

HEALTH-RELATED QUALITY OF LIFE IN MORPHEA

by

NATASHA KLIMAS

In collaboration with Angela D. Shedd, M.D., Ira H. Bernstein, Ph.D., and Heidi T. Jacobe, M.D., M.S.C.S.

DISSERTATION

Presented to the Faculty of the Medical School

The University of Texas Southwestern Medical Center

In Partial Fulfillment of the Requirements

For the Degree of

DOCTOR OF MEDICINE WITH DISTINCTION IN RESEARCH

The University of Texas Southwestern Medical Center

Dallas, TX

TABLE OF CONTENTS

ABSTRACT	iii
INTRODUCTION	iv
MATERIALS AND METHODS	v
RESULTS	x
DISCUSSION	xiii
KEY MESSAGES.....	xvi
TABLES AND FIGURES.....	xvii
ACKNOWLEDGEMENTS	xxvi
REFERENCES.....	xxvii

ABSTRACT

Objective: Little is known about health-related quality of life (HRQOL) of patients with morphea (localized scleroderma). We determined the impact of morphea on HRQOL and clinical and demographic correlates of HRQOL.

Methods: Cross sectional survey of Morphea in Adults and Children (MAC) cohort.

Results: Morphea impairs HRQOL. Patients were particularly affected with respect to emotional well-being and concerns that the disease will progress to their internal organs. Patients with morphea had worse skin-specific HRQOL than those with other skin diseases, including non-melanoma skin cancer, vitiligo, and alopecia (lowest $P < .0001$). The morphea population was found to have significantly worse global HRQOL scores than the general U.S. population for all subscales (all $P \leq .004$) with the exception of bodily pain. Comorbidity ($r = .35-.51$, $P \leq .0029-.0001$) and symptoms of pruritus ($r = .38-.64$, $P \leq .001-.0001$) and pain ($r = .46-.74$, $P < .0001$) were associated with impairment in multiple domains of skin-specific and global HRQOL. Physician-based measures of disease severity correlated with patient-reported HRQOL.

Conclusion: Patients with morphea have negative impact on HRQOL particularly if symptoms or concerns regarding internal manifestations are present. Providers should be aware of this when evaluating and treating patients.

INTRODUCTION

Morphea, otherwise known as localized scleroderma, is an idiopathic inflammatory disorder that produces sclerosis of the skin and subcutaneous tissues. Recent studies have examined predominately physician based outcome measures in morphea including clinical and radiology based outcomes. Few, however, have examined the impact of morphea on health-related quality of life (HRQOL), particularly in adults.

It is well-known that cutaneous disease impacts HRQOL (1-3). Further, the importance of patient based outcomes has been underscored in numerous publications (4). Yet HRQOL in morphea is poorly described, and existing studies largely focus on children (5-7). Existing pediatric studies indicate that morphea has modest effect on life quality, while studies in adults report negative impact on life quality and emotional distress (6, 8). Conclusions from these studies are limited by incomplete information regarding patient demographics and clinical features or by use of unidimensional measures (6, 8-11). No studies to date have examined the impact of morphea on overall HRQOL in adults, thus comparison of impact of morphea with that of systemic disease is limited. Further, correlation between newly validated clinical scoring systems with patient perceived disease impact is poorly described. Examination of the impact of morphea on HRQOL using newer multidimensional instruments in a large group of well characterized patients is important for optimizing patient care. Further, correlation between patient based outcomes such as HRQOL and physician based measures such as clinical scores can help determine the relevance of these scores to patients.

The objective of this study was to determine the impact of morphea on HRQOL in adults as measured by multidimensional HRQOL scales (Skindex-29+3 and SF-36) and ascertain how well these measures correlated with physician based outcomes. We also determined demographic and clinical features correlated with HRQOL.

MATERIALS AND METHODS

Participants

The institutional review board-approved Morphea in Adults and Children (MAC) cohort contained 322 adults (≥ 18 years old at enrollment) and children (≤ 17 years old at enrollment) as of March 2012 and is in compliance with the Declaration of Helsinki principles. Criteria for inclusion in this study included: eligibility for enrollment in MAC cohort (the details of eligibility have been reported previously)(8, 12), age ≥ 18 years at time of enrollment, presence of sufficient information for analysis including baseline Skindex- 29+3 and SF-36 HRQOL surveys, and English language/literacy skills. Of the 322 of patients in the cohort, 249 were excluded due to the following: age < 18 years ($n=79$), English language/literacy skills ($n=4$), and insufficient data on variables of interest ($n=166$, specifically due to the fact that the Skindex-29+3 and SF-36 were not administered at the outset of the cohort).

The cohort was designed to capture prevalent and incident cases of morphea. Patients are recruited from within the UT Southwestern Medical Center system encompassing two dedicated pediatric care facilities, a county hospital, and a faculty-based clinic practice. In addition, patients are routinely enrolled through regional

referrals from private practitioners. This represents a conscious effort to enroll patients of varied disease severity, subtypes, and socioeconomic backgrounds.

The MAC database contains the following domains: demographic, clinical, medical history, immunologic, immunogenetic, DLQI, Skindex-29+3, SF-36, physician based determinants of disease severity (modified Rodnan skin score and LoSCAT) (13, 14), and cosmetic and functional status. These variables were assessed by direct physician interview/examination and use of validated questionnaires.

After patients signed consent, all data were abstracted using a comprehensive clinical report form designed prior to the study, including demographic, clinical, medical history, and family history data. All patient reported histories were also confirmed by review of medical records. At the time of enrollment, all patients were examined by one examiner with expertise in morphea (H.J.), who assigned subtype and clinical scores. Subtype classifications used in this investigation are presented in Table I.

Variables of Interest

Skindex-29+3

Skin-specific HRQOL was evaluated with the previously-validated Skindex-29 (15). The Skindex-29 assesses the following three subscales: emotions, symptoms, and functioning in the month preceding administration. A fourth, 3-item subscale was added to characterize morphea-specific concerns: (1) activity limitation as a result of disease, (2) concern for involvement of internal organs and (3) feelings of isolation. Each subscale score ranges from 0 to 100; higher scores indicate poorer HRQOL.

DLQI

Skin-specific HRQOL was also measured with the previously-validated (16) Dermatology Life Quality Index (DLQI). This questionnaire evaluates the impact of skin disease on HRQOL over the course of the week prior to administration. Individual items are summed to yield a total score ranging from 0 to 30. Higher scores indicate poorer HRQOL.

SF-36

HRQOL as it pertains to general health was measured via the SF-36 (17). This 36-item questionnaire evaluates the following eight health domains: physical functioning (PF), role-physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role-emotional (RE), and mental health (MH). The eight scales of the SF-36 may be incorporated into two summary measures, the Physical Component Summary (PCS), and the Mental Component Summary (MCS). SF-36 scores range from 0 to 100; lower scores indicate poorer HRQOL.

SCQ

The burden of patients' comorbidities was measured with the Self-Administered Comorbidity Questionnaire (SCQ) (18, 19). Scores range from 0 to 45, with higher scores indicating maximal comorbidity (19).

Pruritus and Pain

Physical symptoms of pruritus and pain were assessed on a visual analog scale (VAS) of 1-10, with 10 representing greatest severity. Visual analog scales for patient reported symptoms were utilized because they have extensive validation and history of

use in skin disorders, including prior studies with morphea in the form of the Impact of Chronic Skin Disease on Daily Life (ISDL)(9, 10, 20-22).

Physician Based Measures

Patients were scored by the same investigator (H.J.) using the modified Rodnan Skin Score (mRSS)(13) and the newly validated Localized Scleroderma Cutaneous Assessment Tool (LoSCAT)(14). Because the LoSCAT was not validated at the time of the inception of the cohort, patients enrolled before 2008 were only assessed with the mRSS. Although the mRSS is not validated in morphea, it was selected because its components offer an assessment of disease severity based on body sites affected and the degree of skin thickening or hardening. After 2008, MAC patients were assessed with both the mRSS (for continuity with initial assessments) and the LoSCAT. The LoSCAT contains measures of activity (Localized Scleroderma Skin Severity Index [LoSSI] and Physician Global Assessment-Activity [PGA-A]) and damage (Localized Scleroderma Skin Damage Index [LoSDI] and Physician Global Assessment-Damage [PGA-D]). Higher scores on all physician-based measures indicate greater disease severity (14, 23).

Cosmetically sensitive areas were identified as lesions on the face and neck. Functional limitation was defined as having at least one of the following: (1) limited joint mobility (clinically appreciable limited range of motion of a joint secondary to skin and subcutaneous tissue involvement, but not due to abnormality of the joint itself and/ or contracture), (2) limb-length discrepancy or (3) contracture.

Socioeconomic Variables

Through use of the subjects' residential postal zip codes and 2007-2011 U.S. census data (<http://factfinder2.census.gov>), annual household income was obtained for each zip code tabulation area as an aggregation of census tracts using previously published methods (24, 25). As census data is not normally distributed, median values were used and classified as \leq \$24,999/year, \$25,000-\$49,999/year, \$50,000-\$99,999/year, and \geq \$100,000/year. Insurance classifications have been widely employed as markers for socioeconomic status (26, 27). We categorized the insurance types of our patients as public, private, or uninsured based on review of the subject's medical record.

Statistical Analysis

Overall HRQOL in morphea was evaluated by summary statistics of the Skindex-29+3 and assessing correlations among subscales. HRQOL in morphea was compared with historical HRQOL in other dermatologic diseases by comparing means of the three Skindex-29 subscales (emotions, symptoms, and functioning) (21, 28). HRQOL in morphea was compared with that of other medical conditions, and with the general U.S. population using norm-based scores of the SF-36 (29). Data for comparison was obtained from previous articles evaluating HRQOL as measured by the SF-36 (30-32). Means were compared using a two-tailed, two-sample *t* test; to minimize experiment-wise error rate, comparisons between morphea and other diseases were evaluated with statistical significance designated as $P < .01$.

We also evaluated the relationship between HRQOL (defined as a dependent variable through use of Skindex-29+3, DLQI, and SF-36 summary measures) and several independent variables. These included age, gender, income class, employment,

insurance type, lesion pain, lesion itch, functional limitation as complication of disease, involvement of a cosmetic site, morphea subtype, LoSSI, LoSDI, PGA-A, PGA-D, and SCQ scores. Associations with HRQOL were assessed using analysis of variance (ANOVA), two-tailed, two-sample *t* tests, and Pearson correlations. Current treatments were divided into topical/intralesional therapy, systemic immunosuppressive agents/phototherapy, both topical/intralesional therapy and systemic/phototherapy, or no active therapy groups and compared with respect to HRQOL using two-way ANOVA. Calculations were completed using SAS 9.3 (SAS Institute, Cary, NC).

RESULTS

Patient Characteristics

Seventy-three patients out of 322 met inclusion criteria for this study, the majority of whom were female (85%). White patients made up the largest racial group, at (71%). Morphea subtypes included plaque (12%), linear (29%), and generalized (59%). Nineteen subjects were treated with topical or intralesional therapy, 16 were treated with systemic immunosuppressive agents or phototherapy, 14 were treated with both topical/intralesional therapy and systemic/phototherapy and 24 were not receiving active therapy. Details of study participants are available in Table 1. Overall, there was little correlation between patient demographics and HRQOL.

Skin-Specific HRQOL

Skindex 29+3

With respect to the Skindex-29+3 subscales, highest mean scores occurred in the emotions and morphea-specific domains, with mean (SD) scores of 41 (26) and 37 (29), respectively (Fig.1B, 1D). Within the emotions domain, patients were most

concerned that their skin may get worse (mean score 63, SD 34) or that their condition may be serious (mean score 55, SD 3) (Fig. 1B). Frustration (mean score 53, SD 33) and annoyance (mean score 50, SD 32) were also expressed. In the morphea-specific domain, patients were most concerned that the condition would affect their internal organs (mean score 49, SD 35) (Fig. 1D). Results from the symptoms domain are available Fig. 1A.

Skindex-29 scores in morphea were compared to patients with other dermatologic conditions and those without skin disease. Patients with morphea had greatest impairment in the emotions domain, with Skindex-29 scores (mean score 41, SD 26) similar to those with acne vulgaris (mean score 41, SD 25), eczema (mean score 41, SD 27) and psoriasis (mean score 39, SD 27). HRQOL in morphea was significantly poorer across all subscales of the Skindex-29 than those without dermatologic disease ($P < .0001$) (Table 2).

DLQI

With respect to the DLQI, 34 patients (47%) experienced moderate or greater impact on HRQOL (DLQI > 5). The mean (SD) DLQI score of our participants, 7 (7), is consistent with a moderate impact on life quality (16). The details of studies examining DLQI in this cohort were previously published (8).

Overall HRQOL

SF-36 scores in morphea were compared with the general U.S. population, healthy individuals, and those with 9 other medical conditions (Table 3). With respect to physical health related subscales (PF, RP, BP, GH), patients with morphea were similar to those with hypertension, back pain, and rheumatoid arthritis and significantly worse

than the general U.S. population and healthy population (31). Patients with morphea had greatest impairment in the mental health domain. With regard to mental health related subscales (VT, SF, RE, MH), scores of patients with morphea were similar to those with rheumatoid arthritis and systemic sclerosis, and significantly poorer than the general U.S. population (30, 31). Similarly, summary PCS and MCS scores also reflected poorer HRQOL in morphea overall (Table 3).

Correlations between patient-based measures of HRQOL

Patient-based measures of HRQOL (Skindex-29+3, DLQI, SF-36), were highly correlated with one another, ($P < .0001$). Correlation among the emotions, symptoms, functioning, and morphea-specific Skindex 29+3 subscales was of relevant magnitude of effect, as high scores in one subscale were associated with high scores in others ($r = .44770-.6995$, $P < .0001$) (Table 4A).

Clinical Variables Correlated with HRQOL

Patient-reported comorbidity as identified by the SCQ correlated with impaired HRQOL across 3 Skindex- 29+3 subscales, the DLQI, and both summary measures of the SF-36 (Table 4B). Lesion pain was associated with impairment in the SF-36 PCS, DLQI and all Skindex-29+3 subscales with the exception of emotions. Presence of itch was associated with worse SF-36 PCS, Skindex 29+3 symptoms and morphea-specific Skindex-29+3 scores.

Increased severity of active disease as measured by the activity domains of the LoSCAT correlated with worse HRQOL (Table 4C). The LoSSI was associated with worse symptoms and morphea-specific Skindex-29+3 subscores and worse SF-36 PCS scores. There was little correlation with HRQOL and the damage domains of the

LoSCAT with exception of the SF-36 PCS. Physician-assessed functional limitation was associated with worse morphea-specific Skindex-29+3 scores and SF-36 PCS scores (Table 4B).

Patients with generalized disease had significantly poorer HRQOL than those with the plaque subtype in the Skindex 29+3 morphea-specific domain (Fig 2D). There were no significant differences in HRQOL between treatment groups.

DISCUSSION

In this cross sectional study of adults enrolled in the MAC cohort we determined the impact of morphea on HRQOL and associated demographic and clinical features. Our results demonstrate that morphea has negative impact on HRQOL of adult patients similar to disorders such as eczema and rheumatoid arthritis, especially in the domain of emotions and mental health. The presence of comorbid conditions, increased morphea activity, and symptoms were correlated with impaired HRQOL across all measures, while treatment was associated with less impact on HRQOL.

The results of the present study identified demographic and clinical features of morphea which put adult patients at risk for impaired life quality. We confirmed prior observations that symptoms associated with morphea, particularly pain and itch are strongly associated with poor HRQOL (8-10). In fact, pain and itch were stronger correlates of HRQOL than the location of lesions in cosmetically or functionally sensitive sites. This likely reflects the notion that physical symptoms are known pervasive, chronic stressors linked with anxiety, depression, and impairment of activities of daily living (33-35). Similar to prior observations in our cohort, itch was significantly correlated with lesion activity (as measured by the LoSSI component of the LoSCAT), suggesting

that pruritus might be an effective marker of active disease. Patients with generalized morphea experience relatively greater impairment than other subtypes which is likely a function of the greater body surface area involvement and frequency of symptoms (both of which were also correlated with impact on HRQOL). Similar to studies in other disorders, the presence of greater comorbidity was correlated with impairment (36). The finding that socioeconomic status was not associated with impact on HRQOL was unexpected, as these factors are known to strongly affect HRQOL in a number of diseases (37). However, despite our efforts to recruit a diverse patient population, our sample was predominately Caucasian and relatively affluent. This might have limited our ability to determine the effect of these variables.

To the extent of our knowledge, no prior study has examined the effect of morphea on global HRQOL in adults preventing comparison between morphea and other medical conditions. We found that morphea impacts overall HRQOL, particularly its mental domains, to an extent comparable to a number of medical and/or autoimmune conditions with frequent internal manifestations. Similarly, comparison of Skindex-29 scores reveals morphea has impact resembling other chronic skin conditions.

We have also found that increased disease activity as measured by the LoSCAT is linked with poor HRQOL in morphea. Our results are similar to those of Szramka-Pawlak et al, who found a correlation between the activity domain of the LoSCAT (LOSSI) and skin-specific HRQOL in their population as measured by the Skindex-29 (11). In contrast to previous observations in our cohort in which DLQI scores were correlated with the presence of damage as measured by the LoSCAT, the results of the present study suggest that active disease is more closely linked with HRQOL than

damage as measured by the Skindex and SF-36 (8). This emphasizes the importance of addressing active lesions in clinical practice.

A notable finding from our study which has not been previously reported is that patients demonstrate a high level of concern that morphea may affect their internal organs. In the information era, this may reflect the ability of patients to independently research morphea, at which point they likely encounter sources referring to morphea interchangeably with localized scleroderma, systemic sclerosis, and scleroderma which produces confusion with regard to diagnosis and prognosis. This highlights the need for providers to educate patients about their disease and its prognosis..

The importance of addressing HRQOL issues is underscored by the heightened presence of anxiety and depression in those with cutaneous disease (38, 39). This has been illustrated by the notion that poor skin-specific HRQOL is linked with suicidal ideation (40). Further, physical symptomatology, and adherence to therapeutic regimens, may be adversely influenced by comorbid psychiatric conditions (41, 42).

The present study includes a number of limitations. Sample size limits conclusions in subgroups of patients. Further, although there is some indication that treatment does not improve HRQOL in morphea, longitudinal studies are needed to confirm these results.

To conclude, our study demonstrates that morphea exerts a profound influence on HRQOL, particularly in the domain of emotions and mental health. With this in mind, physicians caring for patients with morphea can be better equipped to recognize this condition's effect on life quality and thus address its impact more effectively with their patients.

KEY MESSAGES

- Disease severity, comorbidity, and symptoms are closely linked with HRQOL.
- Individuals with morphea worry about the progression of their condition.
- HRQOL issues in morphea should be addressed. Physicians can intervene with patient education.

TABLES AND FIGURES

Table 1. Patient characteristics

	n	%
Gender n, %		
Female	62	85%
Male	11	15%
Age	73	47 (mean)
Ethnicity n, %		
White	52	71%
Hispanic/Latino	11	15%
African American	4	5%
Asian and Others	6	8%
Employment Status n, %		
Employed	41	56%
Unemployed	26	36%
N/A	6	8%
Income n, %		
Less than \$25,000	4	6%
\$25,000-49,999	18	27%
\$50,000-100,000	40	61%
Over \$100,000	4	6%
Insurance Status n, %		
No Insurance	4	6%
Public	17	24%
Private	50	70%
Morphea Subtype n, %		
Plaque	9	12%
Linear	21	29%
Generalized	43	59%
LoSCAT mean (SD)		
LoSSI	12	(15)
PGA-A	28	(27)
LoSDI (mean)	19	(16)
PGA-D	30	(22)
MRSS	6	(5)
Current Therapy n, %		
Topical/Intralesional (IL) Therapy	19	26%
Systemic Agents/Phototherapy	16	22%
Both Topical/IL and Systemic/Phototherapy	14	19%
No Active Therapy	24	33%

Table 1. Patient characteristics

Patients on multiple therapies were counted more than once. Topical/Intralesional therapy includes calcipotriene, imiquimod, topical tacrolimus, intralesional and topical corticosteroids. Systemic Immunosuppressives include methotrexate, systemic and intramuscular corticosteroids. Nine patients were excluded from LoSSI analysis, 7 from PGA-A analysis, 6 from MRSS analysis, 9 from LoSDI analysis, and 8 from PGA-D analysis as these scores were not calculated on same visit as HRQOL instrument administration. Income and insurance data were unavailable for 7 and 2 patients, respectively.

Table 2. Skin-specific HRQOL in morphea compared with other dermatologic conditions

	Sample Size	Symptoms, mean (SD)	<i>P</i> value	Emotions, mean (SD)	<i>P</i> value	Functioning, mean (SD)	<i>P</i> value
Morphea	73	32.8 (22.8)	—	40.8 (26.2)	—	22.0 (22.9)	—
Without skin disease	107	14 (12)*	<.0001	9 (13)*	<.0001	4 (8)*	<.0001
Vitiligo	245	13.9 (14.6)*	<.0001	35.9 (23.6)	.1475	16.7 (19.5)	.0558
NMSC/AK	136	29 (20)	.2238	20 (19)*	<.0001	9 (14)*	<.0001
Acne vulgaris	63	30 (19)	.4299	41 (25)	.9688	16 (16)	.0883
Alopecia	7	31 (24)	.5702	27 (33)*	.0001	14 (23)	.0108
Rosacea	29	33 (20)	.9644	33 (20)	.0533	16 (18)	.0883
Cutaneous lupus erythematosus	178	41.3 (24)	.0115	49.1 (28)	.0430	28.4 (26)	.1014
Psoriasis	44	42 (21)	.0128	39 (27)	.6494	23 (27)	.7989
Dermatomyositis	41	44.9 (24)*	.0002	50.4 (26)*	.0069	28.2 (27)	.0545
Lichen sclerosus	262	46.8 (19)*	<.0001	38.2 (20)	.5206	33.6 (19)*	.0024
Eczema	102	48 (23)*	<.0001	41 (27)	.9636	26 (26)	.2700
Epidermolysis bullosa	75	49 (25)*	<.0001	35 (26)	.0954	31 (24)*	.0095
Vulvodynia	280	50 (17)*	<.0001	50 (20)*	.0004	44 (22)*	<.0001

Table 2. Skin-specific HRQOL in morphea compared with other dermatologic conditions

Mean (SD) Skindex-29 scores for patients with morphea and other dermatologic diseases (21, 28). *P* values are shown as a comparison between mean Skindex-29 subscores of morphea patients and those of other skin conditions. *NMSC/AK*, Non-melanoma skin cancer/actinic keratosis. *Significant finding ($P < .01$)

Table 3. Norm-based SF-36 scores of morphea patients compared with general U.S. populations, including healthy adults and selected diseases

	N	PF Mean (SD)	P value	RP Mean (SD)	P value	BP Mean (SD)	P value	GH mean (SD)	P value
Morphea	73	45.65 (12.85)	—	45.20 (12.14)	—	51.75 (12.99)	—	45.43 (12.00)	—
General U.S. Population	1982	50.00 (10.00)*	.0003	50.00 (10.00)*	<.0001	50.00 (10.00)	.1472	50.00 (10.00)*	.0001
Healthy population	571	54.67 (5.61)*	<.0001	54.68 (4.98)*	<.0001	56.27 (6.89)*	<.0001	55.37 (7.05)*	<.0001
Back pain, sciatica	766	46.60 (11.31)	.4843	46.44 (11.43)	.3637	44.55 (9.28)*	<.0001	46.46 (10.55)	.4172
Depression	256	43.54 (12.72)	.1649	43.04 (11.91)	.1297	42.93 (10.74)*	<.0001	40.86 (11.41)*	.0009
Hypertension	503	43.80 (11.93)	.1948	46.07 (11.75)	.5347	46.50 (10.49)*	<.0001	45.68 (10.43)	.8439
Rheumatoid arthritis	133	42.52 (12.65)	.0392	43.17 (12.37)	.1702	42.19 (10.25)*	<.0001	43.24 (11.97)	.1259
Diabetes	169	42.26 (11.30)	.0129	44.60 (12.00)	.6762	44.89 (10.61)*	<.0001	41.19 (10.91)*	.0013
Heart disease	184	39.39 (12.80)*	<.0001	42.23 (12.04)	.0397	43.18 (10.42)*	<.0001	40.47 (10.98)*	.0002
Systemic sclerosis	504	36.40 (11.8)*	<.0001	40.1 (12.1)*	.0004	43.0 (10.0)*	<.0001	37.7 (10.7)*	<.0001
Systemic lupus erythematosus	1316	52.7 (30.6)	.0501	36.3 (41.5)	.0677	48.5 (24.1)	.2522	37.5 (23.0)*	.0034
Fibromyalgia	2733	40.7 (26.3)	.1095	19.2 (32.3)*	<.0001	34.3 (19.5)*	<.0001	39.2 (22.1)	.0166

Table 3., Continued

	N	VT mean (SD)	P value	SF mean (SD)	P value	RE mean (SD)	P value	MH mean (SD)	P value
Morphea	73	44.97 (11.17)	—	46.35 (12.65)	—	46.54 (13.02)	—	45.32 (11.08)	—
General U.S. Population	1982	50.00 (10.00)*	<.0001	50.00 (10.00)*	.0025	50.00 (10.00)*	.0042	50.00 (10.00)*	<.0001
Healthy population	571	54.36 (8.05)*	<.0001	54.06 (6.10)*	<.0001	52.85 (7.11)*	<.0001	53.04 (7.56)*	<.0001
Back pain, sciatica	766	46.52 (10.21)	.2045	46.87 (11.16)	.7002	47.60 (11.25)	.4312	47.63 (10.88)	.0751
Depression	256	40.51 (9.99)*	.0002	39.01 (11.95)*	<.0001	39.27 (12.37)*	<.0001	36.51 (11.28)*	<.0001
Hypertension	503	48.34 (10.28)*	.0063	47.75 (11.32)	.3039	48.84 (11.12)	.0850	49.60 (10.41)*	.0006
Rheumatoid arthritis	133	47.11 (10.67)	.0944	44.75 (12.28)	.2748	45.40 (13.15)	.4689	47.46 (11.25)	.1114
Diabetes	169	45.90 (11.68)	.5037	44.93 (12.30)	.3327	46.33 (12.83)	.8924	48.10 (11.99)	.0521
Heart disease	184	45.63 (10.28)	.5912	43.95 (12.29)	.1023	45.88 (12.80)	.6673	48.10 (11.62)	.0452
Systemic sclerosis	504	45.5 (10.9)	.6832	42.8 (11.80)	.0120	44.9 (12.40)	.2695	47.6 (10.3)	.0642
Systemic lupus erythematosus	1316	35.9 (23.1)*	.0009	62.0 (27.9)*	<.0001	54.5 (43.9)	.1222	67.1 (20.3)*	<.0001
Fibromyalgia	2733	27.1 (21.1)*	<.0001	51.8 (28.2)	.1005	43.9 (43.9)	.6086	62.5 (21.8)*	<.0001

Table 3., Continued

	N	PCS Mean (SD)	P value	MCS Mean (SD)	P value
Morphea	73	47.70 (12.48)	—	45.37 (11.41)	—
General U.S. Population	1982	50.00 (10.00)	.0565	50.00 (10.00)*	<.0001
Healthy population	571	55.83 (5.34)*	<.0001	52.48 (7.25)*	<.0001
Back pain, sciatica	766	45.60 (10.84)	.1062	47.95 (10.97)	.0490
Depression	256	45.13 (12.54)	.0863	36.78 (11.60)*	<.0001
Hypertension	503	44.08 (11.56)*	.0090	50.63 (10.00)*	<.0001
Rheumatoid arthritis	133	41.66 (11.37)*	<.0001	48.11 (11.22)	.0418
Diabetes	169	42.05 (11.49)*	<.0001	48.24 (12.00)	.0454
Heart disease	184	39.36 (11.31)*	<.0001	48.84 (11.44)	.0115
Systemic sclerosis	504	36.7 (11.2)*	<.0001	49.0 (11.7)*	.0094
Systemic lupus erythematosus	1316	36.3 (11.5)*	<.0001	44.3 (11.8)	.4476
Fibromyalgia	2733	31.9 (9.6)*	<.0001	41.9 (12.5)	.0197

Table 3. SF-36 scores of morphea patients compared with general U.S. populations, including healthy adults and those with selected diseases

Mean (SD) SF-36 scores for patients with morphea and other populations (30-32). *P* values are shown as a comparison between mean norm-based SF-36 scores of morphea patients and those of other populations. One patient's GH scale score was excluded from the analysis, as the patient did not complete sufficient SF-36 items for its computation. *PF*, physical functioning; *RP*, role-physical; *BP*, bodily pain; *GH*, general health; *VT*, vitality; *SF*, social functioning; *RE*, role-emotional; *MH*, mental health; *PCS*, physical component summary; *MCS*, mental component summary. *Significant finding ($P < .01$)

Table 4A. Correlations (p values) among HRQOL measures in morphea

	Skindex-Symptoms	Skindex-Emotions	Skindex-Functioning	Skindex-Morphea-Specific	DLQI	SF-36 PCS	SF-36 MCS	
Skindex-Symptoms	1	—	.4477 (<.0001)*	.6040 (<.0001)*	.6463 (<.0001)*	.6129 (<.0001)*	.5235 (<.0001)*	.4440 (<.0001)*
Skindex-Emotions	.4477 (<.0001)*	1	—	.6708 (<.0001)*	.6116 (<.0001)*	.6097 (<.0001)*	.1233 (.2985)	.6050 (<.0001)*
Skindex-Functioning	.6040 (<.0001)*	.6708 (<.0001)*	1	—	.6995 (<.0001)*	.8255 (<.0001)*	.5283 (<.0001)*	.5624 (<.0001)*
Skindex-Morphea-Specific	.6463 (<.0001)*	.6116 (<.0001)*	.6995 (<.0001)*	1	—	.6739 (<.0001)*	.5706 (<.0001)*	.5396 (<.0001)*
DLQI	.6129 (<.0001)*	.6097 (<.0001)*	.8255 (<.0001)*	.6739 (<.0001)*	1	—	.5446 (<.0001)*	.4917 (<.0001)*
SF-36 PCS	.5235 (<.0001)*	.1233 (.2985)	.5283 (<.0001)*	.5706 (<.0001)*	.5446 (<.0001)*	1	—	.1474 (.2134)
SF-36 MCS	.4440 (<.0001)*	.6050 (<.0001)*	.5624 (<.0001)*	.5396 (<.0001)*	.1474 (.2134)	.1474	.2134	1

Table 4B. Significant correlations (p values) between clinical variables and HRQOL measures in morphea

	Skindex-Symptoms	Skindex-Emotions	Skindex-Functioning	Skindex-Morphea-Specific	DLQI	SF-36 PCS	SF-36 MCS
SCQ	.4430 (.0001)*	.2203 (.0689)	.4655 (<.0001)*	.3552 (.0027)*	.4504 (.0001)*	.5066 (<.0001)*	.3534 (.0029)*
Pain	.7441 (<.0001)*	.1966 (.1055)	.4555 (<.0001)*	.4813 (<.0001)*	.5289 (<.0001)*	.4755 (<.0001)*	.2402 (.0468)
Itch	.6439 (<.0001)*	.1263 (.3012)	.2188 (.0709)	.3818 (.0012)*	.2308 (.0583)	.2225 (.0662)	.2053 (.0907)
Functional Limitation	.1793 (.1292)	.0642 (.5895)	.1101 (.3537)	.3599 (.0018)*	.1750 (.1414)	.3754 (.0011)*	.0376 (.7519)

Table 4C. Correlations (p values) between LoSCAT and HRQOL measures in morphea

	Skindex-Symptoms	Skindex-Emotions	Skindex-Functioning	Skindex-Morphea-Specific	DLQI	SF-36 PCS	SF-36 MCS
LoSSI	.5570 (<.0001)*	.0885 (.4866)	.2665 (.0333)	.3376 (.0064)*	.2750 (.0292)	.4163 (.0006)*	.1905 (.1316)
PGA-A	.5930 (<.0001)*	.2222 (.0729)	.3887 (.0013)*	.3738 (.0020)*	.3948 (.0011)*	.3708 (.0022)*	.2860 (.0199)
LoSDI	.1282 (.3127)	.0937 (.4615)	.0872 (.4935)	.1907 (.1312)	.1337 (.2960)	.3949 (.0012)*	.0773 (.5436)
PGA-D	.1171 (.3529)	.1000 (.4280)	.2099 (.0933)	.1632 (.1941)	.1782 (.1588)	.2812 (.0233)	.0602 (.6341)
MRSS	.3191 (.0085)*	.0288 (.8189)	.2228 (.0700)	.3050 (.0121)*	.1959 (.1149)	.4548 (.0001)*	.0782 (.5294)

Table 4. Multivariable Analysis

A. Pearson correlation coefficients between patient-based HRQOL measures. Absolute value of correlation is shown, though there was an inverse relationship between SF-36 scores and other HRQOL measures. Lower SF-36 scores indicate poorer HRQOL, whereas lower Skindex-29+3 and DLQI indicate better HRQOL

B. Clinical variables significantly correlated with impaired HRQOL in one or more Skindex-29+3 or SF-36 subscales as designated by Pearson correlation coefficients $\geq .30$ and $P < .05$ are depicted. C. Pearson correlation coefficients between disease severity as measured by the LoSCAT and HRQOL measures are shown. *Significant finding ($r \geq .30$, $P < .01$)

FIGURE 1

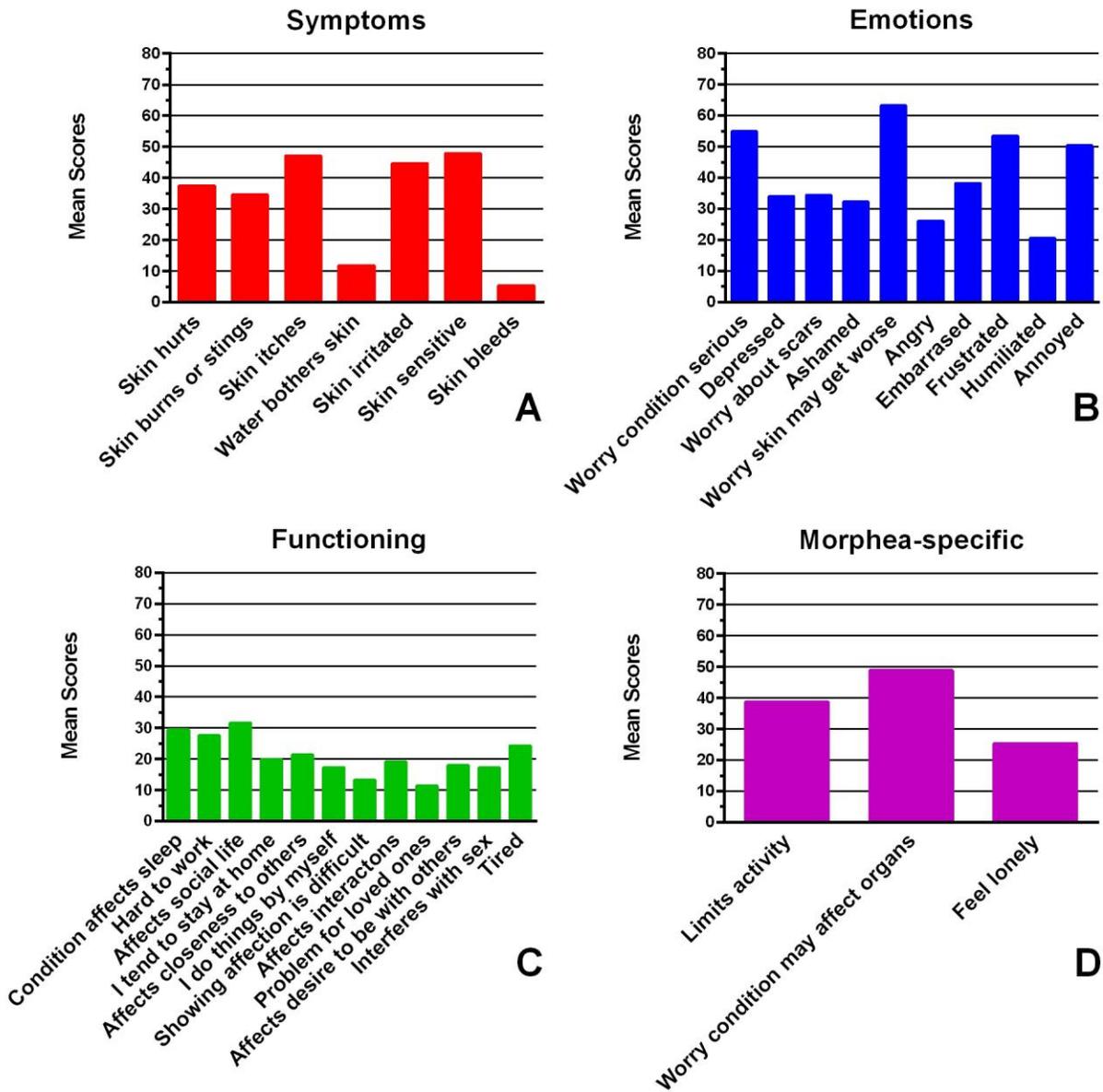


Figure 1. Details of HRQOL in morphea as assessed by the Skindex-29+3. Mean scores of individual questions within each subscale are depicted: (A) symptoms, (B) emotions, (C) functioning, and (D) morphea-specific.

FIGURE 2

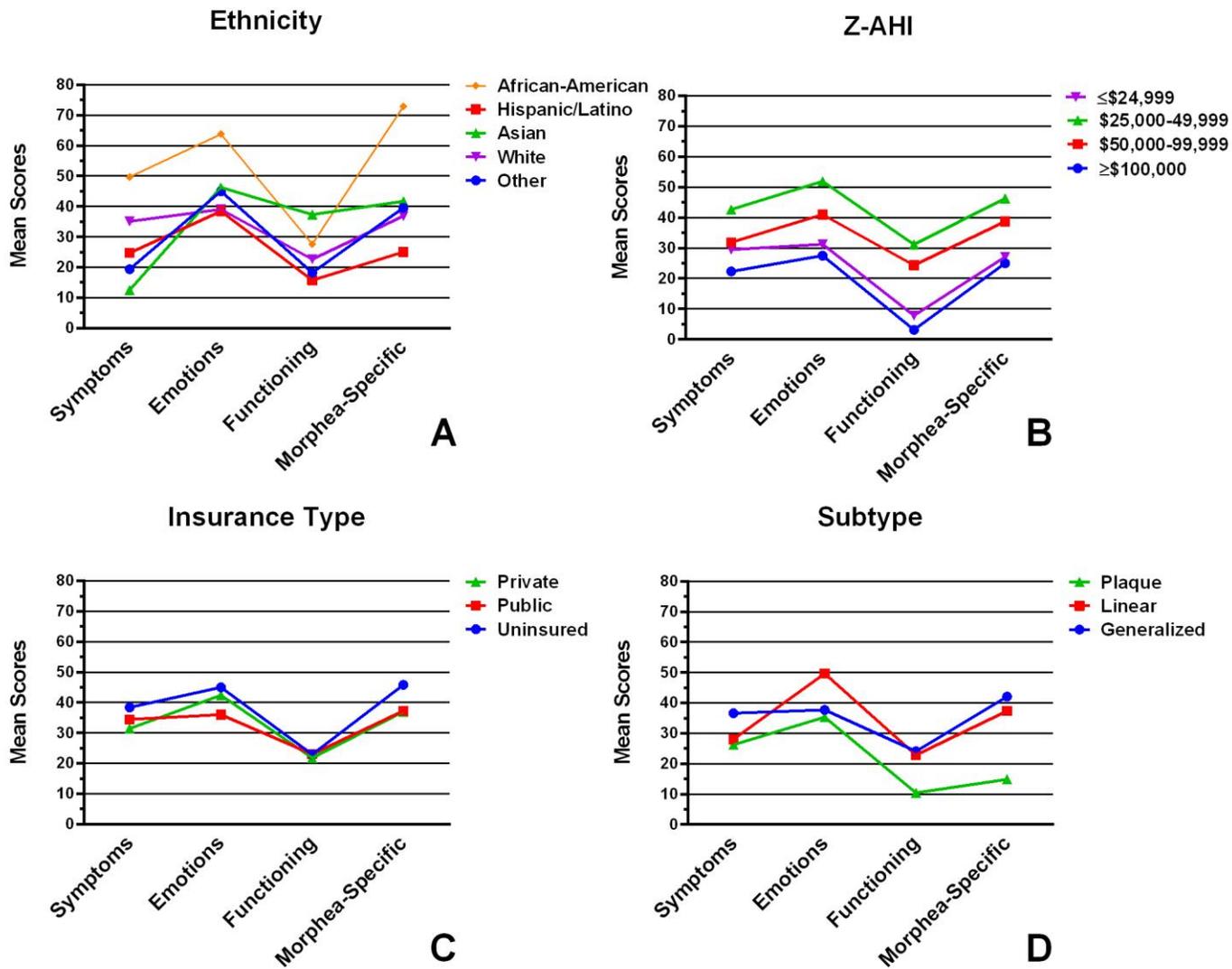


Figure 2

Factors related to HRQOL as measured by the Skindex-29+3. Mean Skindex-29+3 scores are given for (A) ethnicity, (B) Z-AHI, (C) insurance type, and (D) disease severity.

ACKNOWLEDGEMENTS

Foremost, I would like to express my sincere gratitude to my mentor, Dr. Heidi Jacobs for her continuous support, patience, and immense knowledge. I am also indebted to my other co-authors/collaborators, Drs. Angela Shedd and Ira Bernstein, as well as Rose Cannon, Daniel Grabell, Simer Grewal, Kara Pretzlaff, as well as Drs. Andrew Kim and Rebecca Vasquez, for their invaluable contributions.

REFERENCES

1. Finlay AY. Quality of life assessments in dermatology. *Seminars in Cutaneous Medicine and Surgery*. 1998 12//;17(4):291-6.
2. Grozdev I, Kast D, Cao L, Carlson D, Pujari P, Schmotzer B, et al. Physical and mental impact of psoriasis severity as measured by the compact Short Form-12 Health Survey (SF-12) quality of life tool. *The Journal of investigative dermatology*. 2012 Apr;132(4):1111-6.
3. Klein R, Moghadam-Kia S, Taylor L, Coley C, Okawa J, LoMonico J, et al. Quality of life in cutaneous lupus erythematosus. *J Am Acad Dermatol*. 2011 May;64(5):849-58.
4. Deshpande PR, Rajan S, Sudeepthi BL, Abdul Nazir CP. Patient-reported outcomes: A new era in clinical research. *Perspectives in clinical research*. 2011 Oct;2(4):137-44.
5. Orzechowski NM, Davis DM, Mason TG, 3rd, Crowson CS, Reed AM. Health-related quality of life in children and adolescents with juvenile localized scleroderma. *Rheumatology (Oxford, England)*. 2009 Jun;48(6):670-2.
6. Saxton-Daniels S, Jacobe HT. An evaluation of long-term outcomes in adults with pediatric-onset morphea. *Archives of dermatology*. 2010 Sep;146(9):1044-5.
7. Uziel Y, Laxer RM, Krafchik BR, Yeung RS, Feldman BM. Children with morphea have normal self-perception. *The Journal of pediatrics*. 2000 Nov;137(5):727-30.
8. Das S, Bernstein I, Jacobe H. Correlates of self-reported quality of life in adults and children with morphea. *J Am Acad Dermatol*. 2014 May;70(5):904-10.
9. Kroft EB, de Jong EM, Evers AW. Psychological distress in patients with morphea and eosinophilic fasciitis. *Archives of dermatology*. 2009 Sep;145(9):1017-22.
10. Kroft EB, de Jong EM, Evers AW. Physical burden of symptoms in patients with localized scleroderma and eosinophilic fasciitis. *Archives of dermatology*. 2008 Oct;144(10):1394-5.
11. Szramka-Pawlak B, Danczak-Pazdrowska A, Rzepa T, Szewczyk A, Sadowska-Przytocka A, Zaba R. Health-related quality of life, optimism, and coping strategies in persons suffering from localized scleroderma. *Psychology, health & medicine*. 2013 Feb 11.
12. Johnson W, Jacobe H. Morphea in adults and children cohort II: patients with morphea experience delay in diagnosis and large variation in treatment. *J Am Acad Dermatol*. 2012 Nov;67(5):881-9.
13. Furst DE, Clements PJ, Steen VD, Medsger TA, Jr., Masi AT, D'Angelo WA, et al. The modified Rodnan skin score is an accurate reflection of skin biopsy thickness in systemic sclerosis. *The Journal of rheumatology*. 1998 Jan;25(1):84-8.
14. Arkachaisri T, Vilaiyuk S, Torok KS, Medsger TA, Jr. Development and initial validation of the localized scleroderma skin damage index and physician global assessment of disease damage: a proof-of-concept study. *Rheumatology (Oxford, England)*. 2010 Feb;49(2):373-81.
15. Chren MM, Lasek RJ, Flocke SA, Zyzanski SJ. Improved discriminative and evaluative capability of a refined version of Skindex, a quality-of-life instrument for patients with skin diseases. *Archives of dermatology*. 1997 Nov;133(11):1433-40.
16. Basra MK, Fenech R, Gatt RM, Salek MS, Finlay AY. The Dermatology Life Quality Index 1994-2007: a comprehensive review of validation data and clinical results. *The British journal of dermatology*. 2008 Nov;159(5):997-1035.
17. Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Medical care*. 1992 Jun;30(6):473-83.
18. Katz JN, Chang LC, Sangha O, Fossel AH, Bates DW. Can comorbidity be measured by questionnaire rather than medical record review? *Medical care*. 1996 Jan;34(1):73-84.
19. Sangha O, Stucki G, Liang MH, Fossel AH, Katz JN. The Self-Administered Comorbidity Questionnaire: a new method to assess comorbidity for clinical and health services research. *Arthritis and rheumatism*. 2003 Apr 15;49(2):156-63.

20. Evers AW, Duller P, van de Kerkhof PC, van der Valk PG, de Jong EM, Gerritsen MJ, et al. The Impact of Chronic Skin Disease on Daily Life (ISDL): a generic and dermatology-specific health instrument. *Br J Dermatol*. 2008 Jan;158(1):101-8.
21. Goshi R, Chock M, Foering K, Feng R, Okawa J, Rose M, et al. Quality of life in dermatomyositis. *J Am Acad Dermatol*. 2011 Dec;65(6):1107-16.
22. Gniadecki R, Robertson D, Molta CT, Freundlich B, Pedersen R, Li W, et al. Self-reported health outcomes in patients with psoriasis and psoriatic arthritis randomized to two etanercept regimens. *J Eur Acad Dermatol Venereol*. 2012 Nov;26(11):1436-43.
23. Arkachaisri T, Vilaiyuk S, Li S, O'Neil KM, Pope E, Higgins GC, et al. The localized scleroderma skin severity index and physician global assessment of disease activity: a work in progress toward development of localized scleroderma outcome measures. *The Journal of rheumatology*. 2009 Dec;36(12):2819-29.
24. American Fact Finder [database on the Internet]. U.S. Census Bureau. [cited July 14, 2013]. Available from: http://factfinder2.census.gov/faces/nav/jsf/pages/community_facts.xhtml.
25. Jolly M, Mikolaitis RA, Shakoor N, Fogg LF, Block JA. Education, zip code-based annualized household income, and health outcomes in patients with systemic lupus erythematosus. *The Journal of rheumatology*. 2010 Jun;37(6):1150-7.
26. Harnick DJ, Cohen JL, Schechter CB, Fuster V, Smith DA. Effects of Practice Setting on Quality of Lipid-Lowering Management in Patients With Coronary Artery Disease. *The American Journal of Cardiology*. 1998 6/15;81(12):1416-20.
27. Heffernan DS, Vera RM, Monaghan SF, Thakkar RK, Kozloff MS, Connolly MD, et al. Impact of socioethnic factors on outcomes following traumatic brain injury. *The Journal of trauma*. 2011 Mar;70(3):527-34.
28. Klein R, Moghadam-Kia S, Taylor L, Coley C, Okawa J, LoMonico J, et al. Quality of life in cutaneous lupus erythematosus. *Journal of the American Academy of Dermatology*. 2011 5//;64(5):849-58.
29. Ware JE, Snow KK, Kosinski M, Gandek B, Institute NEMCHH. SF-36 health survey: manual and interpretation guide. The Health Institute, New England Medical Center; 1993.
30. Hudson M, Thombs BD, Steele R, Panopalis P, Newton E, Baron M. Quality of life in patients with systemic sclerosis compared to the general population and patients with other chronic conditions. *The Journal of rheumatology*. 2009 Apr;36(4):768-72.
31. Ware JE KM, Keller SK. SF-36® Physical and Mental Health Summary Scales: A User's Manual. Boston, MA; 1994.
32. Wolfe F, Michaud K, Li T, Katz RS. EQ-5D and SF-36 quality of life measures in systemic lupus erythematosus: comparisons with rheumatoid arthritis, noninflammatory rheumatic disorders, and fibromyalgia. *The Journal of rheumatology*. 2010 Feb;37(2):296-304.
33. Becker N, Bondegaard Thomsen A, Olsen AK, Sjogren P, Bech P, Eriksen J. Pain epidemiology and health related quality of life in chronic non-malignant pain patients referred to a Danish multidisciplinary pain center. *Pain*. 1997 Dec;73(3):393-400.
34. Zachariae R, Lei U, Haedersdal M, Zachariae C. Itch severity and quality of life in patients with pruritus: preliminary validity of a Danish adaptation of the itch severity scale. *Acta dermato-venereologica*. 2012 Sep;92(5):508-14.
35. Kini SP, DeLong LK, Veledar E, McKenzie-Brown A, Schaufele M, Chen SC. The impact of pruritus on quality of life: The skin equivalent of pain. *Archives of dermatology*. 2011;147(10):1153-6.
36. Xuan J, Kirchdoerfer LJ, Boyer JG, Norwood GJ. Effects of comorbidity on health-related quality-of-life scores: an analysis of clinical trial data. *Clinical therapeutics*. 1999 Feb;21(2):383-403.
37. Burstrom K, Johannesson M, Diderichsen F. Health-related quality of life by disease and socio-economic group in the general population in Sweden. *Health policy (Amsterdam, Netherlands)*. 2001 Jan;55(1):51-69.

38. Aktan S, Ozmen E, Sanli B. Psychiatric disorders in patients attending a dermatology outpatient clinic. *Dermatology (Basel, Switzerland)*. 1998;197(3):230-4.
39. Picardi A, Abeni D, Melchi CF, Puddu P, Pasquini P. Psychiatric morbidity in dermatological outpatients: an issue to be recognized. *The British journal of dermatology*. 2000 Nov;143(5):983-91.
40. Picardi A, Lega I, Tarolla E. Suicide risk in skin disorders. *Clinics in dermatology*. 2013 Jan-Feb;31(1):47-56.
41. Gupta MA, Gupta AK, Schork NJ, Ellis CN. Depression modulates pruritus perception: a study of pruritus in psoriasis, atopic dermatitis, and chronic idiopathic urticaria. *Psychosomatic medicine*. 1994 Jan-Feb;56(1):36-40.
42. Renzi C, Picardi A, Abeni D, Agostini E, Baliva G, Pasquini P, et al. Association of dissatisfaction with care and psychiatric morbidity with poor treatment compliance. *Archives of dermatology*. 2002 Mar;138(3):337-42.