Role of Depression in Quality of Life for Patients with Psoriasis

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Key Words

Depression • Stress, illness-related • Quality of life • Psoriasis • Severity of illness index

Abstract

Background: It has been proposed that depression plays a role in how psoriasis affects quality of life. However, primary data are limited. **Objective:** To investigate the role depression plays in how patients experience psoriasis. **Methods:** Cross-sectional study conducted between January and May 2005. Recruitment of 265 adults with prevalent psoriasis through Internet advertisements. Standardized assessment of depressive symptoms, health-related quality of life (HRQL), illness-related stress, and clinical severity of psoriasis using validated scales. **Results:** Thirty-two percent of all participants screened positive for depression. We observed a graded relationship between depressive symptoms and HRQL impairment ($p < 0.001$). Only 16.5% of those with high depression scores were currently treated for depression. Both dissatisfaction with antipsoriatic treatment and illness-related stress were highly associated with depression. After adjustment for HRQL, patients with more severe psoriasis were less likely depressed, although this association failed to reach statistical significance (multiadjusted odds ratio 0.37; 95% CI 0.13–1.02; $p = 0.06$). **Conclusion:** Patients with high subjective distress and low objective measures of psoriasis should be evaluated for depression.

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Background

Psoriasis is a chronic inflammatory, systemic disease that primarily affects the skin. Currently incurable, psoriasis can occur at any age [1]. It is equally distributed between men and women, and has a higher prevalence in Caucasians compared to African Americans [2]. With about 4.5 million affected adults in the US and estimated annual cost per patient between USD 650 and 800 the socioeconomic impact of psoriasis is remarkable [3, 4]. The typical thickened, red, scaly plaques are often disfiguring and may cause substantial problems in everyday life [5].

Traditional antipsoriatic treatments include topical and systemic immunosuppressive drugs and UV therapy. Having been almost exclusively discussed in the dermatological literature for several years, the introduction of biologics recently evoked some broader notice of psoriasis [6–11]. The fact that most biologics are approved exclusively for moderate-to-severe psoriasis led to a controversial discussion about the definition of severity in psoriasis [12]. Clinically, the severity of psoriasis is described by the intensity and extent of the psoriatic lesions [13, 14]. From the patient's perspective, however, the impact psoriasis has on their everyday physical, social, and psychological-emotional functioning is most important. A subgroup of patients with objectively mild psoriasis experiences high subjective disease severity [12]. Health-related quality of life (HRQL) describes the perceived influence of illness on everyday functioning, the achievement of life

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goals, and social and subjective feelings of well-being. The growing number of studies that include HRQL as an outcome reflects the current broadening of the conceptualization of psoriasis [15]. Clinical symptoms only account for a relatively small proportion of the total variability in emotional well-being in psoriasis [16]. Illness-related stress – one of the dimensions of HRQL – is a particular problem for many patients with psoriasis. Illness-related stress mainly results from the anticipation of the reactions of others to psoriasis and adversely affects interpersonal activities [17]. Despite substantial research on HRQL, illness-related stress, and clinical severity of psoriasis, it is not known which factors are present in the subset of patients in which the HRQL impairment is not reflected by the clinical severity.

It has been reported that psoriasis has an impact on HRQL that is comparable to depression [16].

However, a recent Italian study suggested that depression itself plays a considerable role in the overall morbidity of psoriasis patients [18]. Demoralization and dissatisfaction with treatment may contribute to depression. Depression affects treatment adherence and also modifies the perception of pruritus, a typical symptom of psoriasis [19, 20].

Although it has been proposed that depression plays a role in how psoriasis affects quality of life, primary data from the US population have not been published. We assessed adult psoriasis patients from the US population on HRQL, clinical disease severity, illness-related stress, treatment satisfaction, and depression. The aim of this study was to investigate what factors account for decreased HRQL in psoriasis patients. We hypothesized that depressive symptoms might explain a substantial proportion of the total variance in HRQL in psoriasis patients. We further speculated that depression might be associated with the high HRQL impairment in a subgroup of patients with clinically mild psoriasis.

Methods

Setting and Study Population

In order to efficiently perform a population-based study on factors that account for decreased HRQL in adults suffering from psoriasis we conducted this cross-sectional study through the Internet. Patients 18 years or older with self-reported psoriasis who accessed the Internet from the US were eligible. This was technically possible through registration of the Internet protocol address of the user, which provides information about the geographical region from which the Internet is accessed. Study subjects were recruited between January and May 2005. Recruitment included an advertisement at google.com that appeared on the

screen when 'psoriasis' or related search terms were entered. The exact wording and size of the advertisement was: 'Johns Hopkins Study: Psoriasis & Quality of Life – 30 min Questionnaire – get your report back'. By clicking the web link of the advertisement, participants could enter the interactive study Internet page. A total of 361 patients were recruited, 74% (n = 267) of which completed the entire study questionnaire. All participants provided informed consent before starting to answer the study questionnaires. After finishing the questionnaires, participants received standardized feedback on their HRQL score and likelihood of depression. Persons with high and moderately high probability of depression were instructed to seek further advice from a health professional. Additionally, the investigators' contact information as well as resources for additional information on psoriasis and depression were provided.

Approval from the Office for Research Subjects, Johns Hopkins Bloomberg School of Public Health, Baltimore, Md., was received prior to initiating the study.

Assessments

HRQL was assessed with the Dermatology Life Quality Index (DLQI), a widely used instrument with adequate psychometric properties (e.g. validity, reliability, sensitivity to change) [21–23]. It consists of 10 questions considering the following domains: symptoms and feelings, daily activities, leisure, work and school, personal relationships, and the effects of treatment on daily life. Depression is not assessed in this instrument. The DLQI score ranges from 0 to 30 with higher scores reflecting worse quality of life [21, 23].

The Center for Epidemiologic Study Depression Scale (CES-D) is a 20-question instrument to assess symptom severity of depression [24]. It has been validated in different settings and has already been used in an Internet study [24–27]. The CES-D score ranges from 0 to 60 with higher scores indicating higher likelihood of depression. A common cutoff for a positive test is a score greater than 16. At this level, sensitivity ranges from 86 to 100%, and specificity from 84 to 53% in different studies [24, 28, 29]. Because of the relatively high false-positive rate seen in patients with medical conditions, we created three levels of probability of depression: low-to-moderate probability (score <16), moderate-to-high probability (score 16–21), and high-to-very high probability (score ≥22) [25].

Illness-related stress was measured using the Psoriasis Life Stress Inventory (PLSI), a psoriasis-specific instrument with excellent psychometric properties [30, 31]. The PLSI consists of 15 pairs of questions. The first asks whether a potentially stressful feeling or situation related to psoriasis was encountered within the past 4 weeks (e.g. people commenting on their skin lesions, people avoiding physical contact). If such an event was encountered, the participant is also asked to score the degree of stress experienced because of this situation on a 4-point Likert scale. The PLSI ranges from 0 to 45 with higher scores reflecting higher levels of illness-related stress. As proposed by the developers of the scale, we used a score of 10 as a cutoff to define high stress [30].

The self-administered Psoriasis Area and Severity Index (SAPASI) is a patient-rated instrument with adequate psychometric properties to assess the clinical severity of psoriasis [32–36]. To be applicable in the Internet setting, the SAPASI was slightly modified: as in the original version, patients rated the intensity of

erythema, induration, and scaliness on a 12-cm visual analogue scale (VAS) [34]. For estimation of the involved body surface area (BSA), patients were informed that the area of their palmar hand equals roughly 1% of their BSA. Participants then were asked to estimate the percentage of their body covered with psoriatic plaques. As in the original PASI, the percent BSA involvement was recategorized into a semiquantitative score with 0 indicating no BSA involvement, 1 = 1–9%, 2 = 10–29%, 3 = 30–49%, 4 = 50–69%, 5 = 70–89% and 6 = 90–100% [37]. The SAPASI was calculated using the formula: $[(VAS\text{-erythema} + VAS\text{-scaliness} + VAS\text{-induration})/3] \cdot BSA\text{ score}$.

The SAPASI score ranges from 0 to 72 with higher scores indicating higher clinical disease severity. Severe psoriasis was defined as SAPASI >12, a score between 7 and 12 as moderate psoriasis, and a score of less than 7 as mild psoriasis.

Information on sociodemographic characteristics included age, sex, ethnicity, annual household income, education level, marital status, and living arrangements. Smoking status and current alcohol use were also measured. Information on specific disease characteristics of psoriasis included age at onset, diagnosis by physician, joint involvement, current treatment, presence/absence of facial and genital lesions within the past 14 days, family history of psoriasis, and global severity rating of psoriasis within the past 14 days on a 5-point Likert scale. Participants were also asked to indicate their satisfaction with current antipsoriatic treatment, and to rate the intensity of pruritus caused by psoriatic lesions within the past 14 days on a VAS scale ranging from 0 to 10. Information on personal history of depression and current antidepressive treatment was collected. To increase internal validity, participants were also asked to indicate whether they had answered all questions honestly and whether they had completed the study questionnaire more than once. Participants indicating they had not answered honestly or had participated more than once were excluded from the analysis. The questionnaire was designed in a way that allowed proceeding to the next set of questions only if all previous questions had been answered. Therefore no data were missing for our analysis.

Statistical Analysis

We first compared the 265 subjects who completed the entire study questionnaire with those who only partially completed the study questionnaire ($n = 94$) by sociodemographic characteristics, disease characteristics of psoriasis, personal history/current treatment of depression, smoking status, and alcohol abuse to explore the presence of possible selection bias. χ^2 test and Fisher's exact test were used for binary variables. Wilcoxon rank-sum tests were performed for continuous variables due to positively skewed distributions [38].

The population for the main analysis consisted of the 265 individuals who had complete observations. Spearman correlation coefficients were calculated to describe the univariate association of DLQI, CES-D, PLSI, and SAPASI. Univariate and multivariate analyses were performed to describe factors associated with HRQL impairment and the likelihood of depression. A DLQI of 10 and a CES-D of 22 were used as cutoffs [23–25]. Univariate analyses included Wilcoxon rank-sum, χ^2 , and Fisher's exact tests, as appropriate. Separate multivariate logistic regression models were fitted to predict HRQL (DLQI) and the severity of depressive symptoms (CES-D). Independent variables for CES-D included sociodemographic characteristics, DLQI, SAPASI, pruritus, pres-

ence of genital/facial psoriatic lesions, and alcohol abuse. Important covariates considered for the prediction of HRQL included sociodemographic characteristics, CES-D, SAPASI, presence of genital/facial lesions, pruritus and alcohol abuse. The fit of the final models was assessed by Hosmer-Lemeshow χ^2 tests [38].

The study web page was programmed in PERL 5. Javascript was used for real-time data analysis. The data were recorded in an SQL database and transferred to Stata statistical software 8.0 for Windows, which then was used to perform the statistical analysis [39].

Results

Of the 361 participants who started answering the questionnaires, 267 (74%) completed the study. Two participants (0.7%) indicated that they did not answer all questions honestly and therefore were excluded from the analysis. There were no statistically significant differences between participants who completed the study and those who did not with respect to age, gender, socioeconomic status, disease characteristics of psoriasis, personal history and current treatment of depression, smoking status, and alcohol abuse (table 1). Whites were more likely to complete the study questionnaire compared to other ethnic groups ($p = 0.006$). A higher dropout rate, particularly at the beginning of the study questionnaire, was found for each nonwhite ethnic group (data not shown). Patients with non-physician-diagnosed psoriasis were less likely to complete the survey (85 vs. 96%; $p = 0.001$).

The following results are based on 265 complete observations. The majority of the sample was female, predominately white and less than 50% had completed a college education. Eleven participants (4.1%) did not report to have physician-diagnosed psoriasis. Thirty-one percent ($n = 84$) screened positive for depression when using the conservative (CES-D ≥ 22) and 48.7% ($n = 129$) when using the conventional cutoff (CES-D >16). The mean DLQI score was 10.8 (± 7.1) with 50.3% ($n = 133$) scoring in the high HRQL impairment (DLQI ≥ 10) category. The mean PLSI score was 9.5 (± 9.5). About half of the patients (48.7%, $n = 129$) were classified as having clinically mild, 24.5% ($n = 65$) moderately severe, and 26.8% ($n = 71$) severe psoriasis (SAPASI 9.9 ± 9.4).

HRQL, depressive symptoms, and psoriasis-related stress were highly interrelated with correlation coefficients between 0.58 and 0.81 ($p < 0.001$ for each combination). Statistically significant correlations were also found between clinical severity of psoriasis and patient ratings of depression and HRQL (table 2).

Table 1. Comparison of sociodemographic characteristics of participants who completed the study versus those who did not complete the study (n = 359)

Variable	Participants who completed questionnaire n = 265	Participants who did not complete questionnaire n = 94 ^b	z/χ^2 ^a	p value
Gender, % females	63.4	72.3	2.46	0.12
Age (mean $\pm$ SD), years	42.6 $\pm$ 13.3	40.7 $\pm$ 15.7	1.29	0.20
Annual household income <USD 30,000, %	22.3	29.8	2.14	0.14
Race, % white	91.3	78.7	10.44	0.006
Education level, %				
No degree	7.6	10.7	4.02	0.13
High school	46.8	55.3		
College	44.7	34.0		
Living alone, %	14.3	10.6	0.821	0.37
Married, %	60.4	59.3	0.056	0.81
	n = 265	n = 64 ^c		
Diagnosis of psoriasis by physician, %	95.9	84.4	11.36	0.001
Diagnosis of psoriatic arthritis by physician, %	21.1	23.4	0.16	0.69
Age at onset of psoriasis (mean $\pm$ SD), years	27.4 $\pm$ 15.6	26.3 $\pm$ 14.1	0.15	0.88
Severity rating of psoriasis, % severe	42.6	39.1	0.27	0.60
Positive personal history for depression, %	33.6	27.7	0.35	0.55
Currently treated against depression, %	15.9	17.2	0.07	0.79
	n = 265	n = 49 ^d		
Positive family history for psoriasis, %	39.3	32.7	0.76	0.38
Rating of overall health state, % poor or fair	27.6	18.4	1.81	0.18
Medications (mean $\pm$ SD)	1.6 $\pm$ 2.0	1.2 $\pm$ 1.5	1.13	0.26
Current smoking, %	44.5	35.4	1.38	0.24
Alcohol (mean $\pm$ SD), days having 6 or more drinks within past month	3.1 $\pm$ 6.6	3.3 $\pm$ 6.8	0.31	0.76

^a Wilcoxon rank-sum test, χ^2 test (as appropriate).
^b Patients who completed page 1 of the study questionnaire.
^c Patients who completed page 2 of the study questionnaire.
^d Patients who completed page 3 of the study questionnaire.

Factors Associated with HRQL

Among patients with high HRQL impairment, 51.9% (n = 69) screened positive for depression using a conservative cutoff (CES-D $\geq$ 22) and were 5 times more likely to screen positive than those with low HRQL impairment.

The mean CES-D in the subgroup with high HRQL impairment was 24.0 compared to 11.7 in participants with lower HRQL (p < 0.001). The subgroup of patients with high HRQL impairment reported having encountered significantly more potentially stressful situations related to their psoriasis, and also experienced significantly more illness-related stress in the past 28 days (mean PLSI 15.5 $\pm$ 9.5 vs. 3.5 $\pm$ 4.3; p < 0.001) (table 3).

Table 2. Correlation matrix (Spearman correlation coefficients of DLQI, CES-D, PLSI, and SAPASI; n = 265)

	DLQI	CES-D	PLSI	SAPASI
DLQI	1.00			
CES-D	0.58	1.00		
PLSI	0.81	0.68	1.00	
SAPASI	0.61	0.33	0.56	1.00

p < 0.001 for each combination.

Table 3. Comparison of sociodemographic characteristics, disease characteristics and psychosocial comorbidity of participants by HRQL impairment (DLQI ≥ 10 vs. DLQI < 10 ; n = 265)

Variable	Total (n = 265)	Higher HRQL impairment (DLQI ≥ 10) (n = 133)	Lower HRQL impairment (DLQI < 10) (n = 132)	z/χ^2 *	p value
<i>Sociodemographics</i>					
Gender, % females	63.4	66.2	60.6	0.88	0.35
Age (mean $\pm$ SD), years	42.5 $\pm$ 13.3	40.0 $\pm$ 12.2	45.2 $\pm$ 14.0	3.21	0.002
Annual household income <USD 30,000, %	22.3	30.1	14.4	9.41	0.002
Race, % white	91.3	92.5	90.2	0.45	0.50
Education level, %					
No degree	7.6	9.8	5.3		
High school	46.8	47.4	46.2	2.23	0.33
College	45.7	42.9	48.5		
Living alone, %	14.3	15.0	13.6	0.11	0.75
Current smoking, %	44.5	55.6	33.3	13.34	<0.001
Alcohol (mean $\pm$ SD), days having 6 or more drinks within past month	3.1 $\pm$ 6.6	3.8 $\pm$ 7.7	2.3 $\pm$ 5.2	1.40	0.16
<i>Characteristics of psoriasis</i>					
Objective severity (SAPASI; mean $\pm$ SD)	9.9 $\pm$ 9.4	14.2 $\pm$ 10.4	5.6 $\pm$ 5.7	7.54	<0.001
Mild (SAPASI <7), %	48.7	25.5	72.0		
Moderate (SAPASI 7–12), %	24.5	30.1	18.9	63.4	<0.001
Severe (SAPASI >12), %	26.8	44.4	9.1		
Psoriatic arthritis, %	21.1	27.1	15.2	5.64	0.02
Psoriatic lesions on face within past 14 days, %	33.6	40.6	26.5	5.89	0.02
Psoriatic lesions on genitals within past 14 days, %	41.5	57.1	25.8	26.88	<0.001
Pruritus of psoriatic lesions within past 14 days (VAS; mean $\pm$ SD)	5.7 $\pm$ 2.9	6.9 $\pm$ 2.5	4.5 $\pm$ 2.8	6.74	<0.001
Antipsoriatic treatment within past 14 days, %					
None	22.6	19.6	25.8		
Topical	55.9	57.9	53.8	2.33	0.51
Systemic	15.5	15.0	15.9		
Phototherapy	6.4	7.5	4.6		
Satisfaction with treatment within past 14 days, %					
Satisfied	7.2	1.5	12.9		
Undecided	28.3	20.3	36.4	25.71	<0.001
Dissatisfied	64.5	78.2	50.8		
<i>Psychosocial and psychiatric comorbidity</i>					
Positive personal history for depression, %	33.6	41.4	25.8	7.22	0.007
Currently treated against depression, %	15.9	16.5	15.2	0.10	0.76
CES-D score					
Total (mean $\pm$ SD)	17.8 $\pm$ 13.2	24.0 $\pm$ 13.4	11.7 $\pm$ 9.8	8.21	<0.001
Depression screening, %					
Positive, CES-D > 16	48.7	70.7	26.5	51.72	<0.001
Highly positive, CES-D ≥ 22	31.7	51.9	11.4	50.23	<0.001
Illness-related stress (PLSI; mean $\pm$ SD)	9.5 $\pm$ 9.5	15.5 $\pm$ 9.5	3.5 $\pm$ 4.3	8.21	<0.001

* Wilcoxon rank-sum test, χ^2 test (as appropriate).

Younger age, lower annual family income, and current smoking were also associated with high HRQL impairment. Forty-four percent of the patients with high DLQI scores were classified as having clinically severe psoriasis, as compared to 9.1% of the patients with lower HRQL im-

pairment ($p < 0.001$). Facial and genital psoriatic lesions, as well as the intensity of pruritus within the past 14 days were strong predictors for decreased HRQL ($p < 0.001$ for each). There were no differences by HRQL impairment regarding receipt of antipsoriatic treatment. However,

Fig. 1. Likelihood of depression for participants by HRQL impairment (n = 265).
* p value for trend <0.001 for all strata.

Table 4. Multi-adjusted logistic regression on HRQL (DLQI ≥10; n = 265)

Covariate	OR	95% CI	p value
Likelihood of depression			
Low (CES-D <16)	reference		
Moderate (CES-D 16-21)	1.94	0.86; 4.39	0.11
High (CES-D >21)	6.16	2.80; 13.55	<0.001
Objective severity of psoriasis			
Mild (SAPASI <7)	reference		
Moderate (SAPASI 7-12)	2.41	1.13; 5.14	0.02
Severe (SAPASI >12)	6.64	2.82; 15.14	<0.001
Genital lesions	1.97	1.01; 3.83	0.05
Pruritus of psoriatic lesions (VAS) ^a	1.21	1.07; 1.37	0.002
Hosmer-Lemeshow χ^2_{12} (p value)		10.18 (0.43)	

Adjusted for age, gender, and annual household income.
^a Modeled as continuous covariate.

those with high HRQL impairment were more likely to indicate they were dissatisfied with their current treatment for psoriasis (table 3).

Figure 1 shows the likelihood of depression stratified by HRQL tertiles. A clear dose-response relationship between depressive symptoms and HRQL impairment was observed (p values for trend <0.001 for all strata). More than 70% of the participants in the highest DLQI tertile had a positive depression screen at the higher CES-D cut-off (fig. 1).

In the final multiadjusted logistic regression model predicting HRQL, depressive symptoms (CES-D), clinical severity of psoriasis (SAPASI), presence of genital lesions, and intensity of pruritus were positively and independently associated with HRQL impairment (table 4).

Age, gender, and annual household income were included in the final multivariate logistic regression (MLR) model due to results from the univariate analysis and considerations regarding potential confounding. The adjusted odds ratio of high HRQL impairment for participants with a CES-D score of 21 or more compared to those with lower likelihood of depression (CES-D <16) was 6.16 (95% CI 2.80; 13.55; p < 0.001).

Factors Associated with Positive Depression Screening Test

Younger age, lower annual family income, current smoking, and alcohol abuse were positively associated with a higher likelihood of depression (table 5). Clinical severity of psoriasis was also positively associated with

Table 5. Comparison of sociodemographic characteristics, disease characteristics and psychosocial comorbidity of participants by likelihood of depression (CES-D ≥ 22 vs. CES-D < 22 ; n = 265)

Variable	Total (n = 265)	Higher likelihood of depression (CES-D ≥ 22) (n = 84)	Lower likelihood of depression (CES-D < 22) (n = 181)	z/χ^2 *	p value
<i>Sociodemographics</i>					
Gender, % females	63.4	66.7	61.9	0.57	0.45
Age (mean $\pm$ SD), years	42.5 $\pm$ 13.3	44.6 $\pm$ 12.2	38.3 $\pm$ 14.0	3.76	<0.001
Annual household income <USD 30,000, %	22.3	35.7	16.0	12.86	<0.001
Race, % white	91.3	90.5	91.7	0.11	0.74
Education level, %					
No degree	7.6	9.5	6.6		
High school	46.8	48.8	45.9	1.17	0.56
College	45.7	41.7	47.5		
Living alone, %	14.3	14.3	14.4	0.01	0.99
Current smoking, %	44.5	65.5	34.5	21.85	<0.001
Alcohol (mean $\pm$ SD), days having 6 or more drinks within past month	3.1 $\pm$ 6.6	4.4 $\pm$ 5.2	2.4 $\pm$ 5.6	2.03	0.04
<i>Characteristics of psoriasis</i>					
Objective severity (SAPASI) (mean $\pm$ SD)	9.9 $\pm$ 9.4	14.0 $\pm$ 11.7	8.0 $\pm$ 7.4	4.16	<0.001
Mild (SAPASI <7), %	48.7	11.0	56.9		
Moderate (SAPASI 7–12), %	24.5	37.3	23.2	18.50	<0.001
Severe (SAPASI >12), %	26.8	41.7	19.9		
Psoriatic arthritis, %	21.1	25.0	19.3	1.10	0.29
Psoriatic lesions on face within past 14 days, %	33.6	41.6	29.8	3.60	0.06
Psoriatic lesions on genitals within past 14 days, %	41.5	63.1	36.9	23.60	<0.001
Pruritus of psoriatic lesions within past 14 days (VAS) (mean $\pm$ SD)	5.7 $\pm$ 2.9	6.8 $\pm$ 2.5	5.2 $\pm$ 3.0	4.23	<0.001
Antipsoriatic treatment within past 14 days, %					
None	22.6	15.6	26.0		
Topical	55.9	55.3	57.1	13.08	0.004
Systemic	15.5	14.3	16.2		
Phototherapy	6.4	13.1	2.8		
Satisfaction with treatment within past 14 days, %					
Satisfied	7.2	2.4	9.4		
Undecided	28.3	19.0	32.6	11.40	0.003
Dissatisfied	64.5	78.6	58.1		
<i>Psychosocial and psychiatric comorbidity</i>					
Positive personal history for depression, %	33.6	60.7	21.0	40.58	<0.001
Currently treated against depression, %	15.9	22.6	12.7	4.23	0.04
Quality of life (DLQI) (mean $\pm$ SD)	10.8 $\pm$ 7.1	16.6 $\pm$ 6.8	5.8 $\pm$ 6.4	8.16	<0.001
Illness-related stress (PLSI) (mean $\pm$ SD)	9.5 $\pm$ 9.5	17.7 $\pm$ 10.0	3.5 $\pm$ 4.3	9.22	<0.001
* Wilcoxon rank-sum test, χ^2 test (as appropriate).					

higher likelihood of depression (SAPASI 14.0 $\pm$ 11.7 vs. 8.0 $\pm$ 7.4; $p < 0.001$). Other clinical characteristics of psoriasis that were found positively associated with a positive depression score included presence of genital lesions and intensity of pruritus ($p < 0.001$ for each). Dissatisfaction with antipsoriatic treatment was higher in patients who screened positive for depression ($p < 0.001$). The subgroup of patients with a positive depression score had sig-

nificantly more HRQL impairment (DLQI 16.6 $\pm$ 6.8 vs. 5.8 $\pm$ 6.4; $p < 0.001$) and had also experienced more illness-related stress in the past 28 days (PLSI 17.7 $\pm$ 10.0 vs. 3.5 $\pm$ 4.3; $p < 0.001$) (table 5).

In the final multivariate model on depressive symptoms, HRQL (DLQI), illness-related stress (PLSI), and genital lesions were independent positive predictors (table 6). A qualitative change in the direction of the rela-

Table 6. Multi-adjusted^a logistic regression on depression (CES-D ≥ 22 ; n = 265)

Covariate	OR	95% CI	p value
Impairment of health-related quality of life			
Low (DLQI <7)	reference		
Moderate (DLQI 7–12)	1.61	0.54; 4.79	0.39
High (DLQI >12)	5.32	1.54; 18.27	0.008
Illness-related stress			
Low (PLSI <4)	reference		
Moderate (PLSI 4–12)	2.81	0.99; 8.01	0.05
High (PLSI >12)	8.08	2.40; 27.24	0.001
Objective severity of psoriasis			
Mild (SAPASI <7)	reference		
Moderate (SAPASI 7–12)	0.45	0.18; 1.15	0.10
Severe (SAPASI >12)	0.37	0.13; 1.02	0.06
Genital lesions	2.35	1.15; 4.80	0.02
Pruritus of psoriatic lesions (VAS) ^b	1.07	0.93; 1.23	0.35
Hosmer-Lemeshow χ^2_{12} (p value)	14.78 (0.14)		
^a Adjusted for age, gender, and annual household income.			
^b Modeled as continuous covariate.			

tionship after multivariate adjustment was observed for clinical severity of psoriasis. After adjustment, lower SAPASI scores were associated with higher CES-D scores. The relative odds of a positive depression screening test for participants with severe clinical psoriasis was 0.37 (95% CI 0.13;1.02; p = 0.06) compared to participants with mild clinical psoriasis (table 6). This was probably due to collinearity between HRQL, illness-related stress, and clinical severity of psoriasis. A dose-response relationship was observed for DLQI, PLSI, and SAPASI (table 6).

Depression was undertreated in the participants of this sample. Sixty percent of those who screened positive for depression reported being told by a health professional that they had depression at some point in their lives. Only 23% of those who screened positive for current depression also reported currently receiving treatment for depression.

Discussion

The present study highlights the critical role of depression in the overall morbidity of patients suffering from psoriasis. Using the standard cutoff for depression on the CES-D, nearly half of all psoriasis patients, and nearly three quarters of the subgroup with high HRQL impairment had a positive depression screening test. Even when applying a more conservative measure of depression with

higher specificity, half of those with high HRQL impairment tested positive for depression.

An important advantage of collecting data over the Internet is that participants are more likely to disclose private issues and harmful health behavior. Collecting information on psychiatric morbidity, stress and social anxiety, and the presence of genital lesions via the Internet may result in data with higher validity compared to other methodologies [40, 41]. Another advantage of an Internet-recruited sample is that patients from all different geographical regions within the US could easily participate. Additionally, the Internet setting offered very high efficiency both in terms of monetary resources and time. For both the Internet and the US healthcare system, significant ethnic and socioeconomic disparities exist regarding access [42–44]. It is possible that patients who are more frustrated with their psoriasis were more likely to take the time to respond to the advertisement and to complete the questionnaire, so that a recruitment bias cannot be excluded. The recruitment ad on google.com did not include any mention of depression or low social functioning. Although this is a general problem associated with surveys rather than a specific disadvantage of an Internet-based study, our results should be interpreted with caution, particularly with respect to generalization to the general US population. As in other internet-based studies, females appeared to be more likely and ethnic minorities less likely to participate [25]. In our study, participants belonging to ethnic minorities

were more likely to drop out. As this study consisted of many different web pages which all needed to be downloaded on the computer, this high early dropout rate might be associated with the use of slower dial-up modems and long waiting times when proceeding through the questionnaires. With respect to HRQL impairment and depression, however, this selection bias is likely to be nondifferential.

An additional possible limitation of the study are questions concerning the validity of a self-reported diagnosis of psoriasis. Almost all of the study subjects reported that psoriasis was diagnosed by a physician. It cannot be ruled out that some participants did not truly have psoriasis. However, in another sample of psoriasis patients, Shikiar et al. [45] observed high construct validity of self-reported data both with respect to each other and to clinical assessments. In order to be applicable for the Internet setting we used a modified version of the SAPASI with direct estimation of BSA involvement. The distribution in our sample of the SAPASI was 9.9 ± 9.4 , which is almost identical to the distribution of the SAPASI in its validation study [34]. DLQI and PLSI both are instruments with adequate psychometric properties, but have not been validated in an Internet setting before. The observed distributions of the DLQI and PLSI scores were highly similar to the distributions observed in other settings [23, 30]. The CES-D has already been used in an Internet setting as a screening instrument for depression [25]. Overall, the quality of the collected data is therefore considered high, particularly with regard to internal validity. However, it is possible that patients with higher HRQL impairment and/or higher illness-related stress overestimate the clinical features of their psoriasis, e.g. erythema, induration, or scaliness. In the presence of such a differential information bias the true association between clinical severity of psoriasis and HRQL impairment would be even weaker. Consequently, the true relative impact of depression in the causal model of HRQL impairment in psoriasis might be even greater than what we observed.

To our knowledge this is the first study that has considered depression and illness-related stress when investigating factors associated with decreased HRQL in psoriasis patients [4, 16, 46–50]. Between 20 and 25% of people with chronic medical conditions will become depressed during the course of their disease [51]. We also found a much higher rate of depression in our sample of individuals with a chronic disease compared to the general population. Studies on suicidal ideation in patients suffering from psoriasis have found rates between 2.5

and 9.7% [52, 53]. These figures are at least as high as what has been reported from other chronic medical conditions, and much higher than in the general population [54, 55]. The only randomized controlled trial that examined antidepressive pharmacological interventions in 60 psoriasis patients found a beneficial effect of moclobemide, a reversible inhibitor of monoamine oxidase type A on objective severity of psoriasis and depressive symptoms [56]. Lithium, however, is a well-known trigger for psoriasis. Exacerbations of psoriasis related to fluoxetine and bupropion have also been described [57–59].

The mismatch of objective and subjective severity of psoriasis in a subset of patients has been extensively discussed in the recent dermatological literature [12, 60–62]. The present study suggests that this mismatch might be explained by prevalent depression.

The positive crude association between CES-D and SAPASI (table 2) not only disappeared after adjustment for DLQI, but qualitatively changed (positive relationship in crude estimate → negative relationship in adjusted estimate) (table 6). Based on this finding we hypothesize that in a subset of patients with psoriasis, dissatisfaction with treatment, chronic problems in everyday life, and (presumably) inadequate coping strategies can cause depression, even though psoriasis may clinically not be severe. As psoriasis does not appear to directly involve the brain except possibly through inflammatory markers it seems plausible that the chronicity of the condition may lead to depression primarily through HRQL impairment. However, this hypothesis is based on a cross-sectional dataset, where causal relationships cannot be established. We also cannot rule out recruitment bias; our findings should, therefore, be confirmed in a different setting and in a prospective study before generalization. There is substantial evidence that dermatologists often do not detect psychiatric comorbidity [63–65]. Lack of attention to psychiatric comorbidity may contribute to the observed high rate of dissatisfaction with current antipsoriatic treatment. Almost two thirds of all patients, and 78.6% of those with a high likelihood of depression expressed dissatisfaction with their antipsoriatic treatment. Our data indicate that less than half of the patients with psoriasis and depression are receiving any treatment for depression.

The data presented highlight that depression might play a critical role in the life of psoriasis patients. We found that concurrent depression affects HRQL of patients suffering from psoriasis at least as much as the clinical severity of their psoriasis. Most of these psoriasis pa-

tients with depression also indicated a lot of stress experiences related to their psoriasis and dissatisfaction with psoriasis treatment. Depression might also at least partially account for the frequently observed mismatch of objective and subjective severity of psoriasis. Depression appears undertreated, suggesting that integrated treatment models including dermatologists, primary care

physicians and mental health specialists might be most effective. Our findings suggest that not only antidepressants, but also enhancing coping strategies might help depressed psoriasis patients to improve their HRQL. This appears to be another situation where we need to develop and evaluate models of care that address all the needs of patients.

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