

## CLINICAL REPORT

# Disutility in Patients with Hidradenitis Suppurativa: A Cross-sectional Study Using EuroQoL-5D

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**Disutility reflects the disability caused by a disease. The EuroQoL-5D (EQ-5D) questionnaire is a measure of health-related overall utility. The questionnaire has only been applied previously to a small number of patients with hidradenitis. In this study a survey of 421 patients with hidradenitis suppurativa was conducted using the EQ-5D questionnaire. Questions regarding pain, malodour and pruritus were included to determine quantitatively whether these factors are associated with low EQ-5D index and visual analogue scale (VAS) scores. The index and VAS scores obtained were compared with reference values for the general population in Denmark. A significantly decreased utility in patients with hidradenitis suppurativa was found for all age group levels, except for 65–74-year-olds. The total index score in the cohort was 0.705 (population mean 0.887) and the VAS was 62.25 (population mean 82.6). Multivariate analysis found significant associations between loss of utility and pain, malodour and pruritus ( $p < 0.0001$ ). Patients with hidradenitis suppurativa had a significantly decreased EQ-5D compared with the background population. Malodour and pruritus were found to be associated with low index values, and pain and malodour with low VAS. Patient-reported pain and discomfort had the most negative overall effect on mean index scores. *Key words: hidradenitis suppurativa; EQ-5D; utility; health-related quality of life.***

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Diseases cause different disabilities, a term which covers impairments, activity limitations, and participation restrictions. The comparative disability caused by different diseases is therefore of importance when assessing the impact of different diseases and the resources allocated to their management.

Hidradenitis suppurativa (HS) is a skin disease manifested by recurrent deep-seated painful abscesses, fistulas scarring and malodours suppuration, which is often debilitating (1). Affected areas usually include the intertriginous regions of skin, i.e. axillae, groin, perianal

area and inframammary regions. Prevalence of HS is estimated at 1–4% in a European population (2–4), with onset usually at the beginning of the third decade of life (5). Risk factors for HS include smoking and overweight (6–8). Quality of life (QoL) is often impaired in HS (9). Von der Werth & Jemec (10) examined QoL using the Dermatology Life Quality Index (DLQI) questions and reported HS to have a significant adverse effect on QoL compared with various dermatological diseases, such as psoriasis, atopic dermatitis and acne. Esmann & Jemec have qualitatively described the issues that reduce QoL for patients with HS (11), including smell, scarring, itching and pain. Co-occurrence between HS and depression has also been demonstrated in several studies, and it is therefore hypothesized that the disease has a significant impact on the psycho-social functioning of patients.

Disutility is an important aspect of disability. Disutility is an economic term defined as “the adverse or harmful effects associated with a particular activity or process, especially when carried out over a long period” (12). The EuroQoL-5D (EQ-5D) questionnaire is a well-established general measure of health-related overall utility. The EQ-5D is not diagnosis-specific, i.e. specifically aimed at cardiac or dermatological diseases, thus comparison between groups of diseases is possible (13, 14). Although not aimed exclusively at dermatology, the EQ-5D has been used and validated for dermatological diseases (15). Reference values for the EQ-5D for the general population and for specific age groups are available for many countries.

The EQ-5D has previously been examined in small samples of patients with HS (16, 17). The principal aim of the current study is to examine the EQ-5D index and EQ-5D visual analogue scale (VAS) scores for a large cohort of patients with HS, and to compare the findings with the established reference values for the general population in a Danish cohort of patients with HS as well as the results of the previous studies of patients with HS. In addition, the study reports the distribution of the index score, in order to estimate the individual effect of each of the 5 questions on the mean index score and to determine the effect of age on disutility in patients with HS.

## MATERIALS AND METHODS

This study was designed as a cross-sectional survey of overall life utility as measured by the EQ-5D. In addition, information

regarding malodour, pain and pruritus was obtained in order to determine the effect of each of these factors on utility.

### Patients

All patients with HS ( $n=421$ ) registered at the Department of Dermatology, University Hospital of Roskilde, regardless of severity and comorbidities were contacted by post and invited to answer a questionnaire, which included the EQ5D-3L questions.

### Questionnaire

Patients were asked to rate the intensity of pain (at the skin), itching, malodour and joint pain, for the past week on a 0–10 VAS scale. For each of these aspects patients were asked on how many of the past 30 days they had been affected.

Two months after the initial inquiry, a reminder letter with a new questionnaire was sent to non-responders. After a further month, patients who had not responded to the first 2 reminders were contacted by phone to ask if they agreed to be sent a new questionnaire. A total of 299 (71% response) replies were received. Three replies were missing more than one variable of the EQ-5D-3L questions and were excluded for the purposes of this study.

### EuroQoL-5D

The EQ-5D-3L questionnaire is divided into 2 sections. The first section contains 5 questions about mobility, self-care, usual activities, pain/discomfort and anxiety/depression. For each question problems within the domain are evaluated on a 3-level basis. Responders can choose between “no problems”, “some problems” or “extreme problems”.

The second part is a VAS score, which records the responder’s self-evaluated health, where 0 is worst imaginable health and 100 is best imaginable health. Scoring is calculated as an index value between –0.624 and 1 (1 = perfect health) using the Danish Time Trade-off coefficient (TTO) (18).

The population norms for the Danish population, provided by EuroQol, were used as reference values (19).

### Statistical analysis

All statistical analyses were performed using SPSS version 22.0 (IBM Software, USA). One-sample  $t$ -tests were performed for comparison of the EQ-5D index and VAS scores with the population means. Multiple linear regressions were performed to identify factors separately influencing the index and VAS scores, taking into account that a pain score is an integral part of the EQ-5D.

Before proceeding with the multiple regression analysis, the data were examined for collinearity in a scatter plot matrix with each variable opposing each of the others. A histogram was applied to examine the normal distribution for each variable, and tested for heteroscedasticity in a scatter plot with the predicted values on the x-axis and the standardized residuals on the y-axis.

Using the stepwise, forward and backward method in linear regression the best model was determined by comparing the adjusted coefficient of determination for each model. A  $p$ -value of  $<0.05$  was considered as significant.

The index and VAS means were compared for groups 1 and 2. A Kolmogorov–Smirnov (KS) and a Shapiro–Wilk (SW) test for both index values and VAS was performed to test whether the data was normally distributed within the groups. To compare the means of two not normally distributed populations a Mann–Whitney  $U$  test was performed.

The effect on utility for each aspect was calculated by multiplying frequency with TTO coefficients.

Table I. Some characteristics of the 294 patients with hidradenitis suppurativa

Age, years, mean $\pm$ SD	42.38 $\pm$ 12.12
Females/males, $n$	232/62
Disease duration, years, mean $\pm$ SD	22.2 $\pm$ 12.7
Family history of HS/No family history, $n$	119/177
Years of education <sup>a</sup> , years, mean $\pm$ SD	4.37 $\pm$ 2.79
Pain VAS, mean $\pm$ SD	3.91 $\pm$ 3.18
Days with pain in the last 30 days, mean $\pm$ SD	9.51 $\pm$ 9.67
Itching VAS, mean $\pm$ SD	3.72 $\pm$ 3.17
Days with itching in the last 30 days, mean $\pm$ SD	10.35 $\pm$ 10.56
Malodour VAS, mean $\pm$ SD	2.87 $\pm$ 3.34
Days with malodour in the last 30 days, mean $\pm$ SD	8.12 $\pm$ 10.76
Joint pain VAS, mean $\pm$ SD	3.42 $\pm$ 3.44
Days with joint pain in the last 30 days, mean $\pm$ SD	10.63 $\pm$ 11.98

<sup>a</sup>Does not include patients currently in education.

VAS: visual analogue scale 0–10; SD: standard deviation.

The effect on utility for each aspect was calculated by multiplying the frequency of each answer by the appropriate coefficient, using the Danish TTO coefficients (18).

### Ethical considerations

Danish law does not require ethical committee approval of questionnaire studies. The survey was registered with the Danish Data Protection Agency according to requirements.

## RESULTS

### Patient characteristics

Participating patients ( $n=294$ ; 232 females, 62 males) had a mean age of 42.4 (age range 19–77) years (see Table I for additional data).

### Comparison with the general population

The mean index score for each age group is shown in Table II, together with the population mean provided by EuroQol for comparison. The mean difference for each age group and  $p$ -values are included in Tables III and IV, for index and VAS score, respectively. There was a significantly decreased utility in patients with HS compared with the general population at all age group

Table II. Mean EuroQoL-5D (EQ-5D) index and visual analogue scale (VAS) score by age group for patients with hidradenitis suppurativa (HS) and general population

Age group	$n$	HS patients		General population	
		EQ-5D index (SD)	EQ-5D VAS (SD)	EQ-5D index	EQ-5D VAS
18–24 years	17	0.730 (0.262)	73.8 (0.193)	0.928*	88.5*
25–34 years	67	0.663 (0.283)	58.5 (0.261)	0.927*	88.4*
35–44 years	87	0.698 (0.241)	63.2 (0.238)	0.901*	84.5*
45–54 years	79	0.710 (0.263)	61.3 (0.256)	0.882*	82.2*
55–64 years	31	0.731 (0.199)	58.5 (0.244)	0.870*	79.9*
65–74 years	14	0.809 (0.114)	76.9 (0.146)	0.847	76.6
>75 years	1	0.162	30.0	0.794	69.1
Total	294	0.705 (0.25)	62.0 (24.75)	0.887	82.6

\*Indicates a significant difference between the general population and the HS cohort. SD: standard deviation.

Table III. EQ-5D frequency distribution of answer

Level	Mobility n (%)	Self-care n (%)	Usual activities n (%)	Pain/discomfort n (%)	Anxiety/depression n (%)
1	200 (67.57)	248 (84.07)	161 (54.95)	62 (21.02)	177 (60.00)
2	94 (31.76)	45 (15.25)	119 (40.61)	188 (63.73)	102 (34.58)
3	2 (0.68)	2 (0.68)	13 (4.44)	45 (15.25)	16 (5.42)

1: no problems, 2: some problems, 3: extreme problems.

Table IV. Effect of each aspect on index score and effect of each aspect compared with effect of mobility

	Mobility	Self-care	Usual activities	Pain/discomfort	Anxiety/depression
Effect on index	-0.0196	-0.0109	-0.0259	-0.099	-0.0434
Comparative effect	1 (ref.)	0.56	1.32	5.05	2.21

levels, except for 65–74-year-olds. Fig. 1 shows the index and VAS scores by age.

Multiple regression analysis

Multivariate analysis revealed that intensity of itching and malodour, and the number of days patients experienced these problems could be considered as possible predictors for index score. Pain was not considered to be a predictor for index score due to the fact that one of the aspects considered for index score is the level of pain. The intensity of pain (in the skin), itching, malodour and joint pain, and the number of days in the past month that patients experienced these problems were considered as possible predictors for the EQ5D VAS score.

Index score

When determining predictors of the index value, the adjusted coefficient of determination was 0.287 regardless of using the forward, backward or stepwise method. All 3 models determined that statically significant predictors of index score were: intensity of malodour on a VAS scale (m.VAS), and intensity of itching (i.VAS). These scores were statistically significant in determining the index value. The regression equation for index score is:  $index = 0.869 - 0.023 m.VAS - 0.017 i.VAS$ .

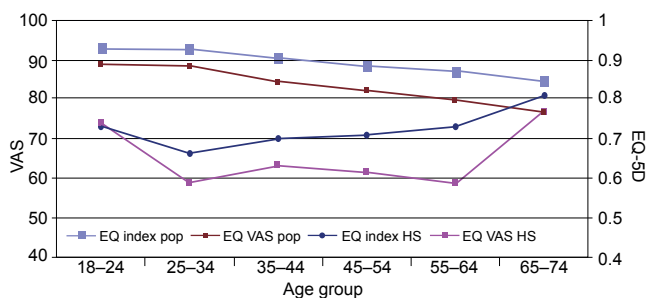


Fig. 1. Mean visual analogue scale (VAS) and EuroQoL-5D (EQ-5D) index for patients with hidradenitis suppurativa (HS) (n=296) and the general population (n=16,861).

VAS scores

For the EQ-5D VAS scores the stepwise and forward methods yielded the same regression equation. Because the adjusted coefficient of determination was only slightly higher than the backward model, 0.261 vs. 0.255 for stepwise and forward methods, both are reported.

Backward model. Statically significant predictors were skin-related pain VAS scores for the past week (p.VAS), malodour VAS score for the past week (m.VAS), and the numbers of days in the last month with joint pain (jp.days).

The regression equation for EQ-5D VAS scores is:  $EQ-5D VAS score = 79.308 - 1.916 p.VAS - 1.297 m.VAS - 0.578 jp.days$ .

Forward and stepwise model. Statically significant predictors in this model were skin-related pain VAS scores for the past week (p.vas), the numbers of days in the last month with skin-related pain (p.days), and the intensity of joint pain in the past week (jp.VAS). The regression equation for EQ-5D VAS scores is:  $EQ-5D VAS score = 79.004 - 1.4562 p.VAS - 0.554 p.days - 1.798 jp.VAS$ .

Distribution and effect of each aspect. The distribution of self-reported problems within each aspect are shown in Table III and Fig. 2 and the effect of each aspect on index score in Table IV.

DISCUSSION

Patients with HS in our cohort have significantly decreased EQ-5D index and VAS scores in all age groups except for 65–74 year olds. The total index score in the cohort was 85% of that of the general population (0.705 compared with the population mean of 0.887) and the VAS score was 75% (62.25 compared with 82.6), indicating significant disability.

The reduced index and VAS scores might be expected due to the debilitating nature of the disease, but this

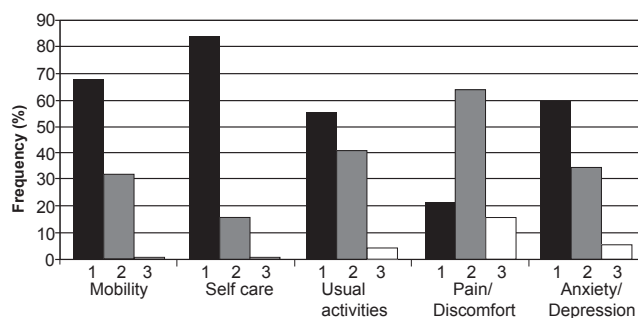


Fig. 2. Frequency distribution for the EuroQoL-5D questionnaire in relation to specific aspects and level of problem.



quantitative investigation reports the degree to which the patients are affected. In agreement with previous qualitative studies (11) we found that pain/discomfort had the most adverse effect on overall mean index values.

Findings regarding index scores for the HS population were in agreement with earlier, smaller studies. In a study of 27 persons from the general population suspected of HS on the basis of a validated questionnaire, Vinding et al. (16) found a mean EQ-5D index of 0.82 (95% confidence interval (CI): 0.74–0.90) and a mean VAS score of 79.56 (95% CI: 72.89–86.22). It is speculated that the participants had less severe disease than those in the present hospital-based study because they were drawn from the general population. This is supported by the greater disutility found by Matusiak et al. (17), in which 54 hospital-based Polish patients with HS (28 women, 26 men) with a mean age of  $39.94 \pm 11.63$  years, completed the EQ-5D questionnaire. The authors found a mean  $\pm$  SD index and VAS score of  $0.66 \pm 0.23$  and  $56.78 \pm 18.84$ , respectively. No statistical differences were found between the results of these 3 studies, due to the considerable standard deviation.

#### *Effect of age*

In contrast to the general population, disutility in patients with HS did not appear to increase with age. It may be speculated that this is due to the natural fluctuation of HS, as studies indicate that the disease decreases in severity with age (3). The observations may therefore be interpreted as a reflection of the reduced prevalence with increasing age, i.e. as the disease subsides, the utility of HS patients approaches that of the general population.

#### *Predictors for index and VAS scores*

In this report pain, malodour and pruritus are used as a surrogate measurement for severity. Hurley score was not used, as over 75% of the patients had Hurley stage II, making comparisons between groups statistically impossible.

Itching and malodour VAS scores for the past week appeared to be significant predictors of the index score. Using the backward model, we found that predictors for the EQ-5D VAS were VAS for skin pain and malodour, and the number of days in the last month with joint pain and skin pain. Using the forward and stepwise model, we, found the predictors to be pain VAS scores related to skin and joints, and the number of days with pain related to skin.

Pain is a well-known factor for decreased QoL (20, 21), and this study supports these findings. We found that pain and discomfort had the highest impact on index score, almost twice the impact of anxiety and depression, which had the second highest impact.

These findings highlight the need for pain management in patients with HS, and emphasize the psychological impact of this disease.

This study shows that itching, and especially malodour, have a significant negative effect on EQ-5D index and VAS scores and, ultimately, QoL. Most studies of HS mention malodour but, to the best of our knowledge, it has not previously been shown in a quantitatively defined way to affect the patients.

#### *Comparison with other dermatological conditions*

Only 3 other skin diseases have been examined using the EQ-5D questionnaire. Most reports concern psoriasis, and index values range from 0.52 to 0.9 (22). Meta-analysis of these results are difficult, as not all of these studies list a standard deviation of their results.

A review of the data appears to indicate that hidradenitis and psoriasis have similar adverse effects on utility, as the results for HS are within the ranges of index scores described in psoriasis.

Walters et al. (23) found a mean  $\pm$  SD index score of  $0.57 \pm 0.18$  in 233 patients with chronic leg ulcers. Moberg et al. (24) found a mean index score of 0.782 (CI 0.77–0.79) in 2,457 patients with hand eczema, while Klassen et al. (25) found a mean  $\pm$  SD index score in 56 acne patients of  $0.82 \pm 0.16$  pre-treatment and 0.89–0.17 post-treatment.

The mean  $\pm$  SD index score found in this study was  $0.71 \pm 0.25$ . The large SD suggests that HS patients are affected in a more heterogeneous manner than patients with acne, chronic leg ulcers and hand eczema. The data also suggests that HS has a greater adverse effect on utility than either hand eczema or acne, but less effect than chronic leg ulcers.

#### *Study limitations and strengths*

Selection bias may have influenced the results. The patients were referred for specialist care by general dermatologists. A wide range of clinical severities was represented, and the patients were, for the most part, undergoing treatment for HS.

The large number of patients in this study strengthens the results. However, patients with a low utility might be disinclined to answer questionnaires. The questionnaire had 29% non-responders, which could represent a healthy-worker bias, although responders and non-responders were not statistically different regarding age and gender (data not shown).

When testing for co-linearity between the variables in the multiple linear regressions, a slight trend was noted towards co-linearity between pain VAS score and days of pain during the past month. The same applies to the other questions; higher itching VAS score and days with itching, malodours VAS score and days bothered

by malodour, etc. We did, however, decide to retain the regression model. Co-linearity remains minimal, and we wish to examine both aspects of the disease, as both are important. Given the slight co-linearity it may have been more optimal to have a single measurement for skin/joint pain, pruritus and malodour. It was not possible to construct such a measurement *post hoc*, however, as VAS scores are ordinal data, which would invalidate a simple multiplication.

This study found a significantly decreased EQ-5D in patients with HS compared with the background population, and these findings are in agreement with other studies on the subject. Furthermore, malodour and pruritus were found to be predictive of low EQ-5D index values, and pain and malodour predictive of low VAS scores.

*The authors declare no conflicts of interest.*

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