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## Quality of Life in Psoriasis

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Delia Colombo and Renata Perego

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### 1. Introduction

Psoriasis has a profound impact on patients' everyday life. The burden of the disease extends beyond physical manifestations and includes significant physical, social and psychological impairment. Numerous studies have demonstrated the significant negative impact of psoriasis on quality of life (QoL) [1-5]. Furthermore, as a chronic disease, psoriasis affects the QoL of both patients and their close relatives in a cumulative way [6]. The family members of patients with psoriasis experience a wide range of detrimental effects on their lives with regards to psychological social and lifestyle modifications, interpersonal relationships, financial issues, family activities, sleep and issues related to the practical care of the patients.

Various factors may contribute to the lower QoL of patients with psoriasis. The chronic nature of the disease and the lack of control over unexpected outbreaks of the symptoms are among the most bothersome aspects of psoriasis [7]. Patients may feel humiliated when they need to expose their bodies during intimate relationships, swimming, using public showers, or anyway living in conditions that do not provide adequate privacy [8]. Thus psoriasis affects patients' social life, daily activities, and sexual functioning [9]. Treatment of psoriasis, as it may be associated with risk for adverse effects, is also an important component of the QoL of psoriasis patients [10]. By utilizing the Short Form-36 (SF-36), a generic QoL instrument, it has been demonstrated that psoriasis may cause as much disability as other major medical diseases, including heart disease, diabetes, and cancer [11].

Psoriasis is also related to several co-morbidities, especially cardiovascular diseases and psychiatric disorders. Moreover, cardiovascular risk factors are strongly associated with the severity of inflammation and the duration of disease [12-14].

Improving the QoL in psoriasis patients is an extremely important goal. Therefore, the interventions to improve the process of care of this population should also assess QoL outcomes, such as social functioning and emotional well-being, adjusting for the effects of co-existing

chronic conditions. Disease-specific measures may be sensitive enough to detect and quantify small changes that are important to clinicians and patients [15]. Healthcare professionals have a crucial role in identifying and supporting affected patients and families. In order to establish a good relationship with family members and to be able to improve patients' compliance, dermatologists should develop greater insight into the lives of psoriasis patients and their relatives.

In this chapter, the impact of the different aspects of psoriasis on QoL will be reviewed.

## 2. Skin symptoms

Research found that large percentages of patients with psoriasis reported considerably skin pain and discomfort [16,17]. Skin pain was reported by up to 42%, and skin discomfort by up to 37% of psoriasis patients [16, 18,19]. Skin pain and discomfort had a negative impact on functions such as sleep, mood and enjoyment of life [16]. Studies suggested that other psoriasis-related sensory skin symptoms were associated with sleep disturbances, psychological distress and impaired health related QoL (HRQoL) [20-25].

Ljosaa et al. [17] showed that physiological factors such as skin pain and disease severity were significantly associated with HRQoL and that the association between skin pain and HRQoL was partly mediated by sleep disturbance, while less by psychological distress.

Other skin symptoms of psoriasis can significantly affect physical functioning, perception of disease, and QoL. These symptoms include itching, "skin shedding", tightness, redness, dryness, and bleeding [2, 21]. In particular, a direct correlation between pruritus severity and depression has been shown [26]. Psoriatic lesions of the vulva were found in women with psoriasis, resulting in itching, burning and vulvar discomfort, and women with these symptoms more frequently demonstrated depressive symptoms [27].

Psoriatic skin lesions are often perceived by patients as making their physical appearance unsightly; skin lesions make them feeling disfigured and apprehensive that others will avoid or exclude them, resulting in low self-esteem and self-confidence [28, 29].

When psoriasis involves the palms and soles, which occurs in approximately 40% of patients, the pain and discomfort result in significantly greater physical disability than is experienced by patients without palmoplantar involvement [30]. Nail involvement, which is present in up to 50% of patients, may also limit daily activities such as basic self-care activities and housekeeping [31, 32].

## 3. Psoriatic arthritis

Psoriatic arthritis (PsA) is a painful disease of the joints and connective tissue affecting 10-30% of patients with psoriasis, and is mainly localized at fingers, toes, wrists, hips and

back [2, 3, 31, 33]. PsA can result in damage to bone and synovial membranes, pronounced disability, and increased mortality [33]. Patients with PsA have a significantly worse QoL than those without PsA, as measured by different questionnaires [31, 34].

#### 4. Psychological disturbances and psychiatric co-morbidities

Psoriasis is associated with a variety of psychological difficulties, including poor self-esteem, sexual dysfunction, anxiety, depression, and suicidal ideation [35]. The psychiatric morbidity in psoriasis may be primary or secondary to the impact of the disease upon the patients' QoL.

High depression/anxiety scores, obsessionality and difficulties with verbal expression of emotions, especially anger, social stigmatization, high stress levels, depression, and other psychosocial co-morbidities experienced by patients with psoriasis are not always proportional to, or predicted by, other measurements of disease severity, such as body surface area involvement or plaque severity [36-46]. In general, psychological disturbances, including perception of stigmatization and depression, are stronger determinants of disability in psoriasis patients than are disease severity, location and duration [47]. The Italian PSYCHAE study, which measured psychological distress (PD) in 1580 patients with psoriasis by the General Health Questionnaire-12 (GSQ-12) and the Brief Symptom Inventory (BSI), found that there was no association between disease severity and PD [48].

It is not surprising that perceived stress in patients with psoriasis, as well as with other chronic disease, predicts poorer QoL [49]. On the other hand psoriasis is generally thought to be made worse by stress. Various studies have reported an association between stress and psoriasis. In a study of 132 patients with psoriasis, 39% recalled a significant stressful event within one month before the first episode of psoriasis [50]. In contrast, a more recent prospective clinical study demonstrated that there was no direct relationship between stress and exacerbation of psoriasis, showed no clear relationship between stress levels and worsening of psoriasis and found no time relationships between stress and the appearance of psoriasis [51]. A factor analysis of the Psoriasis Life Stress Inventory revealed two stress-related factors contributing to the psychosocial impact of psoriasis: stress associated with anticipation of the reaction and avoidance by others, and stress associated with patients' experience or beliefs about being evaluated exclusively on the basis of their skin [52]. So, stress is largely secondary to the cosmetic disfigurement associated with psoriasis, with great impact on QoL and possibly resulting in psychological morbidity.

Studies on the relationship between psychological factors and psoriasis severity have primarily been focused on depression, with conflicting results: some authors have found depression correlated with objective measures of disease severity [49], while others have not [53]. Anyway, relatively high rates of depression are reported in patients with psoriasis [54, 55]. Controlled studies found notably higher degree of depression in patients with psoriasis than in controls [56-58].

Suicidal ideation and cases of completed suicide have been reported in psoriasis. The prevalence of suicidal ideation has been reported to be 2.5% among less severely affected outpatients with <30% of their body surface involved and 7.2% among the more severely affected inpatients as compared to 5.2% in acne patients, 2.1% in atopic dermatitis patients and 0% in alopecia areata patients [57, 59]. Death wishes and suicidal ideation were associated with higher depression scores.

Some reports suggest a higher prevalence of alcohol abuse and cigarette smoking among psoriatic patients [60,61]. In one study, there was an 18% prevalence of alcoholism in patients with psoriasis compared to 2% among dermatologic controls [60]. Several studies have shown that treatment outcomes are worse in heavy drinkers [62-64]. Abstinence alone has been shown to possibly induce psoriasis remission, whereas restarting drinking may cause disease relapse [62, 65].

Concerning the evolution of PD in psoriasis, the longitudinal phase of the PSYCHAE study, that specifically evaluated this aspect in 1500 psoriatic patients during up to 12 months, showed that minor PD halved during the observation period, possibly due to improvement of clinical symptoms, while major PD remained stable [66]. The same authors investigated patients' coping strategies and found that planning, active coping and acceptance were strategies most commonly employed by their patients while denial, behavioural disengagement, and substance abuse were the least frequent attitudes [48]. During the 12-month follow-up, active coping and avoiding dramatization by recourse to humor were predictive factors of amelioration of PD [66].

## 5. Stigma

A stigma is severe social disapproval of a person based on a distinguishing characteristics [67]. It has also been defined as a biologic or social mark that sets a person off from others [68]. Visible lesions cause feelings of stigmatization which can lead to psychological stress and social withdrawal [69]. Psoriasis patients, even those with relatively mild symptoms, experience high stigmatization as compared to sufferers of other skin diseases, with significant impact on outcomes such as QoL, depression and disability [70-72]. Stigmatization has many forms: Ginsburg and Link identified different dimensions, including anticipation of rejection, feeling of being flawed, sensitivity to others' attitude, guilt and shame, reduction of self-esteem [73].

Among the themes at the basis of the stigma experience, shame has an important role. In different studies, patients with psoriasis reported feelings of embarrassment and shame compared to healthy controls [74, 75]. Shame is one of the most reported emotions, especially by women and by patients with a long disease duration [74]. Feelings of shame can have a strong impact on social life, since they can result in avoidance of public spaces, thus reducing social opportunities, even concerning employment [76].

Boehm et al. [67] have found that it is stigmatization that mediates between symptom severity and QoL, in particular the stigmatization parameters 'reduction of self-esteem' and 'rejection'.

## 6. Gender

Psoriasis does not discriminate by gender. Studies generally show no difference in the severity of physical symptoms suffered by men and women. However, women and men have different subjective perceptions of how symptoms affect their social interactions, emotional states and, ultimately, their QoL.

Men can find it easier to distance themselves from the social effects of psoriasis. Women, in contrast, are more likely to report feeling 'upset', 'disturbed' or 'ashamed' in social settings [77]. Stress research provides another way of understanding differences between men and women's reactions to psoriasis. Women may be more prone to perceive stress and may be more likely to perceive a greater impact on mental QoL [78]. Other authors have shown that women may have a higher likelihood of being stress-reactors [79]. Boehm et al. [67] have found that women reported higher discomfort levels and higher stigmatization, and that, in general, gender differences are observable in the mental component summary score, but not in general-physical or skin-related QoL. The PSYCHAE study, conducted on nearly 1600 Italian psoriasis patients, found that the female gender was the most important predictive factor for psychological distress [48].

## 7. Sexual health

Psoriasis may involve genital skin. In a Netherlands study, of 1943 patients with psoriasis, over 45% reported genital involvement at some time during the course of the disease [80]. Relatively few studies have evaluated the impact of psoriasis on sexual health, however, according to these studies, psoriasis interferes with sexual relations in 35-50% of patients [76, 81, 82]. Sexual dysfunction and distress are particularly high when genital skin is affected.

Psoriasis has a negative influence on a patient's desire for physical intimacy [83] and causes decreased libido in a substantial proportion of patients [81]. Feelings of shame and embarrassment about physical appearance and reduced sexual desire might play a major role in high distress and dysfunction scores in specific sexual indexes [84]. Impairment of sexual activity is more profound in patients with more severe psoriatic symptoms [85], and appears to be more prevalent in women [1]. The patients who believe psoriasis has a negative effect on their sexual lives have more symptoms of depression [81].

Also the treatments used by patients with psoriasis may cause sexual dysfunction: some publications report that antipsoriatic medication such as methotrexate and etretinate might cause sexual impotence and erectile dysfunction [86-88].



## 8. Impact of QoL on healthcare resources

Psoriasis causes significant occupational disability. Over 17% of patients aged 18-54 report psychologic effects in the workplace due to their disease [2], 6% of employed patients with severe psoriasis reported workplace discrimination [2], and 23% reported that psoriasis affected their choice of career [9]. Problems in work were more frequent in patients with palmoplantar psoriasis. Thus, it appears that psoriasis may have a negative impact on work both for psychological and clinical reasons [2, 9]. Wu et al [89] showed that psoriasis patients were more likely to have missed work for health-related reasons, had significantly more health-related work productivity impairment, and more overall work impairment [90]. This can have financial consequences and may limit lifetime earning potential and career. One study found that 86% of patients with severe psoriasis were 'moderately' or 'a lot' concerned with the time and costs of treating psoriasis [91]. Moreover, psoriasis prevents some patients from obtaining employment altogether [92]. Two studies in the UK found a lower rate of employment in patients with severe psoriasis [41, 92]. Patients with psoriasis who are working, however, tend to have a low work QoL [91]. Fleischer et al [93] theorized that the effect of psoriasis on a patient's work life might result in reduced socio-economical standing and limitations and 34% of the study patients reported hardships due to the financial burden of the disease.

## 9. Impact of QoL on healthcare resources

Poorer QoL of psoriasis patients is associated with increased healthcare resource utilization, independent of the clinical severity of the disease [94]. As stated previously in this chapter, measuring clinical severity of skin lesions does not fully capture the effect of the disease on patient QoL [47, 95].

The study by Sato et al. [94] showed that healthcare resource utilization by European patients with plaque psoriasis, in terms of dermatologist visits and hospitalizations, is greater for those with poorer QoL, independent of clinical disease severity, and may decrease if QoL improves. These authors also found that poor QoL is also associated with employment disadvantages, even when controlling for disease severity, suggesting that indirect costs of psoriasis may also be augmented for patients who have a poor QoL.

## 10. QoL in children with psoriasis

In childhood, QoL is greatly influenced by psoriasis. Data on QoL in juvenile psoriasis are limited, however some studies demonstrated the negative influence of psoriasis on the QoL of children by means of the Children's Dermatology Life Quality Index (CDLQI) [96-100]. The social development domain, which is one of the developmental milestones

in a child, is particularly impaired [101]. Moreover, psoriasis in childhood causes a high degree of limitations on recreational activities in at least 15-30% of patients [101]. Itching and problems with treatments were shown to have the highest impact on the children's QoL. The same authors showed that QoL in the long term is not determined by the age of onset of psoriasis.

Other authors demonstrated that the significant negative impact of plaque psoriasis on QoL of children with psoriasis is generally comparable to the impact of other serious pediatric chronic diseases, as arthritis, asthma, and diabetes [102]. The impairment in QoL impacts particularly emotional and school functioning [102].

## 11. Impact of psoriasis treatments on QoL

Only a few clinical trials have been conducted on the effect of treatments for psoriasis on QoL and some of them were not specifically designed to measure QoL but rather inferred the drug impact on QoL from its effect on the clinical symptoms of the disease.

Among topical treatments, calcipotriol-betamethasone gel was reported to improve QoL in patients with scalp psoriasis [103]. Narrowband ultraviolet B (NBUVB) phototherapy administered three times a week for 6 months significantly improved QoL in 95 plaque-type psoriasis patients [104].

Low-dose (3 mg/kg/day), short-term cyclosporine therapy was effective in improving QoL as measured by Skindex-16 and GHQ-28 in 41 patients with mild to severe psoriasis [105]. An Italian longitudinal study on psoriasis patients followed up for 12 months observed that treatment with cyclosporine significantly reduced by 30% the risk for minor psychological distress, while methotrexate and topical corticosteroids were associated with significantly increased risks (33% and 185%, respectively) [66]. Additionally, results from a small study indicate that the use of cyclosporine for the treatment of nail psoriasis can lead to an improvement in QoL [106].

In a Canadian randomized, placebo-controlled trial on 451 plaque psoriasis patients, cyclosporin was reported to improve QoL, assessed by DLQI and Psoriasis Disability Index (PDI) [107].

A recent analysis of Japanese trials on infliximab demonstrates that a Psoriasis Area and Severity Index (PASI) 90 response is necessary to achieve a DLQI of 0 or 1. Since infliximab showed to achieve nearly 50% of PASI 90 responses, the authors infer that it might be useful in meeting the goal of a DLQI of 0 or 1 [108].

An analysis of pooled data from two randomized, placebo-controlled trials evaluated the effects of adalimumab on the risk of symptom worsening in psoriasis and the subsequent impact on HRQoL. The analysis pointed out that clinically relevant worsening of psoriasis symptoms was associated with substantial worsening of HRQoL. Adalimumab treatment was associated with a reduction in risk of clinical worsening of psoriasis, but its specific effect on HRQoL was not reported [109].



A metaanalysis of randomized, controlled trials of etanercept in patients with rheumatoid arthritis, psoriatic arthritis and psoriasis, evaluating among other outcome measures the effect of the drug on HRQoL, treatment with etanercept resulted in improvements in the physical and mental component summary scores (PCS and MCS), as well as in individual SF-36 domains across all indications [110]. The PRESTA trial, conducted in Germany, evaluated the effect of etanercept on a composite measure of skin symptoms, joint manifestations, and QoL [111]. At 24 weeks, around 30% of patients met the triad of efficacy outcomes. In juvenile plaque psoriasis, one randomized, controlled, longitudinal study described a significant positive effect of etanercept on QoL [100].

In a subanalysis of the PHOENIX 1 and 2 trials on ustekinumab in psoriasis, aimed at evaluating the effect on HRQoL and sexual difficulties, ustekinumab treatment was associated with significant improvement in HRQoL and sexual difficulties due to psoriasis [112]. Another post-hoc analysis of the PHOENIX 2 trial showed that ustekinumab decreases work limitations, improves work productivity and reduces work days missed in the 1230 study patients with moderate-to-severe psoriasis [113]. The efficacy of ustekinumab was also evaluated in nail psoriasis and nail-associated QoL in a population treated for cutaneous psoriasis. Together with a statistically significant reduction of the nail psoriasis severity index (NAPSI), a significant improvement of the international onychomycosis QoL scores was observed at all time points up to 40 weeks [114].

In children, in a psoriatic cohort treated in daily clinical practice, QoL was assessed by CDLQI. The results showed that all psoriasis treatments contributed to a significant improvement in children's QoL, which was greatest with dithranol and systemic treatments. The highest positive impact with all treatments was observed on itching and sleep disturbances [115].

## 12. Conclusions and recommendations for clinical practice

Psoriasis is associated with significant psychological distress, psychiatric morbidity, experience of stigmatization and decreased QoL. Several studies have demonstrated the significant negative impact of psoriasis on QoL, which is similar to the impact of other major chronic diseases as heart diseases, diabetes and cancer. Presence of psoriatic arthritis, psychiatric disorders, and other co-morbidities may further worsen QoL and should be taken into account. The association between symptom severity and QoL, though observed by some studies [98,116], is not always strong, and other studies found no significant association at all [48, 95]. Symptom severity has been shown to have a greater direct impact on the physical rather than the mental components of QoL, while the effects of stigmatization on QoL are more strongly mental [67]. Some research has concluded that 'subjective experience of psoriasis is a more powerful determinant of QoL' in comparison to clinical measures [117].

Studies have shown that dermatologists employ a problem-orientated coping style in caring for their patients, and often appear much more interested in investigating the superficial

skin rather than the deep emotions of their patients [48]. On the contrary, it is essential that measures of psychosocial morbidity are included when assessing psoriasis severity.

In clinical practice there is a great challenge for dermatologists to improve the QoL of adults and children with psoriasis. Greater attention should be paid to the possible limitations that these patients experience. The outcome of QoL measurements should be taken into account when deciding on treatment strategies. Dermatology professionals should be encouraged to identify patients, irrespective of gender and of severity of clinical manifestations, who perceive especially high levels of discomfort, indicate problems in maintaining self-esteem and/or have experienced instances of rejection. Specific therapeutic strategies that address issues of self-esteem and social rejection are appropriate especially for these patients. Optimal therapy that leads to long-lasting remission can only be achieved by addressing both the physical and psychosocial effects of psoriasis. The choice of the optimal psoriasis treatment should also take into account the effect of the drug on the patient's psychosocial well-being, and adjunctive psychological interventions before and during treatment may be of benefit for selected patients. It is recommended that psoriasis patients, especially those with severe disease, receive a more holistic, multitarget approach that encompasses both medical and psychological measures.

## Author details

Delia Colombo and Renata Perego

Luigi Marchesi Hospital, Inzago - Milan, Italy

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