impact mental health and socioeconomic status. Adaptive capacities are reduced in response to a perceived loss of control which may serve as a predictor for future complications. Patients may feel powerless in adjusting to life with a wound, leading to psychological distress which negatively affects the physiological wound healing process [42]. Perceived loss of control may contribute to mood disorders like depression, which remains a persistent risk factor for mortality in people with their first diabetic foot ulcer. Early depression treatment may reduce mortality rates in chronic wounds [42]. In a study of 32 subjects with cutaneous wounds divided evenly into groups with and without social support, the group with social support demonstrated lower levels of anxiety and stress hormones as well as faster rates of wound healing [43]. These findings suggest that social support may play a role in improving outcomes in chronic wound healing by mediating the psychological impacts of wounds. Financial factors may also play a role in wound healing through indirect mechanisms. Proper bandaging adherence speeds up wound healing, however, a lack of financial resources and suitable transportation create barriers to access to proper care [38].

Pain is a common, heterogeneous symptom experienced by patients with chronic wounds that has significant impacts on quality of life [44]. Pain and fatigue are recognized limitations in maintaining quality of life [45]. Individuals with chronic wounds face major challenges due to persistent discomfort. These individuals may avoid social interactions due to skin injury, pain, foul smell, and wound drainage leading to decreased social participation. This may lead to feelings of isolation and contribute to the development of anxiety, depression, and other mental health concerns which affect both physical and psychological well-being [42] [45]. Chronic wound pain is frequently undertreated, especially

amongst the elderly [46].

Effective treatment of pain in chronic wounds requires a multidisciplinary team to mitigate the effects of pain on quality of life and wound treatment. Empathy is essential in the treatment of individuals with painful chronic wounds, particularly when addressing pain symptoms [46]. It is recommended that healthcare providers integrate psychological exams as part of the treatment evaluation procedure. This information can help guide treatment plans that include psychological support to improve patient outcomes [45]. Additionally, using non-traumatic bandages to reduce pain and minimizing pain in wound dressing changes is a critical component of care to ensure proper wound care [44] [46]. It is necessary to assess each patient individually to guarantee appropriate interventions for their specific concerns as pain symptoms are heterogeneous in the chronic wound population [42].

In terms of vulnerable populations, the elderly and those with compromised immune systems are more highly susceptible to wound-related complications. Chronic wounds are ideal for the growth of bacterial colonies and biofilms. The injured tissue provides a rich food supply, while the alkaline pH associated with non-healing wounds promotes bacterial growth. Bacteria can also exacerbate wound conditions by increasing the pro-inflammatory environment [1]. Chronic wounds are also prone to wound infections due to stress. Enhanced sensitivity to stress appears to be mediated by a decrease in epidermal antimicrobial peptide synthesis [40]. When bacteria from the wound site enter the bloodstream, it can cause blood poisoning, septicemia, sepsis, or septic shock [1].

Recurrence rates in chronic wounds are high. Diabetic foot ulcers demonstrate a 1-year recurrence rate of 42% and a 5-year recurrence rate of 65% [47]. A study of 80 patients with diabetic foot ulcers demonstrated higher recurrence rates than the general population. Decreased compliance with wound care and diabetes management is suggested mechanisms behind the relationship between wound recurrence and depression [48]. However, other studies indicate weak support for the association between depression and ulcer recurrence [49].

Interdisciplinary techniques addressing stress management, smoking cessation, nutrition, medication management, and structured exercise programs have demonstrated promise in terms of patient satisfaction and quality of life [45]. Psychosocial therapy can help to ease fears and anxiety while also addressing cofactors including genetic susceptibility, obesity, lack of exercise, smoking, diabetes, hypertension, hyperlipidemia, and stress [45]. These findings highlight the importance of taking a comprehensive approach to wound healing, particularly for people with chronic psychiatric illnesses.

2.4. Evaluation of Integrated Biopsychosocial Interventions

Psychological stress has a profound negative impact on wound healing. Several literature reviews, case reports, and case-control studies have investigated the role of integrated biopsychosocial interventions in the improvement of chronic wound healing. There are several interventions that range from psychological

interventions to social support programs and mind-body therapies that demonstrate promise in the treatment of chronic wounds and their psychiatric comorbidities.

2.5. Psychological Interventions

Psychological interventions have been shown to improve immune function and reduce HPA activity and catecholamine levels with varying efficacy [50] [51]. Cognitive behavioral therapy (CBT) is a form of psychotherapy that aims to redirect negative beliefs towards increasingly goal-oriented thinking. CBT fosters problem-solving skills, alters negative cognitive patterns, and shapes coping mechanisms in patients with chronic wounds and ultimately leads to improved quality of life and enhanced healing [52]. Psychological interventions also involve those of Mindfulness-Based Stress Reduction (MBSR). MBSR aims to promote a controlled, non-judgmental evaluation and awareness of experiences. This technique reduces stress and anxiety and contributes to improved quality of life. A randomized control study demonstrated that patients that received MBSR showed overall lower levels of IL-9 and placental growth factor in their wound as well as greater reductions in skin permeability 3 and 4 days after wound induction [28]. The efficacy of psychological interventions in improving the outcomes in chronic wound healing presents a potential non-pharmacological option for patients.

2.6. Social Support Programs

Social interactions and social participation are significantly reduced in patients with chronic wounds [53]. Studies have consistently demonstrated that social isolation impairs wound healing [54]. A systematic review by Robinson *et al.* demonstrated improvement in wound healing with social support, with the extent of the effects dependent on the support type offered to the patient [51]. Social support serves to reduce cortisol levels and stress while increasing levels of oxytocin leading to improved wound healing [55]. Oxytocin promotes wound healing via suppression of HPA activity [54] [55]. In those with chronic venous ulcers, some patients demonstrated wound improvement when engaged in group nursing home activities [56]. The effects of social support on outcomes in chronic wound healing are inconsistent [51] [56]. Involvement of the family in wound care education can also have a powerful impact on wound healing by allowing caregivers to be more active participants in the patient's wound care and to recognize early signs of poor wound healing and infection [57]

2.7. Mind-Body Therapies

Mind-body therapies, including relaxation techniques, yoga, biofeedback, and hypnosis, demonstrate positive impacts on wound healing. Relaxation techniques demonstrate the most significant improvements [51]. A study by Broadbent *et al.* found that a combination of pre-operative music, deep breathing,

muscle relaxation, and guided imagery resulted in decreased overall stress levels and increased hydroxyproline deposition at 7 days of post-operative laparoscopic cholecystectomy [58]. Yoga and expressive writing interventions also show improvements in wound healing [51]. Yoga has a significant therapeutic benefit through normalization of HPA activity and increased mindfulness [59]. Other mind-body therapies such as hypnosis have shown promising effects on wound healing. In a randomized control trial, post-surgical patients receiving hypnosis showed objectively improved wound healing when compared to standard surgical site care protocols [60].

Taken together, these findings indicate the importance of a multidisciplinary approach to the treatment of chronic wounds. Integrated biopsychosocial interventions play an integral role in improving outcomes in patients with chronic wounds by addressing psychiatric comorbidities and reducing the inhibitory effects of psychological distress on wound healing.

2.8. Future Directions for Research

Future research should prioritize identifying the specific psychosocial determinants that most significantly influence wound healing. This includes understanding how factors such as socioeconomic status, social support networks, and individual coping mechanisms directly impact the healing process and patient outcomes. Detailed studies exploring the interaction between these psychosocial elements and biological healing mechanisms could shed light on critical insights into how mental health and social conditions exacerbate or alleviate chronic wound conditions. By pinpointing these determinants, researchers can develop more targeted interventions that address both the psychological and physical aspects of wound care, thereby enhancing the overall effectiveness of treatment protocols.

Additionally, future research should focus on developing and testing novel therapeutic strategies that integrate biopsychosocial models of care. This includes creating personalized treatment plans that are tailored to the unique psychological and social needs of each patient. Investigating the efficacy of combined therapies, such as cognitive-behavioral therapy (CBT) with conventional wound care, could reveal significant improvements in healing rates and patient satisfaction. Furthermore, the implementation of technology-based interventions, like telehealth mental health support and mobile health applications, could provide accessible and continuous psychosocial care for chronic wound patients. By advancing these integrated approaches, the fields of psychodermatology and wound management can offer more holistic and effective solutions, ultimately leading to better health outcomes and quality of life for patients suffering from chronic wounds.

More research is additionally needed to further characterize the longitudinal relationship between psychosocial influences and wound healing. A longitudinal study on the effects of psychological distress in patients with diabetic foot ulcers demonstrated altered immune cell ratios and circulating microRNA expression

in subjects who reported psychological distress. Psychological distress improved by a factor of more than 2.5 following stress-reducing interventions which was followed by a normalization of immune cell levels [61]. Identifying the causal relationship between psychosocial factors and wound healing may mitigate complications of delayed wound healing. Additionally, characterizing long-term psychosocial outcomes in patients with chronic wounds that have healed may guide treatment of chronic wounds and their psychosocial comorbidities.

Research further characterizing the relationships between socioeconomic status, education, pain perception, and social support with chronic wound healing is necessary to improve the way psychosocial factors are addressed in wound treatment. Prior research describes the psychosocial factors of depression, anxiety, and PTSD as delaying wound healing [14] [22] [24]. Some work has been done to explore the roles of socioeconomic status, level of education, and pain perception on wound healing [36] [38]. Additionally, the findings regarding the effects of social isolation and outcomes in chronic wounds are inconsistent [51] [55] [56]. A developed understanding of psychosocial influences on chronic wound healing contributes to a more holistic approach to chronic wound patients. The involvement of an interdisciplinary team with psychosocial care, such as behavioral health professionals and social services, can help expedite the healing process for patients who face adversity related to these psychosocial influences. The psychological and pain symptoms in patients with chronic wounds are heterogeneous, indicating the need for individualized approaches to treatment [44]. This is also an avenue for the use of more digital health technologies to screen patients for factors that may impair wound healing.

Currently, research addressing the use of telehealth interventions for psychiatric comorbidities in the chronic wound population is lacking. Cost, transportation, and time limitations may also limit access to care for patients [38] [62]. Telehealth may play a role in improving access to care, and thus outcomes, for patients with chronic wounds. A systematic review of telehealth and wound care outcomes indicates that the outcomes of telehealth wound care are not inferior to in-person care. However, outcomes are inconsistent indicating a need for further research on the utility of telehealth in chronic wound care [63]. Telehealth interventions increase access to psychological care providers, such as therapists and psychiatrists. Improved access to mental health care for patients with anxiety and depression, particularly in patients with low socioeconomic status, leads to better outcomes than patients who lack care [62]. There are also mobile applications targeted towards patients with chronic wounds, with features such as wound education and wound monitoring. However, the quality of these applications was rated as mediocre by both physicians and patients indicating the need for further application development to improve their utility in patient care [64].

Another avenue for future research and recommendation includes exploration of novel therapeutic treatment agents, necessary for treating chronic wounds due to their complex pathophysiology. The current standard of treatment for chronic

wounds involves debridement, bandages, antibiotic medications, dressing changes, and pain management [65]. As discussed in this review, neuroendocrine pathways, immunity, inflammation, and pain are all involved with chronic wound healing. These aspects can serve as therapeutic targets through biochemical interactions or alternative approaches that do not include medications. Bioactive dressings may aid in chronic wound healing through the immunomodulatory effects of ingredients such as β -glucans, vitamin C, and hydrocortisone at the site of the wound. Dressings enriched with vitamin C and hydrocortisone stimulate wound healing by increasing type I collagen deposition by fibroblasts and promoting fibroblast migration and proliferation [66]. β -glucans stimulate macrophage infiltration, promoting tissue granulation, collagen deposition, and reepithelialization [67]. Stimulation of the healing response directly at the site of a chronic wound shows promise, particularly in the setting of systemic immunosuppression due to stress in chronic wound patients. Vagus nerve stimulation may also promote healing in chronic wounds by promoting cholinergic anti-inflammatory pathways, modulating cytokines, and activating pro-resolution mediators [68]. Additional research into immunomodulatory interventions may improve quality of life in patients with chronic wounds by lessening the duration of healing and minimizing the psychosocial impacts of wounds.

In terms of alternative treatments, some evidence supports the use of topical endocannabinoids to promote wound healing and manage pain in chronic wounds; however, further investigation is necessary to determine their usefulness in the management of chronic wounds [69]. Non-pharmacological interventions for pain reduction in chronic wounds are centered around reducing psychological distress. Stress-reducing interventions that promote relaxation and mindfulness demonstrate promise in the treatment of chronic wounds and associated pain. Decreasing stress improves wound healing and reduces pain without the use of pharmacological agents. These effects are likely mediated by decreases in the elevated levels of cortisol and adrenaline associated with chronic stress [70]. Further characterizing the relationship between stress and pain in chronic wounds may aid in the development of novel targets to modulate pain.

Future research should prioritize identifying specific psychosocial determinants such as socioeconomic status, social support, and coping mechanisms that influence wound healing, exploring their interactions with biological healing mechanisms to develop more targeted, effective interventions. Studies should also focus on integrating biopsychosocial models into personalized treatment plans, examining combined therapies like cognitive-behavioral therapy (CBT) with conventional wound care, and leveraging technology-based interventions such as telehealth and mobile health applications to provide continuous psychosocial care. Additionally, investigating novel therapeutics, including bioactive dressings and vagus nerve stimulation, alongside stress-reducing non-pharmacological interventions, may enhance wound healing and minimize the psychosocial impacts of chronic wounds, ultimately leading to improved quality of life and more

holistic care for patients.

3. Conclusions

Psychosocial factors play a central role in chronic healing processes, with psychiatric conditions and stress hindering the process. Wound healing is a multifaceted mechanism involving neuroendocrine pathways, the immune system, and pain modulation. The baseline complexity of wound healing is further hindered by psychological conditions such as depression, anxiety, and PTSD. Not only do these conditions themselves impact healing, but they also influence behavioral patterns that influence healing. Stress hormones and inflammatory mediators play a vital role in chronic wound healing and present a means for intervention.

Numerous studies have examined the impact of integrated biopsychosocial interventions on chronic wound outcomes, specifically psychological interventions, social support programs and mind-body therapies. Each plays a unique role in addressing the psychosocial factors of wound healing, but the literature overwhelmingly supports the use of mindfulness and relaxation techniques. This further perpetuates the importance of stress hormones in the wound healing process.

Further research outlined in this review highly supports the development of a longitudinal study examining the interplay of psychosocial factors on chronic wound healing. Furthermore, the integration of psychosocial screenings in dermatology clinics and the partnership with behavioral health professionals may serve as an avenue to better identify barriers to wound healing. The complexity of psychosocial factors and their direct role in dermatological conditions hold promise for the advancement of new methods of personalized care.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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