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Title: The role of therapy in impairing quality of life in dermatological patients: a multinational study

Short title: Burden of treatment in skin disease

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CONFLICTS OF INTEREST

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ABSTRACT

Skin disease and its therapy affect health related quality of life (HRQoL). We aimed to measure the burden caused by the dermatological therapy in 3846 patients from 13 European countries. Adult outpatients completed questionnaires, including the Dermatology Life Quality Index (DLQI) which has a therapy impact question. Therapy issues were reported by a majority of patients with atopic dermatitis (63.4%), psoriasis (60.7%), prurigo (54.4%), hidradenitis suppurativa (54.3%) and blistering conditions (53%). The largest reduction in HRQoL attributable to therapy, as percentage of the total DLQI, adjusted for confounders was seen in blistering conditions (10.7%), allergic/drug reactions (10.2%), psoriasis (9.9%), vasculitis/immunological ulcers (8.8%), atopic dermatitis (8.7%), and venous leg ulcers (8.5%). In skin cancer, although having less impact on HRQoL, the reduction due to therapy was 6.8%. Treatment for skin disease contributes considerably to reducing HRQoL: the burden of dermatological treatment should be considered when planning therapy and designing new dermatological therapies.

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Key words: Quality of life, HRQoL, DLQI, dermatological therapy, burden of skin disease, therapy burden

INTRODUCTION

Topical and other dermatological therapies can add to skin disease burden, as they may be time-consuming, messy, intervene with clothing choice and impact health related quality of life (HRQoL) in ways unique to the skin (1, 2). This contrasts with the relatively low burden of oral therapy given for other diseases (3), where for most, oral medication becomes routine. However, even systemic dermatological medications such as cytotoxic drugs, corticosteroids, retinoids, intravenous or injected biologics, may have an associated burden. Topical and injection routes of drug administration show lowest convenience and global satisfaction (4).

Impairment of HRQoL due to dermatologic therapy is little explored, even though the burden caused by skin disease treatment is very important, both to patients and because it contributes to poor adherence (5).

Most generic HRQoL measures were developed without including skin diseases. It is therefore unsurprising that they miss the burden experienced by dermatological patients. In measures designed for use across skin diseases, only the Dermatology Life Quality Index (DLQI) includes a question concerning the impact of treatment on everyday life (6).

The aim of this study was to measure how the therapy of skin disease contributes to reducing HRQoL in outpatients across Europe.

METHODS

Data was used from a cross-sectional multicentre study on patients recruited from 15 dermatological outpatient clinics in 13 European countries: details have been previously reported (7). The study was approved by the Regional Committee for Medical Research Ethics in Norway. Separate ethical approvals were obtained where necessary. The study was conducted in accordance with the Declaration of Helsinki.

Consecutive patients, age above 18 years, understanding the local language and not suffering from severe mental disease were invited to participate on random days, giving written consent. Participants completed questionnaires on sociodemographics (sex, age, ethnicity, education, marital and socioeconomic status), the DLQI and other questionnaires (7-11).

Patients were examined by the dermatologist, who recorded comorbidities: diabetes mellitus, cardiovascular, chronic respiratory, rheumatologic or other disease. Workers from each hospital's service division were invited to participate as control.

The DLQI, a 10 item questionnaire, was used to assess HRQoL impairment. Question 10, which concerns the impact of therapy, was used to assess how treatment impaired HRQoL: '…how much of a problem has the treatment for your skin been, for example by making your home messy, or by taking up time?' with possible answers "very much" (scored 3), "a lot" (2), "a little" (1) or "not at all/not relevant" (0).

The DLQI was not designed for use by healthy individuals. Patients with nevi (n=192) served as 'healthy' controls since there were no significant differences between nevi and the healthy controls (7, 8).

Statistical analysis

Data from all centres were merged. Diagnoses were organized into 35 disease groups (8, 12).

SPSS 24 software was used. Frequencies and means for patient and control characteristics were calculated.

The answers to DLQI question 10 were dichotomized into 'no impairment' (0) or 'impaired' (1, 2 or 3) when calculating frequencies of positive answers.

For each diagnosis mean scores for question 10 and total DLQI were calculated. Their relationship was calculated as ($\frac{mean\ score\ Question\ 10}{mean\ total\ DLQI\ score}$x100), denoted as Q10%.

Comparisons between patients with nevi and healthy controls were performed with the t-test for continuous variables (age) and the x^2-test for categorical variables (sex, marital status, socioeconomic status, comorbidities, economic difficulties, stress, depression and anxiety (7)) and linear (EQ-VAS) and logistic regressions (EQ5D) for comparing HRQoL outcomes (8).

Linear regression was performed to analyze Q10% for each diagnosis adjusting for age, sex, socioeconomic status and comorbidity with 'nevi' as controls.

A search for publications on therapy issues in dermatology using DLQI or other instruments was performed using MEDLINE, EMBASE and Cochrane Library following standard search strategies. Search terms and medical descriptors (MeSH) included skin disease, dermatosis, dermatoses, quality of life, DLQI, skin therapy, topical therapy, photodynamic therapy, cryotherapy, cryosurgery, cryoablation, laser, phototherapy, photochemotherapy, UVB, UVA, UVA_1, PUVA, RePUVA, topical drug administration, parenteral administration, biological therapy, TNF-α inhibitors, infusion therapy, skin cancer therapy, surgical dermatological therapy.

RESULTS

Participants

There were 4010 participants and 1359 healthy controls. Comparative details are previously published (7-11) and briefly given in Supplementary Table I.

DLQI data

There were 3846 (96%) valid answers to DLQI and 5.2% of those had a DLQI>20 (extremely large effect on HRQoL). One fifth (20.3%) experienced at least a very large effect (DLQI>11) and 44.9% had a DLQI>6, meaning at least a moderate effect on HRQoL (13) caused by their skin disease (Supplementary Table II).

The total patient population (n=3846) had a mean DLQI score of 6.73 (Standard Deviation (SD) 6.8), meaning moderately impaired HRQoL. Except for nevi, no skin disease had a mean score <2, so all had at least a small effect on patients' HRQoL. Twenty-seven of the 35 (77%) skin conditions had mean DLQI scores >5, indicating at least a moderate effect on a patient's life (Supplementary Table III).

Higher DLQI values, indicating higher impairment, were seen in females, younger age groups, patients with comorbidities and lower socioeconomic status.

Therapy impact data (DLQI question 10)

Question 10 in the DLQI addresses therapy related issues. Number of patients answering with 'a little', 'a lot' or 'very much', i.e. other than 'no impact/not relevant', are given in Fig.1. More than half of the patients with atopic dermatitis (63.4%), prurigo (60.7%), psoriasis (54.4%), HS (54.3%) and blistering disorders (53%) answered positively. Fifteen of 32 skin conditions had >33.3% patients scoring positively.

The mean scores with SD for question 10 and Q10% for each diagnosis are presented in Table I. There are no existing cut-off values for interpreting results from single questions of the DLQI and isolated values may not give a clear perspective as to how big the impact is. Q10% is not a standardized method for interpreting DLQI data but does give perspective on how therapy issues relate to the total HRQoL impairment. Table I lists the diseases in descending values according to Q10%, adjusted for age, sex, socioeconomic status and comorbidity. The positive standardized β coefficients for all diseases denote influence of therapy on HRQoL even when adjusted. For many diseases the β coefficient was relatively high, indicating robustness of the presented results.

When assessing Q10%, males and older patients showed more impairment, the reverse of what was seen for total mean DLQI. The impairment was highest in patients with comorbidities or of low socioeconomic status.

When considering the impact of therapy on HRQoL, highest mean scores and most positive answers to question 10 were seen in diseases which commonly affect large areas of the skin (e.g. atopic dermatitis, psoriasis, allergic/drug/phototoxic conditions, prurigo, papulosquamous diseases, eczemas, connective tissue disease and vitiligo), as well as diseases accompanied by blisters/erosions, ulceration or crusting (blistering diseases, venous leg ulcer, vasculitis, immunological ulcers and oral diseases) and pruritic dermatoses (prurigo, urticaria and pruritus) (Table I, Figure 1).

Q10% reveals which diagnostic groups are most affected by therapy relative to their total HRQoL impairment. Blistering conditions showed the highest value (10.7), followed by allergic, drug, phototoxic/-allergic reactions (10.2) and psoriasis (9.9), a ranking that differs from total mean DLQI values (Supplementary Table III). This gives insight into the true extra burden of therapy for different diseases.

HS, prurigo, pruritus and urticaria show highest impairment when mean DLQI scores are evaluated but drop in ranking when therapy is assessed. Likewise, acne, rosacea and psychodermatological conditions, scoring among the average impaired as measured by mean DLQI scores, were some of the least affected by therapy. Conversely, blistering conditions, non-melanoma skin cancer (NMSC), actinic keratoses (AK), allergic/drug reactions, vasculitis and venous leg ulcers rank higher when evaluated according to therapy-related impairment.

DISCUSSION

Using a dermatology-specific measure we identified the extent of the reduced HRQoL associated with therapy. For several diseases, patients experience a high burden associated

with therapy (blistering conditions, allergic/drug reactions, psoriasis, vasculitis, vitiligo and venous leg ulcers). Ranking the diseases according to what percentage of the burden is caused by therapy gives new insight into this specific impairment for the separate diagnoses.

Most skin diseases are treated with topical therapy. However dermatological treatments include oral therapy, phototherapy, photodynamic therapy, lasers, cryotherapy, intralesional and surgical procedures and also parenteral administrations, which may be painful, time-consuming or cause infusion reactions. The use of these specific dermatological medications and therapeutic approaches presents issues and challenges unique to skin disease.

Generic HRQoL measures have been developed without specific reference to impact of therapy for skin disease (Table II). Assessment may therefore be inaccurate if this burden experienced by dermatological patients is missed. There are no questions related to the impact of therapy in the most commonly used generic measures. However, the generic measures Treatment Satisfaction with Medicines Questionnaire (SATMED-Q) (3) and Treatment Satisfaction Questionnaire for Medication (TSQM) (4) are designed to address issues with medication, but are little used in dermatology. The DLQI is the only non-disease specific dermatological measure that addresses therapy burden (Table II), but although the DLQI is the most widely used measure in dermatology (14) the issue of therapy is little explored.

There are very few studies evaluating the contribution of therapy to impairment of HRQoL. In three studies (15-17) the generic instrument SF-36 was used in random samples of the population. A large proportion of patients reported dermatological problems and those using topical therapies on prescription showed greater impairment of HRQoL than those not using topical prescription medicines (15).

<u>An overview of the most relevant results for several diagnoses is given below:</u>

Blistering diseases showed the highest impairment due to therapy and positive standardized β values as high as 0.5, in support of the high impairment being caused by the disease and its therapy and not because of the age, sex, comorbidity and socioeconomic status of the patients.

HS results in severely impaired HRQoL (18, 19), has the highest mean DLQI, but scores for Q10% are low. Studies of the same data set rank HS patients with some of the lowest HRQoL (8), highest risk for psychiatric comorbidity (7, 20) and impairment in sexual life (9). Despite very high impairment of HRQoL, therapy contributes little to this burden.

Atopic dermatitis and psoriasis rank highly when mean DLQI, positive answers to therapy issues or Q10% are evaluated, suggesting that these patients suffer equally from all aspects of HRQoL, including therapy.

Diseases affecting small areas of the body, such as facial dermatoses (seborrhoeic dermatitis, rosacea and acne) as well as psychodermatological conditions rank lower on therapy relative to the total DLQI than might be expected, demonstrating that it is the disease itself and not the therapy that is the driving cause of HRQoL impairment. Treating these conditions adequately should alleviate the patient's experienced burden without additional impairment.

In contrast, patients with AK, NMSC, allergic/drug reactions, scars/fibrosis and morphea, who do not report severe impairment of HRQoL as measured by the mean DLQI, rank high in impairment when assessing therapy as a percentage of this total score. AK and NMSC do not apparently have a high impact on HRQoL, nor psychiatric comorbidity (7, 8, 20), but score relatively worse when therapy is assessed, ranking them higher than HS and several other diseases.

Studies evaluating the burden caused by AK and/or NMSC have shown low impact on HRQoL of these diseases (21-24), raising the possibility that currently available measures may be missing therapy issues and that there may be a need for a skin cancer specific HRQoL

measure. Existing disease-specific instruments do not include therapy questions (22, 25) (Table II).

Burdensome treatments have a negative effect on adherence to therapy (5) and can be the reason for undertreatment and relapse of disease. Measuring HRQoL without taking into account therapy issues may not give the true extent of suffering that dermatological patients experience. On the other hand, knowing which diseases have the highest potential to cause therapy issues can alert clinicians to which patients need a different approach, by giving them better information, providing a variety of options, offering training in therapy application or at least acknowledging the issue.

When developing clinical guidelines in dermatology, optimization of therapy and minimising burden of treatment should be considered. Developers of HRQoL instruments should pay attention to therapy issues when measuring HRQoL in some specific diagnoses such as skin cancer, as this burden may go undetected using current available measures (7, 8, 20-23).

Strengths and limitations

The large amount of patients in this study, the unbiased selection of participants and adjusting for confounding factors resulted in robust data on therapy as a factor contributing to impairment in HRQoL. Similar studies on therapeutic issues are lacking and studies using DLQI typically have no healthy control group.

One potential weakness is in the detail of the wording of the DLQI question 10: "(…by making your home messy, or by taking up time)" which might bias the respondents into only considering topical therapy. However, the main question itself is neutral on this point "…how much of a problem has the treatment for your skin been…".

Detailed information on all treatments used by our patients was not systematically obtained. The presented data evaluate therapy issues on a general basis. Further studies evaluating specific dermatological treatments are warranted.

Although we refer to data from each country, the data was based on one centre from each country (apart from Italy and Norway). The recruitment centres may not have been representative of clinical practice across each country. There were large differences between countries in scores assessing impairment which cannot be readily explained. The cross-cultural issue is one that is of relevance to all HRQoL measures (26). The same limitation may apply when comparing diseases (27). The cultural and language factors leading to these differences are not fully understood, though they should be taken into account when making any cross-cultural comparisons and when using HRQoL data as a guide to optimal health policies and creating optimal treatment guidelines. Analysis of the source for country differences may be able to serve as a guide to optimal health policies and creating optimal treatment guidelines.

Conclusion

Treatments for skin diseases contribute to the burden on HRQoL. For some diagnoses, therapy may have a larger impact than was previously known, but we also identify diseases that to a lesser degree are affected by therapy. Older, male patients with lower socioeconomic status and comorbidities suffer more from therapy issues. Our study highlights new aspects to HRQoL that may have been overlooked previously. Clinicians are made aware of the importance in addressing therapy issues and promoting adherence to therapy, pharmaceutical companies to ease of use of their products. Developers of HRQoL instruments should consider including therapy related questions. The ultimate goal would be to reduce the burden of skin disease and promote adherence.

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Table I. Effect of treatment on DLQI. Ranking according to the percentage of Question 10 of the DLQI (therapy issues) to the mean total DLQI (Q10%) for diagnoses with at least 20 valid answers (hyperhidrosis (12), nail diseases (17) and granuloma annulare (13) excluded). Linear regression (standardized β) with 'nevi' as a 'healthy' control group, adjusting for age, sex, socioeconomic status and comorbidity (diabetes mellitus, cardiological, respiratory, rheumatologic or other disease). Mean DLQI and mean score to Question 10 (therapy issues) and standard deviation (SD) given in separate columns.

	Diagnosis	**Q10%[a]**	**Standar-dized β**	**Question 10 Mean (SD)**	**Mean DLQI (SD)**	**Valid N/ Valid N β[b]**
	All patients[c]	7.73	0.06	0.52 (0.8)	6.73 (6.8)	3846/3553
1	Blistering conditions	10.71	0.47	0.92 (1.0)	8.59 (7.4)	66/49
2	Allergic, drug, phototoxic/-allergic reactions	10.21	0.39	0.54 (0.8)	5.29 (4.3)	24/21
3	Psoriasis	9.85	0.19	0.90 (1.0)	9.14 (7.6)	660/615
4	Vasculitis and immunological ulcers[d]	8.78	0.28	0.62 (0.9)	7.06 (6.1)	67/60
5	Atopic dermatitis	8.67	0.33	1.0 (0.9)	11.53 (7.2)	172/150
6	Vitiligo	8.62	0.36	0.33 (0.6)	3.83 (3.7)	24
7	Venous leg ulcers	8.47	0.27	0.80 (1.0)	9.45 (7.3)	113/87
8	Other hair disorders[e]	8.38	0.27	0.42 (0.8)	5.01 (5.4)	82/76
9	Prurigo	8.13	0.33	0.93 (0.9)	11.44 (8.2)	27/24
10	Scars, fibrosis of the skin, morphea	8.11	0.24	0.43 (0.9)	5.3 (4.8)	27
11	Papulosquamous skin diseases[f]	7.69	0.21	0.49 (0.8)	6.37 (6.4)	113/103
12	Connective tissue disease	7.43	0.20	0.58 (0.9)	7.81 (7.0)	91/74
13	Oral conditions[g]	7.39	0.24	0.50 (0.8)	6.77 (6.6)	26
14	Eczema	7.36	0.21	0.62 (0.9)	8.42 (7.2)	234
15	Urticaria	7.09	0.35	0.68 (0.9)	9.59 (6.7)	69/60
16	Hand eczema	7.05	0.18	0.60 (0.9)	8.51 (7.2)	156/146
17	Alopecia areata	6.99	0.18	0.39 (0.8)	5.58 (6.8)	31/30
18	Pruritus	6.84	0.24	0.75 (1.0)	10.97 (7.1)	60/58
19	Non-melanoma skin cancer and actinic keratosis	6.75	0.11	0.16 (0.5)	2.37 (5.0)	401/372
20	Genital (non-venereal)[h]	6.36	0.22	0.56 (0.8)	8.81 (6.4)	32/30
21	Other[i]	6.15	0.20	0.39 (0.7)	6.34 (6.6)	96/67
22	Hidradenitis suppurativa	6.14	0.24	0.78 (0.8)	12.7 (7.6)	46/44
23	Infections of the skin	6.09	0.21	0.38 (0.8)	6.24 (5.8)	253/244
24	Benign skin tumours	5.51	0.09	0.15 (0.5)	2.72 (3.7)	159/154
25	Lichen planus	5.42	0.07	0.33 (0.7)	6.09 (5.4)	46/41
26	Seborrhoeic dermatitis	5.41	0.23	0.34 (0.6)	6.28 (4.4)	75/74
27	Psychodermatological conditions	5.41	0.14	0.46 (0.8)	8.5 (7.1)	34
28	Acne	4.99	0.16	0.31 (0.6)	6.21 (5.2)	234/228
29	Rosacea	4.66	0.09	0.25 (0.6)	5.37 (5.3)	75/68
30	Nevi	4.61	-	0.07 (0.3)	1.52 (2.9)	186
31	Malignant melanoma	4.41	0.03	0.12 (0.4)	2.72 (4.4)	86/75
32	Melasma, pigment disorders	2.01	0.16	0.10 (0.3)	4.97 (4.7)	32/30

	Sex	**Age groups**	**Socioeconomic status**	**Comorbidity**
Q10%[a] (N)	Male: **8.03** (1686)	18-35: **6.62** (1247)	Low: **8.23** (720)	None: **7.33** (2573)
	Female: **7.41** (2168)	36-65: **8.10** (1880)	Middle: **7.4** (2844)	Any: **8.77** (1033)
		>66: **8.7** (652)	High: **8.17** (327)	

Country	Belgium	Denmark	France	Germany	Hungary	Italy	Netherland	Norway	Poland	Russia	Spain	Turkey	UK
Q10%[a] (N)	4.2 (250)	6.8 (265)	2.1 (126)	7.2 (290)	6.7 (261)	9.6 (527)	5.6 (235)	9.8 (534)	8.4 (275)	9 (273)	7.4 (274)	4 (270)	6.5 (213)

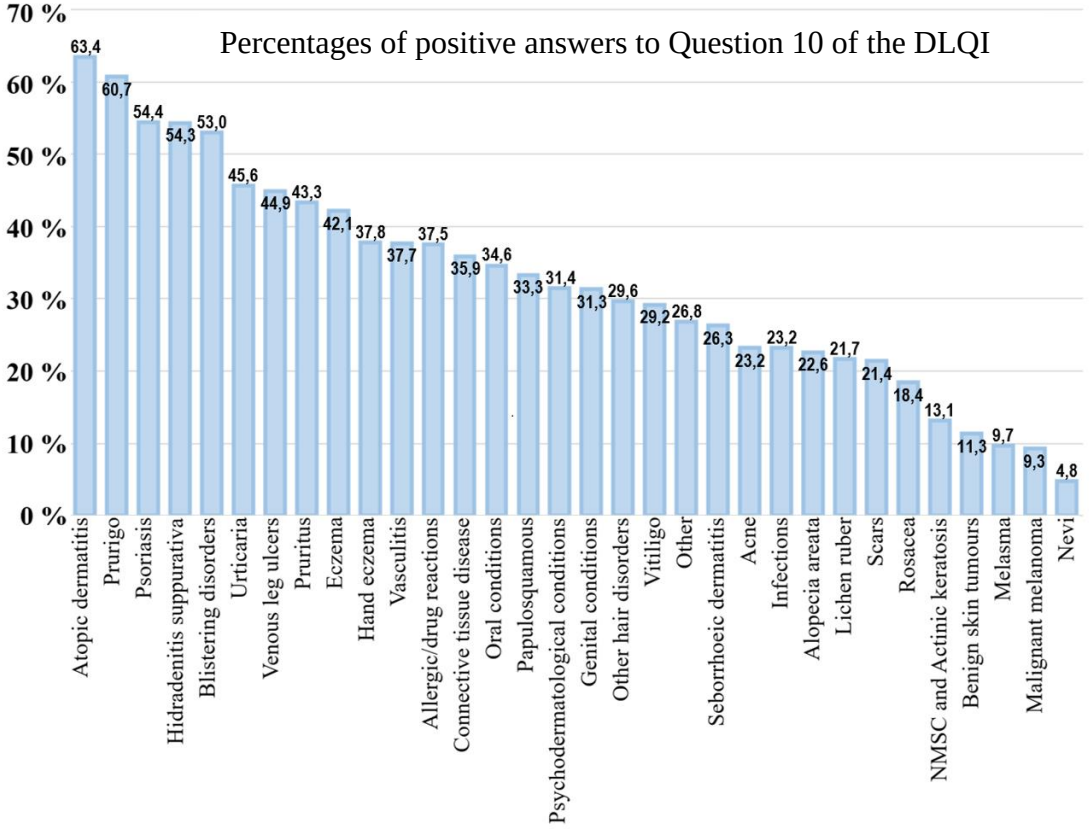
[a]The percentage of the mean score of Question10 (therapy issues) relative to the mean total DLQI score: $\frac{mean\ score\ to\ Question\ 10}{mean\ total\ DLQI\ score}$ x100

[b]Different values due to more missing numbers when regression analysis is performed. [c]Including nail diseases, hyperhidrosis and granuloma annulare. [d]Including pyoderma gangrenosum, Behçet's syndrome, panniculitis, necrobiosis lipoidica. [e]Effluvium, androgenic alopecia, cicatricial alopecia, other hair/scalp conditions. [f]Other than psoriasis: parapsoriasis, pityriasis rubra pilaris, pityriasis lichenoides, pityriasis rosea, Darier's disease. [g]Stomatitis, glossitis, cheilitis, aphthae. [h]Lichen sclerosus, pruritus/eczema vulvae, scroti et ani, balanitis/balanoposthitis. [i]Skin check of organ transplant recipients, other follow-up or uncertain diagnosis.

Table II. Overview of dermatology specific, disease specific and generic instruments assessing quality of life with comments on whether the impact of therapy is addressed in the questionnaire.

Type and name of instrument	Therapy impact	Authors, year
Dermatology specific instruments		
Dermatology Life Quality Index (DLQI)	**Yes**	Finlay et al. 1994 (6)
Skindex, Skindex-29, Skindex-16. Skindex-17	No	Chren et al. 1996 (28) Nijsten et al. 2006 (29)
Dermatology-Specific Quality of Life (DSQL)	No	Anderson et al. 1997 (30)
Dermatology Quality of Life Scales (DQOLS)	No	Morgan et al. 1997 (31)
Disease specific instruments		
Psoriasis Disability Index (PDI)	**Yes**	Finlay et al. 1987 (32)
Psoriasis Index of Quality of Life (PSORIQoL)	**Yes**	McKenna et al. 2003 (33)
Rosacea Quality of Life (RosaQuol)	**Yes**	Nicholson et al. 2007 (34)
The Quality of Life Hand Eczema Questionnaire (QOLHEQ)	**Yes**	Ofenloch et al. 2014 (35)
Venous Insufficiency Epidemiological and Economic Study (VEINES-QOL)	**Yes**	Bland et al. 2015 (36)
Cardiff Acne Disability Index (CADI)	No	Motley et al. 1992 (37)
Dermatology-Specific Quality of Life (DSQL) - Contact dermatitis	No	Anderson et al. 1997 (30)
Dermatology-Specific Quality of Life (DSQL) - Acne version	No	Anderson et al. 1997 (30)
Women with Androgenetic Alopecia Questionnaire (WAA)	No	Dolte et al. 2000 (38)
Acne-specific Quality of Life Questionnaire (Acne-QoL)	No	Martin et al. 2001 (39)
Psychosomatic Scale for Atopic Dermatitis in Adults (PSS-AD)	No	Ando et al. 2006 (40)
Skin Cancer Index (SCI)	No	Rhee et al. 2006 (41)
Alopecia Areata Quality of Life (AAQ)	No	Endo et al. 2012 (42)
Melasma Quality of Life Scale (MELASQoL)	No	Lieu et al. 2012 (43)
The Actinic Keratosis Quality of Life questionnaire (AKQoL)	No	Esman et al. 2013 (25)
Alopecia Areata Quality of Life Index (AA-QLI)	No	Fabbrocini et al. 2013 (44)
Fragrance Allergy QoL instrument (FQL index)	No	Heisterberg et al. 2013 (45)
Vitiligo Quality of Life Index (VitiQoL)	No	Lilly et al. 2013 (46)
Autoimmune Bullous Disease QoL Questionnaire (ABQOL)	No	Sebaratnam et al. 2013 (47)
Generic instruments*		
Treatment Satisfaction Questionnaire for Medication (TSQM)	**Yes**	Atkinson et al. 2004 (4)
Satisfaction with Medicines Questionnaire (SATMED-Q)	**Yes**	Ruiz et al. 2008 (3)
EuroQol (EQ5D)	No	EuroQolGroup 1990 (48)
Medical Outcome Study (MOS) MOS Short-Form 36 (SF-36)	No No	Ware et al. 1992 (49)
WHOQoL-100 WHOQoL-BREF	No No	WHO 1996 (50) WHO 1998 (51)
*Only the most commonly used generic instruments that do not address therapeutic issues are shown here.		

Figure 1. The percentage of positive answers to having therapy issues (Question 10 of the DLQI) for each diagnosis. Diagnoses represented by less than 20 valid answers (hyperhidrosis (12), nail diseases (17) and granuloma annulare (13) excluded.



NMSC – Non-melanoma skin cancer

E-supplements (3 Tables):

Supplementary Table I. Participant characteristics. Reproduced with modification from JID (Dalgard, Gieler et al. 2015) (7)

		Patients	**Controls**	**p-value**
N		**4010**	**1359**	
Sex N (%)	Male	1746 (43.7%)	453 (33.4%)	p<0.05
	Female	2250 (56.3%)	903 (66.6%)	p<0.05
Age Mean (SD)		47.1 (18)	41.1 (13.6)	p<0.05
	Male	48.5 (18.2)	41.1 (14.2)	p<0.05
	Female	46.0 (17.8)	41.1 (13.3)	p<0.05
Socioeconomic status (self-reported)	Low	723 (18.5%)	215 (15.9%)	NS
	Medium	2848 (73.1%)	1012 (75.1%)	NS
	High	327 (8.4%)	121 (9%)	NS
Comorbidities (any)		**1089 (29.1%)**	**170 (16%)**	p<0.05
	Cardiological	667 (17.8%)	78 (7.3%)	p<0.05
	Respiratory	206 (5.5%)	47 (4.4%)	NS
	Diabetes mellitus	224 (6.0%)	24 (2.2%)	p<0.05
	Rheumatological	310 (8.3%)	48 (4.5%)	p<0.05
	Other	609 (16.3%)	111 (10.4%)	p<0.05
NS – Not significant				

Supplementary Table II. Frequencies of DLQI scores N = 3846

DLQI score band descriptors (ref. 6, 13)	**Valid %**	**Number**	**Cumulative % DLQI score**
Extremely large (21-30)	5.2%	200	5.2% > 20
Very large (11-20)	20.3%	782	25.5% >11
Moderate (6-10)	19.4%	745	44.9% > 6
Small (2-5)	26.6%	1023	71.5% > 2
No (0-1)	28.5%	1096	
Total		3846	

Mean DLQI (SD). **N = Valid number of patients**			
Sex	Male: **6.4** (6.7) N=1686	Female: **7** (6.8) N=2168	
Age groups (years)	18-35: **7.34** (6.8) N=1247	36-65: **6.94** (7) N=1880	>66: **5.06** (5.9) N=652
Socioeconomic status	Low: **8.22** (7.2) N=720	Middle: **6.44** (6.6) N=2844	High: **5.88** (5.9) N=327
Comorbidity	None: **6.74** (6.7) N=2573	Any: **6.89** (6.9) N=1033	

Country (in alphabetical order) Mean DLQI (SD)

BE	DK	FR	GER	HU	IT[a]	NLD	NO[b]	PL	RUS	ES	TR	UK
3.38 (3.9)	**5.79** (6.7)	**4.58** (5.3)	**7.14** (7.4)	**7.26** (7.3)	**8.01** (6.7)	**5.09** (5.7)	**6.99** (6.7)	**10.89** (7.8)	**10.38** (7.0)	**2.26** (3.6)	**7.35** (5.6)	**5.23** (6.8)
N=250	265	126	290	261	527	235	534	275	273	274	270	213

[a]Padua and Rome
[b]Oslo and Stavanger
BE-Belgium DK-Denmark FR-France GER-Germany HU-Hungary IT-Italy NLD-The Netherlands NO-Norway PL-Poland RUS-Russia ES-Spain TR-Turkey UK-United Kingdom

Supplementary Table III. Distribution by DLQI score band descriptors for each diagnosis and their effect on quality of life (QoL).

Diagnosis	DLQI Mean (SD)	DLQI ≥ 6 (at least moderate) % (N)	DLQI ≥ 11 (at least very large)	Extremely large effect on QoL (≥20)	Very large effect on QoL (11-20)	Moderate effect on QoL (6-10)	Small effect on QoL (2-5)	No effect on QoL (0 or 1)	DLQI score descriptor
Total N=3846	**6.73 (6.8)**	**44.9% (1711)**	**25.5% (977)**	**5.2% (200)**	**20.3% (777)**	**19.4% (734)**	**26.6% (988)**	**28.5% (920)**	**Moderate**
Hidradenitis suppurativa N=46	12.7 (7.6)	80.4% (37)	58.7% (27)	17.4% (8)	41.3% (19)	21.7% (10)	15.2% (7)	4.3% (2)	Very large (11-20)
Atopic dermatitis N=172	11.53 (7.2)	74.4% (128)	50% (86)	13.4% (23)	36.6% (63)	24.4% (42)	22.7% (39)	2.9% (5)	
Prurigo N=27	11.44 (8.2)	52.9% (17)	48.1% (13)	18.5% (5)	29.6% (8)	14.8% (4)	22.2% (6)	14.8% (4)	
Pruriuts N=60	10.97 (7.1)	74.9% (45)	46.6% (28)	13.3% (8)	33.3% (20)	28.3% (17)	18.3% (11)	6.7% (4)	
Urticaria N=69	9.59 (6.7)	70.9% (49)	40.5% (28)	4.3% (3)	36.2% (25)	30.4% (21)	17.4% (12)	11.6% (8)	Moderate (6-10)[h]
Venous leg ulcers N=113	9.45 (7.3)	66.4% (74)	44.3% (49)	8% (9)	35.3% (40)	22.1% (25)	16.8% (19)	17.7% (20)	
Psoriasis N=660	9.14 (7.6)	57.6% (380)	38.8% (256)	9.4% (62)	29.4% (194)	18.8% (124)	24.1% (159)	18.3% (121)	
Genital (non-venereal)[a] N=32	8.81 (6.4)	65.6% (21)	37.5% (12)	9.4% (3)	28.1% (9)	28.1% (9)	21.9% (7)	12.5% (4)	
Blistering conditions N=66	8.59 (7.4)	54.6% (36)	34.9% (23)	7.6% (5)	27.3% (18)	19.7% (13)	27.3% (18)	18.2% (12)	
Hand eczema N=156	8.51 (7.2)	55.1% (86)	30.8% (48)	10.3% (16)	20.5% (32)	24.4% (38)	32.7% (51)	12.2% (19)	
Psychodermatological conditions N=34	8.5 (7.1)	57.7% (19)	38.2% (13)	2.9% (1)	35.3% (12)	17.6% (6)	29.4% (10)	14.7% (5)	
Eczema N=241	8.42 (7.2)	54% (130)	36.6% (88)	7.1% (17)	29.5% (71)	17.4% (42)	28.6% (69)	17.4% (42)	
Hyperhidrosis N=12	8.08 (7.6)	50% (6)	33.3 (4)	8.3% (1)	25% (3)	16.7% (2)	25% (3)	25% (3)	
Vasculitis, immunological ulcers[b] N=67	7.06 (6.1)	52.2% (35)	25.3% (17)	4.5% (3)	20.9% (14)	26.9% (18)	26.9% (18)	20.9% (14)	
Connective tissue disease N=91	7.81 (7.0)	51.7% (47)	30.8% (28)	7.7% (7)	23.1% (21)	20.9% (19)	24.2% (22)	24.2% (22)	
Oral conditions[c] N=26	6.77 (6.6)	50% (13)	23.1% (6)	7.7% (2)	15.4% (4)	26.9% (7)	23.1% (6)	26.9% (7)	
Papulosquamous diseases[d] N=113	6.37 (6.4)	44.3% (50)	19.5% (22)	7.1% (8)	12.4% (14)	24.8% (28)	28.3% (32)	27.4% (31)	
Other[e] N=96	6.34 (6.6)	43.8% (42)	24% (23)	4.2% (4)	19.8% (19)	19.8% (19)	24% (23)	32.3% (31)	
Seborrhoeic dermatitis N=75	6.28 (4.4)	52% (39)	16% (12)	0	16% (12)	36% (27)	37.3% (28)	10.7% (8)	
Infections of the skin N=253	6.24 (5.8)	45.4% (115)	22.9% (58)	1.6% (4)	21.3% (54)	22.5% (57)	30.4% (77)	23.1% (61)	
Acne N=234	6.21 (5.2)	40.6% (103)	20.6% (48)	1.4% (3)	19.2% (45)	20% (55)	35.5% (83)	20.5% (48)	
Lichen planus N=46	6.09 (5.4)	48.9% (22)	20% (9)	2.2% (1)	17.8% (8)	28.9% (13)	26.7% (12)	24.4% (11)	
Alopecia areata N=31	5.58 (6.8)	38.7% (12)	16.1% (5)	3.2% (1)	12.9% (4)	22.6% (7)	22.6% (7)	38.7% (12)	
Rosacea N=75	5.37 (5.3)	40% (30)	20% (15)	1.3% (1)	18.7% (14)	20% (15)	25.3% (19)	34.7% (26)	Small (2-5)[h]
Scars, skin fibrosis, morphea N=27	5.3 (4.8)	33.2% (9)	18.5% (5)	0	18.5% (5)	14.8% (4)	48.1% (13)	18.5% (5)	
Allergic, drug, phototoxic/-allergic N=24	5.29 (4.3)	41.7% (10)	12.5% (3)	0	12.5% (3)	29.2% (7)	33.3% (8)	25% (6)	
Other hair disorders[f] N=82	5.01 (5.4)	35.3% (29)	15.8% (13)	2.4% (2)	13.4% (11)	19.5% (16)	31.7% (26)	32.9% (27)	
Melasma, pigment disorders N=32	4.97 (4.7)	40.6% (13)	15.6% (5)	0	15.6% (5)	25% (8)	21.9% (7)	37.5% (12)	
Granuloma annulare N=13	4.0 (2.9)	30.8% (4)	0	0	0	30.8% (4)	46.2% (6)	23.1% (3)	
Nail diseases N=17	3.88 (4.3)	35.3% (6)	5.9% (1)	0	5.9% (1)	29.4% (5)	17.6% (3)	47.1% (8)	
Vitiligo N=24	3.83 (3.7)	29.2% (7)	4.2% (1)	0	4.2% (1)	25% (6)	33.3% (8)	37.5% (9)	
Malignant melanoma N=86	2.72 (4.4)	15.2% (13)	8.2% (7)	1.2% (1)	7% (6)	7% (6)	30.2% (26)	54.7% (47)	
Benign skin tumours N=159	2.72 (3.7)	18.8% (30)	5% (8)	0	5% (8)	13.8% (22)	24.5% (39)	56.6% (90)	
Non-melanoma skin cancer and AK[g] N=401	2.37 (5.0)	13.5% (54)	4% (16)	0.5% (2)	3.5% (14)	9.5% (38)	28.4% (114)	58.1% (233)	
Nevi (91.4% - no or small) N=186	1.52 (2.9)	8.6% (14)	2.7% (5)	0	2.7% (5)	5.9% (11)	18.8% (35)	72.6% (135)	

[a]Lichen sclerosus, pruritus/eczema vulvae, scroti et ani, balanitis/balanoposthitis. [b]Including pyoderma gangrenosum, Behçet's syndrome, panniculitis, necrobiosis lipoidica. [c]Stomatitis, glossitis, cheilitis, aphthae. [d]Other than psoriasis: parapsoriasis, pityriasis rubra pilaris, pityriasis lichenoides, pityriasis rosea, Darier's disease. [e]Skin check of organ transplant recipients, other follow-up, or uncertain diagnosis. [f]Effluvium, androgenic alopecia, cicatricial alopecia, other hair/scalp conditions. [g]Actinic keratosis. [h]Values > -.5 rounded upward. Values < -.5 rounded downward.