

# The burden of common skin diseases assessed with the EQ5D™: a European multicentre study in 13 countries

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## Summary

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**Background** Generic instruments measuring health-related quality of life (HRQoL), like EQ5D™, enable comparison of skin diseases with healthy populations and nondermatological medical conditions, as well as calculation of utility data.

**Objectives** To measure HRQoL in patients with common skin diseases and healthy controls across Europe using the EQ5D.

**Methods** This multicentre observational cross-sectional study was conducted in 13 European countries. Each dermatology clinic recruited at least 250 consecutive adult outpatients to complete questionnaires, including the EQ5D.

**Results** There were 5369 participants (4010 patients and 1359 controls). Mean  $\pm$  SD self-rated health state reported by patients was  $69.9 \pm 19.7$ ; for controls it was  $82.2 \pm 15.5$ . When adjusted for confounding factors, including comorbidity, mean patient EQ visual analogue scores were 10.5 points lower than for controls (standardized  $\beta = -0.23$ ). Odds ratio with 95% confidence interval for impairment in all five dimensions of EQ5D adjusted for confounders was doubled for patients compared with controls. Patients with hidradenitis suppurativa (HS), blistering conditions, leg ulcers, psoriasis and eczemas had the highest risk for reduction in HRQoL in most dimensions (2–10-fold). Data on differences of impairment by dimensions offer new insights.

**Conclusions** This study confirms the large impact skin conditions have on patients' well-being, differentiating between aspects of HRQoL. Patients with HS, blistering diseases, leg ulcers, infections and most chronic skin diseases reported reduced HRQoL compared with patients with chronic obstructive lung disease, diabetes mellitus, cardiovascular disease and cancers. These findings are important in the prioritization of resource allocation between medical fields and within dermatological subspecialties.

### What is already known about this topic?

- The EQ5D™ can be used to compare life quality impairment from diseases across a range of specialties and to generate utility data.
- The EQ5D has previously been little used in dermatology.

### What does this study add?

- This study has generated EQ5D data across a range of dermatological diagnoses in a large cohort of patients across Europe.
- Skin diseases affect quality of life differently across different dimensions.
- This EQ5D information may assist appropriate care and resource allocation.

The generic instrument EQ5D™ is increasingly being used as a patient-reported outcome measure across medicine, and by regulatory authorities to calculate utility values. However, there are limited EQ5D data in dermatology. EQ5D data provide insight into the impact skin diseases have and supply robust information for comparison and utility calculations.

The impact of skin disease on a patient's health-related quality of life (HRQoL) can be measured in several ways. Dermatology-specific instruments have been widely used – generic measures to a lesser extent.<sup>1–4</sup> Generic instruments enable comparison of HRQoL between patients and healthy populations, and across patients with different medical conditions.

Generic instruments for measurement of HRQoL are designed to be used across a wide range of diseases and populations. The EuroQol Group, a multidisciplinary team of European researchers, developed the EQ5D with the goal of creating a user-friendly instrument applicable across all medical fields and the general population. The EQ5D has shown extensive cultural and language adaptation, and good validity.<sup>5</sup>

The EQ5D can be used to assess HRQoL across medical specialties, as well as in dermatology. A review by Pereira *et al.* identified 19 articles describing EQ5D usage in atopic dermatitis (AD), acne vulgaris, herpes simplex, psoriasis (PSO), hand eczema and malignant melanoma (MM).<sup>6</sup> However, in a systemic review of HRQoL measured by EQ5D in dermatological patients,<sup>7</sup> only 16 articles met the inclusion criteria, 12 on PSO or psoriatic arthritis (PsA) and one each on acne, hidradenitis suppurativa (HS), leg ulcer and hand eczema. Not all studies evaluated self-reported health state, and the majority of studies evaluated response to an intervention (before and after), while only three assessed the immediate health status. No studies adjusted for somatic and psychiatric comorbidities. The overall validity of the EQ5D was good in patients with skin diseases, especially for PSO and PsA.<sup>7</sup>

Given the small number of dermatological studies assessing HRQoL with the EQ5D, using this generic instrument we aimed to describe the impairment in HRQoL in a large sample of dermatological outpatients across Europe and compare it with controls and other diseases.

## Patients and methods

### Participants and settings

In this cross-sectional multicentre study, patients were recruited from dermatological outpatient clinics in 13 European countries from November 2011 to February 2013. Details of the cohort have been reported previously.<sup>8</sup>

The study protocol was approved by the Regional Committee for Medical Research Ethics in Norway. At each site, ethical approval was sought when necessary. The study was conducted in accordance with the Declaration of Helsinki.

Consecutive patients were invited to participate on random days. Each centre recruited 250 patients, then a further 25, increasing the number of participants. In total, 5442 individuals agreed to participate (79.9% of those invited). Of the initial 4026 patients, 16 were excluded: nine were too young, and seven had missing data. Of the initial 1416 controls, 57 were excluded because they had a skin disease. Data were therefore used from 4010 patients and 1359 controls. For detailed information on participating centres and participant characteristics, see Appendices S1–S3 (online Supporting Information).

Patients were informed of the study and gave their written informed consent. The inclusion criteria were age > 18 years, understanding the local language and not suffering from severe mental disease. Each participant was asked to complete several questionnaires on sociodemographic variables [sex, age, ethnicity, marital status, education and self-reported socioeconomic status (SES)], the EQ5D and other questionnaires as reported elsewhere.<sup>8</sup> Each patient was clinically examined by the dermatologist, who also recorded comorbidities: diabetes mellitus, and cardiovascular, chronic respiratory, rheumatological or other disease, including psychiatric conditions. A control group of healthy workers were invited to participate. Only those willing to participate completed the questionnaires, self-reporting their comorbidities.

## Measures

HRQoL was measured with the EQ5D, a standardized generic instrument consisting of two parts.<sup>9</sup>

The EQ visual analogue scale (EQ-VAS) records respondents' self-rated health on a visual analogue scale, from '0' to '100' (i.e. worst to best imaginable health state). This information can be used as a quantitative measure of health outcome as judged by the individual respondent.

The EQ5D further assesses health status across dimensions of: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Each health dimension has three response levels: 'no problems', 'some problems' and 'extreme problems'. EQ5D reflects the current general health status.

The EQ5D questionnaire is available in 170 languages. Population norms for 24 countries and regions exist. In our study, questionnaires in languages validated for each country involved were used. Further information is available at [www.euroqol.org](http://www.euroqol.org).<sup>9,10</sup>

## Statistical analysis

Data from all centres were merged in a single file, checked and cleaned. The diagnoses were organized into 26 disease groups, in line with the Lambeth study describing skin disease distribution in the community.<sup>11</sup> The skin conditions not fitting into any of the Lambeth study categories, but represented by enough patients, were assigned into separate diagnostic groups.

Comparisons between patients and controls were performed with the t-test for continuous variables and  $\chi^2$  test for dichotomous or categorical variables.<sup>8</sup>

Linear regression was used for continuous variables (EQ-VAS), adjusting for age, sex, SES and comorbidities. EQ5D levels were dichotomized into 'not impaired' and 'impaired'. Multivariate logistic regression was performed to analyse the dichotomized EQ5D domains, calculated for each disease separately, adjusting for age, sex, SES and comorbidity, reporting odds ratio (OR) with a 95% confidence interval (CI). To prevent an  $\alpha$ -error accumulation because of the great number of regression analyses we corrected for multiple testing (Holm correction for  $n = 216$  regression analyses). We report unadjusted P-values, and unadjusted 95% CIs, but only corrected P-values  $< 0.05$  after Holm correction were considered significant.<sup>12</sup>

## Results

Details on participant characteristics have been published previously.<sup>8</sup> Mean patient age was 47 years vs. 41 years for the controls. There were more females in both groups (56.5% of the patients; 66.6% of the controls). Age, sex and comorbidities differed significantly between patients and controls. For detailed participant characteristics, see Appendices S1–S3 (online Supporting Information).

The participants' self-rated health state is shown in Table 1. Patients had lower mean EQ-VAS scores (69.9) than controls

(82.2; European norms 71.9–83.5).<sup>10</sup> Patients with leg ulcers, prurigo, HS and blistering disorders scored the lowest self-reported health (EQ-VAS  $< 60$ ). Pruritus, oral diseases, psoriasis, AD, vasculitis, connective tissue disease and genital disorders, along with eczema, urticaria, hand eczema and several other pruritic, chronic inflammatory conditions, each had a mean EQ-VAS score of  $< 70$ .

Linear regression analysis of EQ-VAS score, adjusted for age, sex, SES and comorbidity (diabetes mellitus, and cardiovascular, respiratory, rheumatic or other disease) is presented in Table 2. Patients reported 10.5 points lower mean self-rated health ( $\beta = -0.23$ ) than controls. Patients with HS registered the lowest self-reported health, followed by those with prurigo and blistering diseases ( $> 20$  points lower than controls). Diseases with the next highest significant impact were leg ulcers, psychodermatological conditions, oral diseases, AD, fibrotic conditions, morphea and scars, hair disorders, psoriasis, pruritus, alopecia areata, urticaria, hand eczema, genital diseases, connective tissue disease, eczema, vasculitis/immunological ulcers and papulosquamous diseases ( $> 10$  points lower than controls).

Impairment for each of the five dimensions of the EQ5D for patients compared with controls is given in Table 3. Significant ORs after Holm correction are reported.

### Mobility

Impaired mobility was highest for leg ulcers (10-fold increased risk), HS (sixfold increased risk), psychodermatological conditions (fourfold increased risk), vasculitis/immunological ulcers and blistering conditions (threefold increased risk), and psoriasis and infections (twofold increased risk). Risk for impaired mobility was similar to controls for acne, rosacea, seborrhoeic dermatitis, naevi, MM, benign tumours, actinic keratosis and nonmelanoma skin cancer (NMSC).

### Self-care

The OR for impaired self-care was increased ninefold for blistering diseases, sevenfold for prurigo, sixfold for leg ulcers, fivefold for HS and hand eczema, fourfold for AD and psoriasis, and twofold for eczema.

### Usual activity

The risk for impairment (OR) in usual activities was highest in leg ulcers (eightfold increased risk), followed by HS (sixfold increased risk), blistering diseases (fivefold increased risk) and hand eczema (fourfold increased risk). AD, psoriasis and connective tissue disease had a threefold increased risk, while eczema, papulosquamous diseases and infections (almost) had a doubled risk.

### Pain/discomfort

This dimension of HRQoL was the most impaired and showed high risk for the majority of skin diseases. Patients with HS

Table 1 Distribution of the EQ visual analogue scale self-reported health status in common skin diseases

Diagnosis	Mean ± SD	n	Mean ± SD age (years)	Male (%)	Missing	Valid
Healthy controls	82.2 ± 15.5	1359	41.1 ± 13.6	33.4	34	1325
All patients	69.9 ± 19.7	4010	47.1 ± 18.0	43.7	297	3713
Leg ulcers	56.0 ± 20.2	125	60.8 ± 15.0	43.9	31	94
Prurigo	56.5 ± 15.9	28	57.4 ± 14.8	60.7	2	26
Hidradenitis suppurativa	56.9 ± 20.7	48	40.3 ± 12.2	20.8	3	45
Blistering diseases	59.0 ± 21.0	68	54.9 ± 14.7	42.6	13	55
Psychodermatological conditions	61.7 ± 19.4	36	47.1 ± 17.0	22.2	0	36
Pruritus	62.6 ± 18.4	61	54.3 ± 15.4	27.9	3	58
Scars, fibrosis of the skin, morphea	63.6 ± 20.3	27	46.3 ± 15.0	32.1	2	25
Oral conditions <sup>a</sup>	63.9 ± 22.6	25	49 ± 14.5	57.7	0	25
Psoriasis	65.6 ± 20.0	682	47 ± 15.6	54.2	41	641
Atopic dermatitis	66.0 ± 19.0	177	35.2 ± 15.0	43.5	11	166
Vasculitis and immunological ulcers <sup>b</sup>	66.4 ± 17.2	70	50.4 ± 16.6	30.0	10	60
Connective tissue disease	66.5 ± 20.2	96	48.5 ± 14.9	20.0	11	88
Genital (notvenereal) <sup>c</sup>	67.4 ± 22.1	35	48.9 ± 16.7	71.4	4	31
Other hair disorders <sup>d</sup>	67.4 ± 21.4	83	41.0 ± 16.6	19.3	5	78
Lichen planus	68.3 ± 18.8	47	54.2 ± 15.0	31.9	3	44
Urticaria	68.4 ± 19.2	69	39.4 ± 14.7	40.6	3	66
Hand eczema	68.9 ± 20.7	158	45.2 ± 15.4	42.4	8	150
Eczema	69.0 ± 19.2	251	48.6 ± 18.2	39.2	13	238
Papulosquamous skin diseases <sup>e</sup>	69.5 ± 20.3	117	44.7 ± 18.4	40.5	7	110
Alopecia areata	69.7 ± 18.1	33	42.8 ± 14.1	33.3	2	31
Allergic, drug and phototoxic/photoallergic reactions	70.6 ± 21.6	27	46.4 ± 18.2	56.0	2	25
Malignant melanoma	72.4 ± 20.2	89	58.2 ± 13.8	46.1	3	86
Hyperhidrosis	72.7 ± 23.2	11	32.1 ± 12.9	25.0	1	10
Granuloma annulare	73.1 ± 13.0	13	51.3 ± 16.7	38.5	0	13
Nonmelanoma skin cancer and actinic keratosis	73.4 ± 19.0	426	65.3 ± 13.0	51.2	37	389
Infections of the skin	73.4 ± 18.0	266	40.4 ± 16.7	53.8	17	249
Nail diseases	73.4 ± 16.2	21	49.6 ± 15.8	33.3	2	19
Rosacea	74.6 ± 14.9	77	49.0 ± 14.5	34.2	2	75
Seborrhoeic dermatitis	75.5 ± 17.5	78	40.1 ± 15.8	43.6	3	75
Benign skin tumours	76.2 ± 16.2	163	49.2 ± 16.2	43.0	13	150
Acne	78.3 ± 16.5	236	24.7 ± 7.5	37.7	4	232
Hyper-/hypopigmentation, melasma	80.3 ± 15.4	32	40.8 ± 13.8	28.1	0	32
Naevi	80.5 ± 14.1	192	39.8 ± 15.2	35.9	10	182
Vitiligo	83.1 ± 10.3	25	36.3 ± 14.0	60.0	0	25
Other skin conditions <sup>f</sup>	67.9 ± 18.2	105	51.3 ± 17.0	45.2	22	83

<sup>a</sup>Stomatitis, glossitis, cheilitis, aphthae; <sup>b</sup>including pyoderma gangrenosum, Behçet disease, panniculitis, necrobiosis lipoidica; <sup>c</sup>lichen sclerosus, pruritus/eczema vulvae, scroti et ani, balanoposthitis; <sup>d</sup>effluvium, androgenic alopecia, cicatricial alopecia, other hair/scalp conditions; <sup>e</sup>other than psoriasis: parapsoriasis, pityriasis rubra pilaris, pityriasis lichenoides, pityriasis rosea, Darrier disease; <sup>f</sup>skin examination after solid organ transplant or for other disease or diagnosis unclear.

had the highest OR (50.28), followed by prurigo (eightfold increased risk), leg ulcers, blistering disorders and oral conditions (all fivefold increased risk), AD, hand eczema, psoriasis, vasculitis/immunological ulcers, urticaria and connective tissue diseases (all fourfold increased risk). A threefold increased risk was seen in psychodermatological conditions, eczema, pruritus, infections, seborrhoeic dermatitis and lichen planus. The risk was doubled for papulosquamous diseases.

### Depression/anxiety

The risk for depression/anxiety was highest for patients with chronic skin conditions; fourfold increased for pruritus, oral

diseases and alopecia areata; threefold for urticaria, psychodermatological conditions and connective tissue disease; twofold for acne, psoriasis, AD, hand eczema, hair disorders, seborrhoeic dermatitis and infections.

### Discussion

Patients across Europe with common skin diseases experience a substantial reduction in self-reported health status. These findings are in agreement with other studies of chronic disorders and chronic skin diseases.<sup>13,14</sup> Leg ulcers, HS, blistering diseases and prurigo had the lowest means (< 60) similar to rheumatoid arthritis pain (56.4),<sup>15</sup> cardiovascular disease (37–

**Table 2** Linear regression EQ visual analogue scale adjusted for age, sex, socioeconomic status and comorbidity (diabetes mellitus, cardiological, respiratory, rheumatic or other disease)<sup>a</sup>

Diagnosis	$\beta$ (95% CI)	Standardized $\beta$	Uncorrected P-value	Valid (n)
All patients	-10.5 (-11.8 to -9.2)	-0.23	< <b>0.001</b>	3418
Hidradenitis suppurativa	-24.2 (-28.9 to -19.5)	-0.28	< <b>0.001</b>	42
Prurigo	-22.3 (-28.7 to -15.8)	-0.20	< <b>0.001</b>	22
Blistering diseases	-21.2 (-25.6 to -16.7)	-0.26	< <b>0.001</b>	48
Leg ulcers	-19.9 (-23.8 to -16.0)	-0.29	< <b>0.001</b>	78
Psychodermatological conditions	-18.1 (-23.2 to -12.9)	-0.20	< <b>0.001</b>	35
Oral (glossitis, stomatitis, cheilitis, aphthae)	-17.0 (-23.0 to -11.1)	-0.17	< <b>0.001</b>	26
Other skin conditions <sup>b</sup>	-18.0 (-23.0 to -13.1)	-0.21	< <b>0.001</b>	38
Hyperhidrosis	-16.8 (-27.2 to -6.3)	-0.09	0.002	8
Atopic dermatitis	-16.1 (-18.6 to -13.4)	-0.32	< <b>0.001</b>	148
Scars, fibrosis of the skin, morphea	-15.6 (-21.4 to -9.7)	-0.15	< <b>0.001</b>	28
Other hair disorders <sup>c</sup>	-15.1 (-18.8 to -11.4)	-0.23	< <b>0.001</b>	73
Psoriasis	-14.6 (-16.4 to -12.8)	-0.37	< <b>0.001</b>	602
Pruritus	-14.3 (-18.6 to -10.1)	-0.19	< <b>0.001</b>	56
Alopecia areata	-12.9 (-18.3 to -7.4)	-0.14	< <b>0.001</b>	30
Urticaria	-12.6 (-16.6 to -8.5)	-0.18	< <b>0.001</b>	58
Hand eczema	-11.0 (-13.8 to -8.2)	-0.21	< <b>0.001</b>	140
Genital (notvenereal) <sup>d</sup>	-10.8 (-16.5 to -5.1)	-0.11	< <b>0.001</b>	29
Connective tissue disease	-10.7 (-14.4 to -6.9)	-0.16	< <b>0.001</b>	70
Eczema	-10.6 (-12.9 to -8.3)	-0.24	< <b>0.001</b>	230
Vasculitis and immunological ulcers <sup>e</sup>	-10.6 (-14.8 to -6.4)	-0.15	< <b>0.001</b>	55
Papulosquamous skin diseases <sup>f</sup>	-10.1 (-13.3 to -6.9)	-0.18	< <b>0.001</b>	100
Allergic, drug, phototoxic/photoallergic reactions	-9.7 (-16.2 to -3.2)	-0.09	0.004	21
Lichen planus	-9.1 (-14.0 to -4.3)	-0.11	< <b>0.001</b>	40
Infections of the skin	-8.7 (-10.9 to -6.5)	-0.21	< <b>0.001</b>	239
Acne	-7.0 (-9.4 to -4.5)	-0.17	< <b>0.001</b>	226
Malignant melanoma	-7.0 (-10.8 to -3.2)	-0.11	< <b>0.001</b>	74
Nail diseases	-7.0 (-14.0 to -0.0)	-0.06	0.050	18
Granuloma annulare	-6.8 (-15.0 to 1.4)	-0.05	0.103	13
Seborrhoeic dermatitis	-6.4 (-10.0 to -2.9)	-0.10	< 0.001	74
Rosacea	-5.6 (-9.3 to -2.0)	-0.09	0.003	67
Benign tumours	-3.9 (-6.5 to -1.2)	-0.08	0.005	146
Nonmelanoma skin cancer and actinic keratosis	-3.1 (-5.8 to -0.6)	-0.08	0.014	359
Hyper-/hypopigmentations, melasma	-2.5 (-7.8 to 2.9)	-0.03	0.365	31
Naevi	-2.1 (-4.5 to 0.2)	-0.05	0.079	172
Vitiligo	-0.07 (-6.1 to 6.0)	-0.001	0.980	24

Bold denotes significance after Holm correction. CI, confidence interval. <sup>a</sup>Patients: 622 missing (3418 valid); controls: 331 missing (1028 valid). <sup>b</sup>Skin examination after organ transplant or for other disease; diagnosis unclear. <sup>c</sup>Effluvium; androgenic alopecia; cicatricial alopecia; other hair/scalp conditions. <sup>d</sup>Lichen sclerosus, pruritus/eczema vulvae, scroti et ani, balanoposthitis. <sup>e</sup>Including pyoderma gangrenosum, Behçet disease, panniculitis, necrobiosis lipoidica. <sup>f</sup>Other than psoriasis: parapsoriasis, pityriasis rubra pilaris, pityriasis lichenoides, pityriasis rosea, Darrier disease.

89),<sup>16,17</sup> cancer (48.0–84.0),<sup>16,18</sup> liver disease (57–70)<sup>16</sup> and chronic obstructive pulmonary disease (COPD; 54.7–58.8).<sup>19</sup> The impairment in mean self-reported health for other chronic skin diseases (psoriasis, atopic eczema, pruritus, hand eczema, connective tissue disease and genital conditions) showed mean values < 70, similar to diabetes mellitus (68.8),<sup>20</sup> cardiovascular disease (37–89),<sup>16,17</sup> anxiety (63.8),<sup>21</sup> cancers (48.0–84.0),<sup>16,18</sup> liver disease (57–70),<sup>16</sup> chronic lymphocytic leukaemia (CLL; 70.3–77.6)<sup>22</sup> and visual impairment (64.0–82.0).<sup>16</sup> As comorbidity was adjusted for, the data indicate how skin disease alone impairs self-reported health. Again, patients with HS, prurigo, blistering disorders and leg ulcers rated their health lowest.

Different diseases lead to differing degrees of impairment for the different health dimensions, reinforcing the need for a selective approach when planning optimal care for outpatients. Overall, patients had a twofold higher risk for experiencing HRQoL impairment in all five dimensions compared with controls, after adjusting for confounding factors. Several diagnoses showed higher risk for impairment in certain dimensions than other diagnoses. Patients with high impairment in one dimension may need a different approach and differently allocated resources than those with other patterns of impairment.

Patients with acne, pruritus, urticaria, prurigo, connective tissue disease, hand eczema, seborrhoeic dermatitis and alopecias show less impairment in mobility and/or self-care,

**Table 3** EQ5D for different diagnoses with odds ratio (OR) and 95% confidence interval (CI) for each dimension<sup>a</sup>

Diagnosis (alphabetical order) and number of patients (n)	EQ5D mobility OR (95% CI) <sup>b</sup>	EQ5D self-care OR (95% CI) <sup>c</sup>	EQ5D activity OR (95% CI) <sup>d</sup>	EQ5D pain/discomfort OR (95% CI) <sup>e</sup>	EQ5D depression/anxiety OR (95% CI) <sup>f</sup>
All patients (3535; 1043 controls)	<b>1.91 (1.5–2.4)</b>	<b>2.86 (2.0–4.1)</b>	<b>2.38 (1.9–2.9)</b>	<b>2.67 (2.3–3.1)</b>	<b>1.96 (1.7–2.3)</b>
Acne (229)	1.03 (0.5–2.1)	1.39 (0.4–4.6)	1.43 (0.9–2.4)	1.43 (1.0–2.1)	<b>2.67 (1.9–3.7)</b>
Allergic, drug, phototoxic/ photoallergic reactions (22)	3.02 (1.1–8.3)	0.09 (0.1–7.3)	3.17 (1.2–8.4)	4.15 (1.6–10.5)	1.0 (0.4–2.5)
Alopecia areata (31)	1.09 (0.4–3.3)	3.07 (0.8–11.2)	2.18 (1.0–5.3)	1.72 (0.8–3.7)	<b>4.19 (2.0–8.9)</b>
Atopic dermatitis (151)	1.9 (1.2–3.1)	<b>4.14 (1.2–7.9)</b>	<b>3.72 (2.5–5.6)</b>	<b>4.99 (3.4–7.3)</b>	<b>2.31 (1.6–3.3)</b>
Benign skin tumours (154)	0.7 (0.4–1.2)	0.84 (0.4–2.0)	0.86 (0.5–1.5)	1.11 (0.8–1.6)	1.16 (0.8–1.7)
Blistering diseases (49)	<b>3.12 (1.6–6.2)</b>	<b>9.73 (4.4–21.6)</b>	<b>5.35 (2.8–10.2)</b>	<b>5.72 (2.9–11.5)</b>	1.87 (1.0–3.4)
Connective tissue disease (75)	2.25 (1.3–4.0)	2.11 (0.9–5.2)	<b>3.01 (1.8–5.2)</b>	<b>4.30 (2.5–7.3)</b>	<b>3.16 (1.9–5.2)</b>
Eczema (237)	1.44 (1.0–2.2)	<b>2.78 (1.6–4.9)</b>	<b>2.64 (1.9–3.8)</b>	<b>3.96 (2.9–5.4)</b>	1.49 (1.1–2.0)
Genital, not venereal (30) <sup>g</sup>	1.34 (0.5–3.6)	2.04 (0.6–7.6)	2.74 (1.2–6.4)	2.42 (1.1–5.3)	1.24 (0.6–2.7)
Granuloma annulare (13)	0.49 (0.1–1.8)	0	1.01 (0.2–4.8)	0.74 (0.2–2.4)	0.52 (0.2–1.6)
Hand eczema (145)	2.10 (1.3–3.3)	<b>5.04 (2.8–9.0)</b>	<b>4.08 (2.7–6.1)</b>	<b>4.53 (3.1–6.7)</b>	<b>2.23 (1.6–3.2)</b>
Hidradenitis suppurativa (44)	<b>6.02 (3.1–11.8)</b>	<b>5.39 (2.1–13.9)</b>	<b>6.26 (3.3–11.9)</b>	<b>50.28 (12.0–211.0)</b>	2.34 (1.3–4.4)
Hyperhidrosis (9)	6.19 (1.5–26.3)	6.08 (0.7–53.5)	7.39 (1.9–28.6)	25.0 (3.1–202.9)	4.26 (1.0–17.5)
Infections of the skin (250)	2.52 (1.7–3.7)	2.78 (1.6–5.0)	<b>1.99 (1.4–2.9)</b>	<b>3.55 (2.6–4.8)</b>	<b>1.77 (1.3–2.4)</b>
Leg ulcers (97)	<b>10.1 (5.6–18.2)</b>	<b>6.49 (3.3–12.6)</b>	<b>8.12 (4.7–14.1)</b>	<b>5.87 (3.2–10.8)</b>	2.04 (1.2–3.4)
Lichen planus (43)	2.03 (1.0–4.2)	2.13 (0.8–5.9)	1.60 (0.8–3.4)	<b>3.42 (1.7–6.9)</b>	1.58 (0.8–3.8)
Malignant melanoma (76)	0.83 (0.4–1.6)	1.2 (0.5–3.1)	1.74 (0.9–3.2)	0.88 (0.5–1.5)	1.22 (0.7–2.1)
Nail conditions (33)	2.34 (0.8–7.1)	0	1.29 (0.4–4.6)	3.23 (1.2–8.8)	1.48 (0.6–3.9)
Naevi (178)	0.59 (0.3–1.1)	0.92 (0.3–2.5)	0.63 (0.4–1.2)	0.84 (0.6–1.2)	0.70 (0.5–1.0)
Nonmelanoma skin cancer and actinic keratosis (372)	1.04 (0.7–1.6)	0.86 (0.4–1.7)	1.14 (0.7–1.7)	0.88 (0.6–1.2)	0.94 (0.7–1.3)
Oral conditions (26) <sup>h</sup>	1.04 (0.3–3.3)	2.07 (0.4–9.8)	3.19 (1.3–7.8)	<b>5.94 (2.4–14.8)</b>	<b>4.60 (2.0–10.6)</b>
Other dermatological conditions (39) <sup>i</sup>	2.88 (1.4–6.0)	2.15 (0.7–6.8)	<b>4.79 (2.4–9.6)</b>	<b>6.56 (2.9–14.8)</b>	2.39 (1.2–4.6)
Other hair disorders (75) <sup>j</sup>	1.16 (0.6–2.4)	1.24 (0.4–4.3)	2.15 (1.2–3.9)	2.13 (1.3–3.5)	<b>2.40 (1.5–3.9)</b>
Papulosquamous diseases (101) <sup>k</sup>	1.52 (0.9–2.7)	1.57 (0.6–3.8)	<b>2.81 (1.7–4.6)</b>	<b>2.18 (1.4–3.4)</b>	2.37 (1.0–2.4)
Prurigo (24)	4.20 (1.7–10.6)	<b>7.35 (2.6–21.1)</b>	3.26 (1.3–8.2)	<b>8.63 (2.8–26.5)</b>	4.90 (1.9–12.4)
Pruritus (58)	2.31 (1.2–4.4)	2.36 (0.9–5.9)	2.28 (1.2–4.3)	<b>3.93 (2.1–7.5)</b>	<b>4.27 (2.4–7.7)</b>
Psoriasis (621)	<b>2.69 (2.0–3.6)</b>	<b>4.05 (2.6–6.3)</b>	<b>3.53 (2.7–4.6)</b>	<b>4.25 (3.4–5.3)</b>	<b>2.58 (2.1–3.2)</b>
Psychodermatological conditions (35)	<b>4.75 (2.2–10.2)</b>	1.92 (0.5–7.1)	1.85 (0.8–4.4)	<b>3.99 (1.9–8.4)</b>	<b>3.43 (1.7–7.0)</b>
Rosacea (67)	1.14 (0.6–2.3)	1.37 (0.5–4.2)	1.61 (0.8–3.1)	1.79 (1.1–3.0)	1.34 (0.8–2.3)
Scars, fibrosis of skin, morphoea (26)	1.71 (0.6–4.8)	1.17 (0.2–9.2)	0.29 (0.2–2)	2.59 (1.2–5.8)	1.56 (0.7–3.5)
Seborrhoeic dermatitis (75)	0.91 (0.4–2.0)	2.28 (0.9–5.9)	1.49 (0.8–2.9)	<b>3.27 (2.0–5.4)</b>	<b>2.21 (1.4–3.6)</b>
Hyper-/hypopigmentations, melasma (31)	0.57 (0.1–2.5)	1.1 (0.1–8.8)	0.86 (0.3–2.9)	0.46 (0.2–1.2)	1.47 (0.7–3.1)
Urticaria (61)	1.27 (0.6–2.8)	1.98 (0.7–6.0)	2.92 (1.6–5.4)	<b>4.10 (2.3–7.2)</b>	<b>3.44 (2.0–5.9)</b>
Vasculitis, immunological ulcers (58) <sup>l</sup>	<b>3.82 (2.1–7.1)</b>	3.84 (1.7–8.8)	3.0 (1.6–5.6)	<b>4.60 (2.4–8.7)</b>	1.25 (0.7–2.2)
Vitiligo (24)	0	0	0.41 (0.1–3.1)	0.81 (0.3–2.3)	1.78 (0.8–4.1)

Bold denotes significance after Holm correction. <sup>a</sup>OR adjusted for age, sex, socioeconomic status and comorbidity (diabetes mellitus, cardiovascular, respiratory, rheumatic or other disease). <sup>b</sup>Missing: 106 patients, 316 controls. <sup>c</sup>Missing: 100 patients, 317 controls. <sup>d</sup>Missing: 104 patients; 317 controls. <sup>e</sup>Missing: 108 patients, 318 controls. <sup>f</sup>Missing: 125 patients, 318 controls. <sup>g</sup>Lichen sclerosus, pruritus/eczema vulvae, scroti et ani, balanoposthitis. <sup>h</sup>Glossitis, stomatitis, cheilitis, aphthae. <sup>i</sup>Skin examination after organ transplant or other disease; diagnosis unclear. <sup>j</sup>Effluvium, androgenic alopecia, cicatricial alopecia, other hair/scalp conditions. <sup>k</sup>Other than psoriasis: parapsoriasis, pityriasis rubra pilaris, pityriasis lichenoides, pityriasis rosea, Darrier disease. <sup>l</sup>Including pyoderma gangrenosum, Behçet disease, panniculitis, necrobiosis lipoidica.

but are at high risk for pain/discomfort and depression/anxiety. For these patients, the dermatologist should be aware of the need for psychiatric support, in order to enhance HRQoL. In contrast, patients with leg ulcers, HS, vasculitis/immunological ulcers and blistering conditions have a high risk of impairment in mobility, self-care, usual activities and pain/discomfort but less for anxiety/

depression. These patients suffer more from the somatic aspect of their disease (even when correcting for comorbidities), but are at a lower risk for anxiety/depression than skin conditions of the face, hair disorders, hand eczema, oral or pruritic conditions. Therefore, this group of patients will need targeted strategies for managing discomfort, mobility and self-care issues.

This study has provided EQ5D data on a wide variety of dermatological diagnoses, correcting for confounding factors, most importantly for comorbidities. Owing to the relatively high level of comorbidity in dermatological patients, which may (partly) explain a lower HRQoL in this population, correcting for comorbidity is important in order to calculate the independent impact that the skin condition has on self-reported health. Using these data enables us to identify more precisely the specific support that different dermatological patient groups may need.

Patients with psoriasis in this study showed reduced self-reported health and reduced life quality. Several studies have evaluated mental health and impaired life quality in patients with psoriasis.<sup>6,7,23</sup> Generic, dermatology-specific and psoriasis-specific measures have confirmed psoriasis patients' reduced HRQoL. Differences between studies regarding degree of impairment may be explained by studies being carried out with different psoriasis populations, such as hospitalized patients vs. outpatients, or with differing severity of disease. Our study confirms the results of Møller *et al.*,<sup>16</sup> who showed life quality impairment in patients with psoriasis to be similar to those with other chronic diseases (cardiovascular, end-stage renal and liver diseases, diabetes, cancer and visual disorders).<sup>16</sup> As we also adjusted for confounding factors for each dimension, a more precise estimate of HRQoL impairment in patients with psoriasis attending dermatology clinics across Europe was obtained. Adjusting for comorbidities is important as psoriasis may be associated with several other diseases.

Patients with AD, a chronic, inflammatory, extensive skin disease, show lower mean EQ-VAS; fourfold increased OR for impairment in dimensions self-care, activity and pain/discomfort; and a twofold risk for depression/anxiety. Self-reported health, when corrected for age, sex, SES and comorbidities was lower than for controls. There are fewer studies on HRQoL in adult patients with AD than in children or their families. Our results are in agreement with other adult studies, even when other HRQoL instruments were used.<sup>24–27</sup>

Patients with leg ulcers had the lowest mean EQ-VAS, which remained considerable even after adjusting for confounding factors. Adjusted values for all dimensions of the EQ5D, except depression/anxiety, gave an OR of impairment of 5–10-fold. Iglesias *et al.* reported impaired HRQoL in all EQ5D dimensions and significant improvement in HRQoL in patients whose ulcers were healing.<sup>28</sup>

Patients with blistering diseases and HS showed extensive impairment of mean EQ-VAS, corrected EQ-VAS and EQ5D in four dimensions (not significant for anxiety/depression). Although the high degree of suffering of these two patient groups is evident to clinicians, few studies have measured HRQoL. As in our study, severely reduced HRQoL in HS when using EQ5D has been confirmed in other studies, which showed mean EQ-VAS scores close to those obtained in the present study.<sup>29,30</sup> Further investigation of HRQoL in this group is necessary.<sup>29–31</sup> There is little information on HRQoL in bullous diseases: one study reported severe impairment of life quality, which is consistent with our findings.<sup>32</sup>

Patients with pruritus, urticaria and prurigo had low EQ-VAS and adjusted EQ-VAS scores, similar to those with psoriasis, AD and connective tissue diseases. OR for pain/discomfort and depression/anxiety was 3–8-fold. Other studies confirm the large impact on HRQoL in patients with chronic pruritus and urticaria.<sup>33,34</sup>

Self-reported health was reduced in patients with hand eczema, as measured by mean and adjusted EQ-VAS. EQ5D in these patients showed a 4–5-fold risk of reduced self-care, activity and pain/discomfort, and a twofold risk for anxiety/depression. Our study showed severe impairment, in accordance with other studies on hand eczema in which different instruments were used.<sup>35–37</sup>

Patients with acne, facial dermatoses (seborrhoeic dermatitis, rosacea) and hair disorders reported EQ-VAS scores similar to healthy controls. The mobility, self-care, activity and pain/discomfort dimensions were not severely impaired, except for pain/discomfort in seborrhoeic dermatitis. However, the dimension of depression/anxiety showed at least a doubled risk for patients with alopecia areata, acne, seborrhoea and other hair disorders. Good self-reported health for patients with acne reflects the patients' young age and low associated comorbidity risk for facial dermatoses. However, this group suffers more from depression and anxiety, as also shown by other studies.<sup>8,38–42</sup>

Patients with benign tumours, naevi, NMSC, actinic keratosis and MM, had mean self-reported health similar to healthy controls. Although MM and NMSC are serious conditions, patients assessed their health to be higher than those with most other skin diseases. Adjusted EQ-VAS was slightly reduced for MM, but not for the other three conditions. All five dimensions of EQ5D showed results similar to controls. Likewise, other studies have shown relatively low impairment of HRQoL and low psychological comorbidity in solitary lesions (tumours), even when malignant.<sup>43,44</sup> This is probably explained by the nonchronic nature and radical treatments available for solitary tumours. Good correlation between instruments and results similar to ours, have been found when patients with actinic keratosis were evaluated with disease-specific, dermatology-specific and generic HRQoL instruments.<sup>44</sup>

Pain, itch, impaired mobility, stigmatization, scaling, malodour, and sex and intimacy issues due to a skin condition affect patients' social lives, daily work and relationships differently than nondermatological diseases do. The few EQ5D studies evaluating HRQoL impairment in skin diseases report results similar to ours.<sup>6,7,23,30,36,45</sup> Generic instruments enable comparison with nondermatological diseases. The impairment for several skin conditions is similar to the reduced HRQoL caused by diabetes mellitus,<sup>20</sup> cardiovascular disease,<sup>16,17</sup> COPD,<sup>19</sup> arthritis pain,<sup>15</sup> anxiety,<sup>21</sup> some cancers,<sup>16,18</sup> renal and liver diseases,<sup>16</sup> visual impairment,<sup>16</sup> and cytostatic, other or no treatment of CLL.<sup>15–22</sup> See Appendix S4 (online Supporting Information) for a detailed description of these studies.

This unique European multicentre study shows in a robust way that adult patients with common skin diseases, such as

chronic inflammatory skin conditions, leg ulcers, HS and blistering diseases, have significantly impaired life quality and self-reported health state. The most impaired dimensions in patients with chronic dermatoses were self-care, usual activities and pain/discomfort. Consultations, treatments and resource allocation should be adjusted to meet the specific needs of these patients adequately.

The high number of patients in this study provides sound data on the European dermatological population. Patients were included without any previous selection, reflecting the reality of dermatological practice for the participating centres and thus reducing bias. Existing studies have used EQ5D for calculating differences before and after an intervention or a specific treatment, but without comparing with other dermatoses. Our study corrected for comorbidity, showing the true impact skin diseases have on dermatological patients' HRQoL.

There are some limitations. Results are not presented separately for each country because of the different distribution of skin diseases across the separate centres. The number of patients/diagnoses per centre was too small for optimal analysis or for comparing data between centres.<sup>8</sup> Much larger studies would be required in individual countries to make such comparisons.

Some diagnostic groups were represented by a lower number of patients. Results should therefore be interpreted with caution. We chose to present these results because for many of the diagnoses there have been no previously published EQ5D or other data.

Patients with inflammatory skin diseases have significantly reduced life quality and health status. Dermatological patients report reduced life quality comparable with patients with other chronic diseases. We show the large and specific impact that skin diseases have on patients' well-being, changing our view of the needs of these patients. Caring for dermatological patients should not solely focus on symptom reduction and psychological support, but also include strategies for improving HRQoL and meeting patients' specific needs. These findings are important in the prioritization of resource allocation in the care of patients with skin disease.

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## Supporting Information

Additional Supporting Information may be found in the online version of this article at the publisher's website:

**Appendix S1.** Participant characteristics.

**Appendix S2.** Participants: patients and controls, characteristics by country.

**Appendix S3.** Distribution of some of the diagnoses by country.

**Appendix S4.** Studies on health-related quality of life using EQ5D in different medical conditions.

**Video S1.** Author video.

**Video S2.** Author video.