

Challenges Psoriasis and Its Impact on Quality of Life: Challenges in Treatment and Management

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Abstract: Psoriasis, a chronic inflammatory disease affecting approximately 3% of the global population, presents complex challenges that extend beyond its physical manifestations. This comprehensive review examines the multidimensional impact of psoriasis on patients' lives, encompassing physical, psychological, and social aspects. We analyze current therapeutic approaches, from traditional systemic treatments to cutting-edge biological therapies and emerging oral medications, evaluating their efficacy, limitations, and accessibility. The review explores how disease severity correlates with quality of life measures and psychological burden, noting the high prevalence of depression (20%), anxiety (21%), and suicidal ideation (0.77%) among affected individuals. However, emerging evidence suggests that clinical severity, as measured by PASI or BSA, does not always correlate with the psychoemotional burden experienced by patients, highlighting the need for a more comprehensive assessment of disease impact. We discuss the evolution of treatment strategies, highlighting recent developments in targeted therapies, including JAK inhibitors, particularly selective TYK2 inhibitors, and PDE4 inhibitors, which offer promising alternatives to traditional treatments. Additionally, we examine the role of various assessment tools and quality of life measures in evaluating treatment outcomes. The analysis emphasizes the need for a holistic approach to patient care that integrates medical interventions with psychological support, addressing both the visible and invisible burdens of the disease. This review underscores the importance of personalized treatment strategies that consider not only clinical efficacy but also patient preferences, accessibility, and long-term safety profiles.

Keywords: psoriasis, quality of life, treatment challenges, psychological impact, biologics, systemic treatments, TYK2 inhibitors, PDE4 inhibitors

Introduction

Psoriasis, a chronic inflammatory condition affecting approximately 3% of the global population, impacts both the skin and joints. This disease is associated with disability levels on par with major health conditions such as cancer, hypertension, arthritis, diabetes, and heart disease. The physical manifestations of psoriasis include lesions that often cause itching, pain, and soreness, and in severe cases, the skin may fissure and bleed. McKenna, S.P. Measuring patient-reported outcomes: Moving beyond misplaced common sense to hard science.^{1–3}

Beyond the physical symptoms, individuals with psoriasis frequently endure significant psychological distress. This includes social embarrassment, diminished body satisfaction, anxiety, depression, and an increased risk of suicidal behaviors. Such psychological challenges can hinder effective self-management of the condition, emphasizing the need for comprehensive treatment approaches that address both the physical and emotional aspects of psoriasis.^{4,5}

Psoriasis stands as one of the most significant chronic inflammatory skin conditions affecting millions worldwide, with profound implications that extend far beyond its visible manifestations. This immune-mediated disease presents a complex challenge to both patients and healthcare providers, characterized by its unpredictable nature and widespread

impact on various aspects of life.⁶ Understanding the full scope of psoriasis's influence on quality of life and the challenges faced in its treatment has become increasingly crucial for developing effective management strategies.⁷

The Disease Burden

Psoriasis vulgaris is a prevalent chronic, recurrent, inflammatory dermatosis driven by an intricate interplay between genetic predisposition and environmental factors. It is classified as an immune-mediated condition, reflecting its underlying pathogenetic mechanisms.^{8,9}

Clinically, psoriasis is characterized by erythematous-squamous plaques, predominantly, but not exclusively, distributed symmetrically on extensor surfaces, such as the elbows and knees, as well as the scalp and lumbosacral regions.¹⁰ These plaques illustrate key pathological processes, including inflammation, keratinocyte hyperproliferation, and angiogenesis.¹¹ However, current evidence underscores that psoriasis extends beyond cutaneous manifestations, with systemic inflammatory involvement.

In cases of moderate-to-severe psoriasis, elevated levels of pro-inflammatory markers and cytokines—such as TNF- α , IL-6, IL-17, IL-23, and C-reactive protein (CRP) — are observed not only in lesional skin but also in systemic circulation and other biological matrices, including saliva.¹² Advanced imaging techniques, particularly FDG-PET/CT, have demonstrated subclinical inflammatory activity in diverse tissues, including the liver, joints, tendons, subcutaneous tissue, and arteries, indicating global inflammation in affected individuals.¹³

Moreover, psoriasis shares a spectrum of immunological and pathophysiological features with other immune-mediated inflammatory diseases, such as rheumatoid arthritis,¹⁴ and inflammatory bowel disease.¹⁵ Among comorbidities, psoriatic arthritis (PsA) is the most prominent, affecting up to 30% of individuals with psoriasis, thereby underscoring the need for holistic patient management.⁶

Psychological and Social Impact

The psychological and social impacts of psoriasis often rival or even exceed the physical manifestations of the disease, profoundly affecting mental and social well-being. Patients frequently encounter stigma and social isolation, exacerbated by visible lesions, leading to decreased self-esteem and significant effects on personal relationships, career choices, and social interactions. This creates a cycle of stress that can further deteriorate the condition. The research highlights that rates of depression and anxiety are considerably higher among psoriasis patients compared to the general population, emphasizing the critical need for integrated psychological support within their treatment plans.¹⁶

Adding to the complexity of managing psoriasis, numerous studies have identified a significant mental health burden among sufferers. However, emerging evidence suggests that the severity of psoriasis, as measured by PASI or BSA, does not always correlate with psychoemotional distress. Even patients with mild psoriasis may experience significant psychological burden, highlighting the need for a comprehensive and interdisciplinary approach to care.^{17,18} For example, feelings of shame and guilt are linked to increased suicidal thoughts,¹⁹ and patients are more prone to substance abuse, including alcohol, smoking, and the use of sedatives and antidepressants. The severity of the disease tends to amplify mental health issues, which in turn can exacerbate clinical symptoms, creating a challenging cycle that complicates effective management.²⁰ Moreover, patients experiencing mental health issues often show resistance to medical treatments and non-compliance, leading to prolonged and costly treatment processes.¹⁹

A comprehensive review by Liu et al analyzed the global epidemiology of mental health comorbidity in psoriasis patients from 1986 to 2019. This study found a cumulative prevalence of depression, anxiety, and suicidal tendencies at 20%, 21%, and 0.77% respectively among psoriatic adults, with incidence rates per 1000 person-years for depression, anxiety, and suicidal behavior at 42.1, 24.7, and 2.6. Notably, psoriatic patients in North America showed higher relative prevalence rates of depression and suicide, while those in South America were more affected by anxiety.²¹

Research has shown that how patients perceive their illness significantly influences their emotional responses and overall health outcomes.²² However, understanding of psoriasis among patients is often limited, and support is lacking, underlining the necessity for high-quality, theory-based educational materials to improve patient comprehension of the disease and reduce anxiety.²³

While psoriasis is primarily a skin condition, focusing solely on physical symptoms does not adequately address the associated comorbidities and their psychosocial impacts. These include social stigmatization and impaired self-esteem and interpersonal relationships, contributing to significant emotional burdens that adversely affect quality of life.²⁴ Despite the profound impact, the psychosocial effects of psoriasis are frequently underestimated by healthcare providers. Acknowledging and addressing the factors that contribute to depression and suicidal ideation in patients with psoriasis is crucial for enhancing the quality of care and developing treatment plans that encompass psychosocial interventions.

Moreover, the social implications of psoriasis permeate into professional life, where patients may experience workplace discrimination or feel constrained in their career options. The visibility of symptoms can lead to misconceptions and prejudice, while the unpredictable nature of flare-ups can impact work attendance and performance, adding stress that may trigger or exacerbate psoriasis symptoms, thus perpetuating a challenging cycle to break.²⁴

Quality of Life in Psoriasis and Its Measurement

Quality of life (QoL) encompasses all aspects that impact an individual's life, reflecting the degree to which one's hopes and expectations align with their experiences. Health-related quality of life (HRQOL), a subset of QoL, specifically relates to health aspects, including psychological, social, and physical wellbeing. Psoriasis, a chronic inflammatory skin condition, significantly affects HRQOL by limiting daily activities, occupational and sexual functioning, and is known for more severely impairing psychosocial rather than physical activities.²⁵

In addition to limiting daily activities, occupational, and sexual functioning, psoriasis also profoundly affects patients' emotional well-being and social interactions. Visible lesions often lead to stigma and social isolation, contributing to decreased self-esteem and difficulties in maintaining personal and professional relationships. For instance, individuals with psoriasis report feeling ashamed or flawed, with younger patients experiencing heightened guilt and sensitivity to societal opinions.²⁶

The economic impact of psoriasis further compounds its burden. Many patients face challenges related to work productivity, absenteeism, and presenteeism. Studies utilizing tools such as the Work Productivity and Activity Impairment (WPAI) questionnaire have shown that moderate-to-severe psoriasis is associated with significant reductions in workplace efficiency and activity levels, leading to financial instability for affected individuals.²⁷

Social awareness campaigns and public education could play a pivotal role in reducing stigma and improving the quality of life for those with psoriasis. Enhanced understanding and broader acceptance within society are essential for mitigating feelings of alienation and exclusion experienced by patients.²⁸ Psychological interventions, such as cognitive-behavioral therapy, relaxation techniques, and biofeedback, have shown promise in helping patients manage stress and build resilience, further emphasizing the need for integrated care approaches.²⁶

Despite advancements in therapeutic options, the lack of public awareness and the persistence of misconceptions about psoriasis remain significant barriers to improving patients' quality of life. Collaborative efforts between healthcare providers, patient advocacy groups, and policymakers are essential to address these challenges effectively and holistically.²⁹

Impact of Psoriasis on HRQOL

Psoriasis can be a particularly frustrating disease for both patients and healthcare providers due to its chronic, recurring nature. The unpredictability of flare-ups contributes to a reduced sense of control, a fear of unexpected outbreaks, and a prevailing feeling of hopelessness regarding the possibility of a cure. These factors collectively lead to a diminished HRQOL in psoriasis patients. The psychological and social burdens can be profound, often exceeding the physical discomfort caused by the disease. This encompasses a range of emotional responses from embarrassment and social withdrawal to severe depression and anxiety, which can exacerbate the disease's physical symptoms, creating a challenging cycle of health deterioration.³⁰

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physical discomfort caused by the disease. This encompasses a range of emotional responses from embarrassment and social withdrawal to severe depression and anxiety, which can exacerbate the disease's physical symptoms, creating a challenging cycle of health deterioration.^{28,31}

Moreover, studies have shown that psoriasis significantly disrupts patients' daily lives, impairing their ability to maintain personal relationships and participate in social and professional activities. This disruption is particularly pronounced in patients with visible lesions, such as on the face or hands, which often lead to stigma and discrimination. Patients frequently report feelings of shame and a reduced sense of self-worth, contributing to an elevated prevalence of mental health conditions, including depression and anxiety.^{32,33}

The extent of HRQoL impairment is often linked to the severity and location of psoriatic lesions. For instance, lesions on sensitive or visible areas, such as the scalp or genitals, are associated with higher Dermatology Life Quality Index (DLQI) scores, reflecting greater psychological and social distress. Notably, studies have observed a direct correlation between higher Psoriasis Area and Severity Index (PASI) scores and increased DLQI scores, emphasizing that as disease severity worsens, so does the overall impact on quality of life.^{32,34}

Additionally, psoriasis affects patients beyond the physical manifestations, with its chronic nature leading to significant financial and emotional burdens. The cost of long-term treatment, combined with lost productivity due to absenteeism, exacerbates these challenges. Importantly, the development of novel therapeutic approaches, such as biologics and small molecule inhibitors, has demonstrated potential in improving HRQoL by providing more effective symptom management and reducing disease severity.^{31,32}

Overall, a holistic approach to psoriasis management, which integrates physical treatment with psychological support and addresses social stigmatization, is crucial for improving the HRQoL of affected individuals. Tailoring treatment strategies to address individual needs and preferences can further enhance outcomes, ensuring that care extends beyond mere skin clearance to encompass the emotional and social dimensions of the disease.^{28,32,33}

Assessment of Quality of Life in Psoriasis Through Disease-Specific Measures

Psoriasis profoundly affects the quality of life (QoL) of patients, necessitating the use of specific measures to accurately assess both the physical severity and the psychosocial impact of the disease.³⁵ Here we discuss several psoriasis-specific instruments developed to address these dimensions.

Psoriasis-Specific Quality of Life Measures

1. **Psoriasis Index of Quality of Life (PSORIQoL)** The PSORIQoL is a 25-item dichotomous instrument developed from interviews that assess the individual's capability to satisfy their needs. This tool focuses on the personal impact of psoriasis, gauging how well patients can meet personal health and wellness goals despite their condition.³⁶
2. **Psoriasis Life Stress Inventory (PLSI)** The PLSI is a 15-item questionnaire designed to measure the psychosocial stress associated with managing daily life while coping with psoriasis. With scores ranging from 0 to 45, this instrument helps quantify the stress burden imposed by the disease, reflecting the challenges patients face in their routine activities.³⁷
3. **Psoriasis Disability Index (PDI)** The PDI specifically addresses the self-reported disability across various aspects of life including daily activities, employment, personal relationships, leisure, and the impact of treatments. This 15-item scale provides insights into how psoriasis affects functional status and quality of life.³⁸

Clinical Severity Measures

4. **Psoriasis Area and Severity Index (PASI) and Simplified PASI** The PASI is a clinical tool used to measure the severity of psoriasis based on body surface area involvement and the severity of lesions characterized by erythema, scaling, and induration. The maximum score for PASI is 72, offering a comprehensive view of disease severity. The

Simplified PASI allows patients to self-assess their condition, facilitating ongoing monitoring without clinical intervention.^{39,40}

Skin-Specific Psychosocial Measures

5. **Questionnaire on Experience with Skin Complaints (QES)** The short form of the QES, consisting of 23 items, examines the social and psychological burdens of psoriasis, particularly focusing on stigmatization, a significant concern for many patients. This instrument validates the emotional and social challenges faced by individuals with psoriasis.⁴¹
6. **Dermatology Life Quality Index (DLQI)** The DLQI is a concise self-reported questionnaire encompassing 10 items that assess feelings, daily activities, leisure, work, personal relationships, and treatment effects over the previous week. It measures HRQOL in patients with skin diseases, highlighting the specific impacts of dermatological conditions on overall life satisfaction.^{42,43}

These instruments play a critical role in both clinical practice and research, enabling a better understanding of the comprehensive impact of psoriasis.

Therapeutic Approaches in Psoriasis

The management of psoriasis has evolved significantly in recent decades, with the therapeutic armamentarium expanding to include multiple targeted approaches. Current management strategies for moderate-to-severe psoriasis encompass a variety of systemic therapies, each with distinct mechanisms of action and safety profiles.⁴⁴

Traditional systemic treatments, including methotrexate, cyclosporine A, and acitretin, remain widely utilized but present considerable limitations.⁴⁵ Methotrexate, while effective through its antiproliferative and immunomodulatory properties, requires vigilant monitoring due to potential hepatotoxicity, myelosuppression, and pulmonary complications.⁴⁶ The cumulative toxicity risk necessitates regular laboratory surveillance and may limit long-term use. Cyclosporine A, despite its rapid onset of action through calcineurin inhibition, carries significant risks of nephrotoxicity and hypertension, demanding careful monitoring of renal function and blood pressure.⁴⁷ UV phototherapy is an effective and widely used treatment for psoriasis, particularly emphasizing narrowband UVB (NB-UVB) therapy combined with oral retinoids to achieve shorter treatment duration and fewer side effects. The therapeutic effects of UV radiation include immediate cellular responses such as DNA damage and lipid peroxidation, and delayed immunological changes involving antigen-presenting cells and Th17 cells. PUVA therapy, combining psoralens with UVA, is highly effective but carries risks like increased skin cancer potential, limiting its use.^{48,49}

The advent of biological therapies has revolutionized psoriasis treatment by specifically targeting immune pathways involved in the disease such as TNF- α and the IL-23/IL-17 axis.⁵⁰ As the oldest class of approved biologics in psoriasis treatment TNF- α inhibitors, including etanercept, infliximab, adalimumab, and certolizumab effectively decrease the inflammatory cascade central to the disease pathogenesis. Among TNF- α inhibitors, infliximab exhibits the highest efficacy for plaque psoriasis, followed by similar effectiveness for certolizumab and adalimumab, and then etanercept. However, these medications typically require more frequent subcutaneous dosing compared to newer biologics targeting IL-17 and IL-23. Safety profiles for TNF- α inhibitors are well-established, although vigilance is essential due to associated risks.⁵⁰ IL-17 inhibitors, including secukinumab, ixekizumab, and bimekizumab, are biologics targeting the IL-17 pathway. Secukinumab and ixekizumab specifically inhibit IL-17A, while bimekizumab targets both IL-17A and IL-17F. These agents are characterized by rapid onset, robust responses, and sustained efficacy in treating moderate-to-severe plaque psoriasis and psoriatic arthritis. They are also particularly effective in treating nail psoriasis. Overall, IL-17 inhibitors have an acceptable safety profile without increased risks of serious infections or malignancies.^{50,51} IL-23 inhibitors, including ustekinumab, guselkumab, risankizumab, and tildrakizumab, specifically target the IL-23 cytokine pathway, effectively managing moderate-to-severe psoriasis. Ustekinumab uniquely targets both IL-12 and IL-23 via the shared p40 subunit, whereas guselkumab, risankizumab, and tildrakizumab selectively inhibit the IL-23 p19 subunit. Clinical efficacy for these inhibitors is robust. Overall, IL-23 inhibitors exhibit favorable safety profiles, without

increased risks of serious infections or malignancies. Common, manageable adverse events include nasopharyngitis, upper respiratory infections, headaches, fatigue, and injection site reactions.^{50–52}

Small molecule inhibitors represent an emerging therapeutic class that combines targeted action with the convenience of oral administration. Janus kinase (JAK) inhibitors, particularly selective TYK2 inhibitors like deucravacitinib, have demonstrated promising efficacy by modulating multiple cytokine signaling pathways involved in psoriasis pathogenesis.⁵³ Phosphodiesterase-4 (PDE4) inhibitors, such as apremilast, while showing moderate efficacy, offer a favorable safety profile and may be particularly suitable for patients with mild to moderate disease or those with contraindications to other systemic therapies.⁵⁴

Recent developments in therapeutic approaches include investigation of novel oral agents targeting specific pathways. The PDE family, including PDE4 (comprising PDE4A, PDE4B, PDE4C and PDE4D), is preferentially expressed by keratinocytes and immune lineage cells such as lymphocytes.⁵⁵ In the pro-inflammatory state characteristic of psoriasis, PDE4 catalyzes the hydrolysis of cAMP in keratinocytes, activating the NF- κ B protein complex, which promotes the production of inflammatory cytokines such as IL-2, IL-6, IL-10, IL-12, IL-23, TNF and IFN γ .⁵⁶

The development of selective TYK2 inhibitors has shown particular promise. Recent studies demonstrate that targeting the TYK2 enzyme involved in the IL-23–IL-17 pathway offers improved efficacy and safety compared to earlier JAK inhibitors.^{57,58} Phase III trials of deucravacitinib have shown superior efficacy to placebo and apremilast at both 16 and 52 weeks.^{44,59} The development of selective TYK2 inhibitors has shown particular promise. Recent studies demonstrate that targeting the TYK2 enzyme involved in the IL-23–IL-17 pathway offers improved efficacy and safety compared to earlier JAK inhibitors.⁵⁸ Phase III trials of deucravacitinib have shown superior efficacy to placebo and apremilast at both 16 and 52 weeks.⁴⁴

Additionally, emerging evidence regarding the role of the gut-skin axis in psoriasis pathogenesis has led to interest in microbiome-based therapeutic approaches.⁶⁰ Studies have demonstrated that stool samples from individuals with psoriasis have lower gut microbiota diversity compared to healthy controls, suggesting that gut dysbiosis may trigger a systemic inflammatory response that disrupts skin homeostasis.^{61,62}

Treatment strategies increasingly adopt a personalized approach, taking into account individual patient characteristics and preferences while aiming to achieve and maintain clear or almost clear skin. The availability of multiple therapeutic options with different mechanisms of action allows for sequential or combination approaches when necessary, though more research is needed to optimize such strategies.

Long-term management focuses not only on skin clearance but also on monitoring and managing potential comorbidities.⁶³ Regular assessment of treatment response and safety parameters remains crucial, with treatment modification as needed based on clinical response and tolerability.

The therapeutic landscape continues to evolve, with ongoing research into novel targeted approaches and optimization of existing therapies.⁶⁴ Future directions include development of more selective molecular targets, investigation of biomarkers to guide treatment selection, and exploration of strategies to maintain long-term disease control while minimizing cumulative toxicity risks.

Conclusion

This comprehensive review demonstrates that effective psoriasis management requires a nuanced understanding of its complex pathophysiology and multifaceted impact on patients' lives. The therapeutic landscape has evolved significantly, with traditional systemic treatments being complemented by biological therapies and emerging oral medications. The development of selective TYK2 inhibitors and PDE4 inhibitors represents a promising advance in addressing both efficacy and accessibility challenges.

The psychological burden of psoriasis, evidenced by high rates of depression, anxiety, and social isolation, emphasizes the critical need for integrated care approaches. Quality of life assessment tools play a vital role in evaluating treatment outcomes and guiding therapeutic decisions, moving beyond mere skin clearance to address the overall well-being of patients.

Recent advances in understanding the gut-skin axis and the role of microbiome in psoriasis pathogenesis open new avenues for therapeutic interventions. However, the variability in treatment responses and accessibility issues continue to present significant challenges in clinical practice.

The future of psoriasis management lies in personalized medicine approaches that consider individual patient characteristics, preferences, and circumstances. This includes:

- Selection of appropriate therapeutic agents based on disease severity, comorbidities, and patient-specific factors
- Integration of psychological support mechanisms
- Regular monitoring of both physical and psychosocial outcomes
- Consideration of emerging therapeutic options as they become available

Data Sharing Statement

All relevant data are included within the article.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

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