Acta Derm Venereol 2016; 96: 60–63

INVESTIGATIVE REPORT

Relationship Between Psychosocial Burden of Skin Conditions and Symptoms: Measuring the Attributable Fraction

Francesca SAMPOGNA, Stefano TABOLLI, Patrizia GIANNANTONI, Andrea PARADISI and Damiano ABENI
Health Services Research Unit; Istituto Dermopatico dell'Immacolata, Istituto di Ricovero e Cura a Carattere Scientifico (IDI-IRCCS), Rome, Italy

Skin conditions often have a severe impact on the physical and psychosocial domains of patients' quality of life, but the relationship between these domains has been studied little. This study estimated the fraction of psychosocial burden that may be attributable to symptoms, using the Skindex-17 quality of life questionnaire (symptoms and psychosocial scales) in 2,487 outpatients. The excess proportion of psychosocial burden for each skin condition was computed. Overall, 79.8% of the psychosocial burden of patients with severe symptoms may be attributable to the symptoms. For patients with mild symptoms this figure is 49.7%. A great heterogeneity was observed, from –0.9% for patients with scars, up to more than 90% for conditions such as lichen planus and psoriasis. While these results will have to be confirmed in longitudinal studies, they seem to indicate that, by targeting specific symptoms, a substantial portion of the psychosocial burden of skin diseases could be spared. ***Key words: skin conditions; quality of life; symptoms; psychosocial burden*****.**

Accepted Mar 11, 2015; Epub ahead of print Mar 13, 2015

Acta Derm Venereol 2016; 96: 60–63.

Damiano Abeni, Health Services Research Unit – IDI-IRCCS, Via dei Monti di Creta, 104, IT-00167 Rome, Italy. E-mail: d.abeni@idi.it

Health-related quality of life (HRQoL) is strongly affected by many and diverse skin conditions (1), such as psoriasis (2), vitiligo (3, 4), cutaneous lymphomas (5), pemphigus (6–8), nail conditions (9, 10) and alopecia areata (11). Skin conditions have an impact on both symptomatic and psychosocial aspects of patients' lives, impacting at different levels, depending on the disease. In a previous paper (1) concerning 2,487 outpatients with several skin conditions, we observed that patients with either alopecia areata, naevi, hirsutism, melanoma, or vitiligo reported a very low impact of the disease from a symptomatic point of view, while ectoparasitic infestations, pruritus, psoriasis and dermatitis were the most symptomatic diseases. From a psychosocial point of view, the highest impact was found in patients with hyperhidrosis, hirsutism, ectoparasitic infections, pemphigus, acne, lichen sclerosus and psoriasis.

HRQoL is considered as a multidimensional construct, and the different dimensions are generally treated as separate entities. However, it is clear that their interrelationship is strong and complex, but it has been rarely, if ever, addressed quantitatively. While this relationship is presumably, at least in part, bi-directional (i.e. symptoms may cause psychosocial impairment, and psychosocial impairment may cause symptoms), the former case may be predominant, and this can be reasonably assumed until the contrary is proved.

The aim of the present study was to investigate the relationship between symptoms and psychosocial burden of different skin conditions. For this purpose, in the same large sample of outpatients on which the field performance of the Skindex-17 was performed (12), we estimated the excess fraction of psychosocial burden that may be attributable to the presence of symptoms in different skin conditions.

MATERIALS AND METHODS

The sample for the present study is the same as that described previously in Sampogna et al. (12). In brief, consecutive patients were enrolled at the outpatient clinics of the Istituto di Ricovero e Cura a Carattere Scientifico (IDI-IRCCS), a research hospital and national reference centre for skin conditions in Rome, Italy, during March 2010. The aim of the survey was to describe HRQoL in a significant sample of dermatological outpatients. The study was approved by the institutional ethics committee.

Patients completed the HRQoL questionnaires during the waiting time, and returned them to the dermatologist, who recorded the diagnosis and the Physician Global Assessment on the classical 5-point scale ("very mild", "mild", "moderate", "severe", "very severe").

The symptoms and psychosocial burden of patients was evaluated using the 2 scales of the Italian version of the Skindex-17 questionnaire (13), a refinement of the Skindex-29 (14–17).

Statistical analysis

Skindex-17 scale scores were transformed to a linear scale of 100, to allow direct comparability of the scores on the 2 scales, which would not be possible with the raw scores, since the scales have a different number of items (5 items in the symptoms scale and 12 in the psychosocial scale). A maximum of 1 missing value in the symptoms scale and 2 in the psychosocial scale were accepted, and the missing values were substituted by the mean value of the other items of the same scale.

For each skin condition (or group of skin conditions), a simple linear regression was performed to estimate the crude relation-

 doi: 10.2340/00015555-2094
 ISSN 0001-5555

ship between the symptoms and the psychosocial scores. A multiple linear regression model was then fitted to evaluate such relationship after adjusting for other relevant independent variables (i.e. clinical severity, as evaluated by the Physician Global Assessment, gender, and age). For each skin condition, the Skindex-17 psychosocial score was entered as the dependent variable, and the main independent variable was the Skindex-17 symptoms scores. The resulting regression coefficients therefore represent the estimated change in psychosocial scores for each increase of 1 unit in the symptoms scores.

In a second phase, the symptoms scores were categorized using the cut-off reported in the original paper (i.e. 5 or more, corresponding to 50 or more in the transformed score), but the patients with a score of zero were kept in a separate category, thus obtaining 3 groups: no symptoms (score=0), mild impairment (score 1–49), and severe impairment (score of 50 or more). This "symptoms level" variable was used as the main independent variable in an analysis of covariance, to estimate the adjusted mean psychosocial score in each category of symptoms impairment. The other independent variables were the same as those included in the multiple linear regression models.

After obtaining the adjusted means, the excess psychosocial burden that is observed in the mild and severe levels of symptoms compared with the "no symptoms" category was evaluated by computing the absolute difference in psychosocial scores between the symptoms levels. The excess proportion of psychosocial burden for each skin condition was then computed by adapting the formula for the percent attributable risk in exposed individuals (18) as follows:

$\%\ \text{excess fraction}_{sym} = [(\mu_{severe\text{-}sym} - \mu_{no\text{-}sym})/\mu_{severe\text{-}sym}] * 100$, where $\mu_{severe\text{-}sym}$ is the adjusted mean among patients in the "severe symptoms" category, and $\mu_{no\text{-}sym}$ is the adjusted mean among patients in the "no symptoms" category. The same was done for the patients in the "mild symptoms" group. Using this procedure, the excess fraction (19) of psychosocial burden that may be attributable to the presence of symptoms in several dermatological conditions was estimated.

All analyses were performed using the IBM SPSS program, version 23. For analysis of covariance the EMMEANS subcommand of the generalized linear models/UNIANOVA procedure was used.

Table I. *Beta-coefficients for the Skindex-17 symptoms score from simple and multiple linear regression, with the Skindex-17 psychosocial score as outcome variable*

	n	Skindex-17 symptoms	Crude	Adjusted[a]	*p* (Adj.)
Acne	193	37.0	0.669	0.647	<0.001
Alopecia, androgenetic	77	13.8	0.265	0.267	0.013
Alopecia, areata	52	9.8	0.795	0.670	<0.001
Bacterial infections	53	44.5	0.475	0.495	<0.001
Balanitis	25	37.5	0.498	0.528	0.046
Benign skin neoplasms	175	15.3	0.378	0.385	<0.001
Dermatitis	249	49.2	0.490	0.453	<0.001
Hair loss	27	20.4	0.452	0.443	0.003
Lichen planus	32	38.4	0.521	0.530	<0.001
Mycoses	116	30.8	0.432	0.414	<0.001
Nail conditions	38	18.3	0.301	0.325	0.007
Naevi	306	12.1	0.293	0.313	<0.001
Non-melanoma skin cancer	79	19.3	0.413	0.396	<0.001
Pemphigus/other bullous diseases	17	46.0	0.821	0.828	0.001
Pityriasis rosea	29	30.0	0.427	0.277	0.266
Pruritus	54	53.0	0.375	0.433	0.011
Psoriasis	220	53.7	0.672	0.536	<0.001
Rosacea	60	33.2	0.847	0.853	<0.001
Scabies/ectoparasitic infections	34	55.8	0.772	0.707	0.013
Scars	19	33.2	0.051	–0.015	0.966
Scleroderma/connective tissue disorders	49	40.0	0.645	0.729	<0.001
Seborrhoeic dermatitis	85	35.8	0.463	0.453	<0.001
Urticaria	29	44.8	0.761	0.460	0.185
Viral infections	68	20.4	0.475	0.511	<0.001
Vitiligo/pigmentation disorders	54	11.6	0.221	0.229	0.072
Other dermatoses	60	40.7	0.491	0.592	<0.001
Other diagnoses/missing	287	29.8	0.505	0.511	<0.001
Total	2,487	31.3	0.512	0.486	<0.001

[a]The multiple linear regression model, besides the Skindex-17 symptoms scores, includes also gender, age, and global physician's assessment.

RESULTS

The overall mean Skindex-17 symptoms score was 31.3, with the highest scores observed in patients with pruritus, psoriasis and ectoparasitic infections. The association between the symptoms and the psychosocial Skindex-17 scores by diagnosis is shown in Table I. The overall estimated change in psychosocial scores for each increase of 1 unit in the symptoms scores, represented by the regression coefficients, was overall quite high (crude 0.512, adjusted 0.486), indicating a moderate-to-strong correlation between the 2 scales. The coefficients were not significant ($p \geq 0.05$) only in pityriasis rosea, scars, urticaria, and pigmentation disorders. The highest adjusted coefficients were observed in acne, alopecia areata, rosacea, and connective tissue disorders. The results were heterogeneous, depending on the disease. For example, patients with scars and rosacea reported the same mean symptoms score, but while the regression coefficient was significant in rosacea, it was close to zero in scars, indicating no linear correlation between symptoms and psychosocial aspect in the latter case. This can be seen clearly in Fig. 1, where each dot represents a condition or a group of conditions, and the Skindex-17 symptoms-psychosocial regression coefficients were plotted against the mean level of the symptoms scores by diagnosis. For the same level of symptoms, each disease has a different regression coefficient for the psychosocial scale; however, there is a trend toward an increase in the regression coefficient for higher levels of symptoms.

Table SI[1] shows the adjusted Skindex-17 psychosocial scale mean scores, by level of symptoms score and by diagnosis. For each diagnosis, also, the excess absolute scores and excess fraction for mild and severe symptoms compared with no symptoms are reported. Overall, it can be seen that the psychosocial scores are 2 and 5 times higher in the mild and in the severe symptoms category, respectively, compared with the no

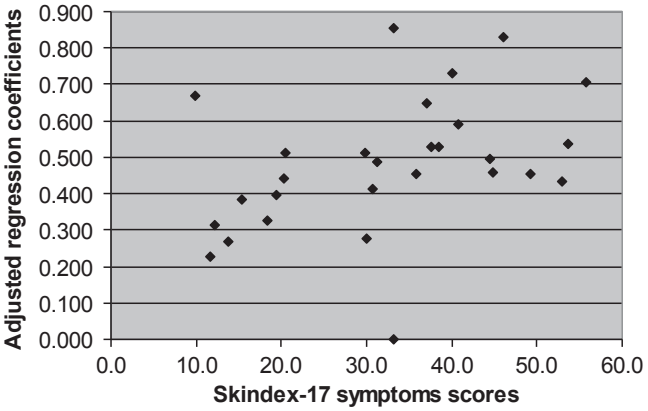

Fig. 1. Relationship between the Skindex-17 symptoms-psychosocial regression coefficients and the mean level of symptoms scores by diagnosis. Each dot represents one of the skin conditions, plus the total estimate, listed in the Tables.

symptoms group. This is reflected in excess fractions of approximately 50% and 80%, respectively.

The highest excess score (severe vs. absent symptoms) was observed in alopecia areata, with an excess fraction of 83.3%, indicating that 83.3% of psychosocial burden may be attributable to the presence of severe symptoms in patients with alopecia areata. The excess fractions were always very high, with several conditions exceeding an estimate of 75%, and namely: acne, alopecia areata, bacterial infections, balanitis, benign skin neoplasms, mycoses, naevi, non-melanoma skin cancer, pemphigus and bullous diseases, seborrhoeic dermatitis, urticaria, and "other dermatoses". Psoriasis, rosacea and scabies exceeded 90%, with the highest levels observed in the scleroderm/connective tissue disorders and lichen planus (97.8% and 95.5%, respectively).

It should be noted that a number of conditions also have an excess fraction greater than 75% when the "mild" symptoms category is considered, with scleroderma/connective tissue disorders, lichen planus, balanitis, and rosacea topping this list.

Finally, although the excess score and the excess fractions were not included in the table for the comparison between the mild vs. severe symptoms group, it is easy to note that for many skin conditions the score in the severe category is 2 times or more higher than in the mild category, so that those excess fractions would exceed 50%.

DISCUSSION

This cross-sectional study found that, among different skin conditions, the relationship between symptoms and psychosocial impairment is highly heterogeneous, and tends to be stronger with a higher burden of symptoms. In addition, the portion of scores on the psychosocial scale that may be linked to the level of the symptoms scores was highly heterogeneous, but tended to be high and particularly relevant for the more symptomatic diseases, e.g. psoriasis, rosacea, scleroderma and lichen, among others.

It is interesting to note that the diagnostic group labelled as "pruritus", in which are classified patients who report this symptom without any cutaneous signs before further examinations are carried out, has no patients in the category of "zero symptoms score": this implies that whatever psychosocial burden is observed is safely attributable to the symptoms. On the other hand, visible conditions with a low symptomatic burden, such as vitiligo or scars, have, if any, a much lower proportion of excess psychosocial burden due to the symptoms.

Symptoms and psychosocial aspects are the main dimensions in the construct of HRQoL (20). They are generally considered as separate scales in quality of life instruments; however. the correlation between the scores of these 2 scales tends to be high. For example, in a study concerning inpatients with psoriasis (21), Pearson correlation coefficient between the Skindex-29 symptoms score and the emotions scale was 0.558, and between the symptoms and the functioning scale was 0.598. A high negative correlation is generally observed between pruritus and quality of life in patients with skin conditions, such as atopic dermatitis (22) and psoriasis (23). However, the other symptoms, such as burning, bleeding and pain are rarely considered.

Moreover, here we tried to quantify the psychosocial burden of the disease due to symptoms, using the concept of attributable risk. The attributable risk indicates the number of cases of a disease among exposed individuals that can be attributed to that exposure. Here we extended this concept, considering symptoms as the exposure, using the mean scores instead of the number of patients, and calculating how much of the psychosocial burden could be attributable to the exposure "symptoms". The percent attributable risk was thus transformed into the excess fraction (19) of psychosocial burden that may be attributable to the presence of symptoms. From a practical point of view, the excess fraction we estimated could be seen as the proportion of psychosocial impairment that could be eliminated by controlling the symptoms. To the best of our knowledge, this is the first time that such concepts and epidemiological procedures have been applied to the relationship between different domains of quality of life in dermatology, and namely between symptoms and psychosocial burden.

Our results, in themselves, could be taken at this point as an educated guess on the "amount" of psychosocial burden that patients could be spared if their symptoms were reduced or eliminated. However, such an educated guess could also be taken as a "prediction", and tested in other samples of patients. Namely, by adopting a

[1]http://www.medicaljournals.se/acta/content/?doi=10.2340/00015555-2094

longitudinal design, it would be possible to evaluate whether, and to what extent, the excess proportions estimated in our cross-sectional study can be translated in an actual improvement of psychosocial burden when the symptoms are reduced or eliminated.

Future research should also determine which symptoms are more significant, in terms of excess psychological burden, in the different skin conditions. That additional knowledge would, in theory, be useful to address specific symptoms in specific conditions in order to achieve the maximum possible benefit in terms of psychosocial wellbeing.

So while these observations, of course, will also have to be replicated and possibly confirmed in other cultural environments and cultural settings, as of now they seem to indicate to clinicians, as well as to drug designers and drug developers, that by targeting the specific symptoms included in the Skindex-17 (i.e. pain, itch, being bothered by water, irritation, and bleeding) a measurable and substantial portion of the psychosocial burden of the skin diseases could be spared.

ACKNOWLEDGEMENTS

The authors are indebted to all the physicians and the patients who participated in the data collection.

REFERENCES

1. Sampogna F, Tabolli S, Abeni D. Impact of different skin conditions on quality of life. G Ital Dermatol Venereol 2013; 148: 255–261.
2. Sampogna F, Tabolli S, Soderfeldt B, Axtelius B, Aparo U, Abeni D. Measuring quality of life of patients with different clinical types of psoriasis using the SF-36. Br J Dermatol 2006; 154: 844–849.
3. Sampogna F, Raskovic D, Guerra L, Pedicelli C, Tabolli S, Leoni L, et al. Identification of categories at risk for high quality of life impairment in patients with vitiligo. Br J Dermatol 2008; 159: 351–359.
4. Ongenae K, Van Geel N, De Schepper S, Naeyaert JM. Effect of vitiligo on self-reported health-related quality of life. Br J Dermatol 2005; 152: 1165–1172.
5. Sampogna F, Frontani M, Baliva G, Lombardo GA, Alvetreti G, Di Pietro C, et al. Quality of life and psychological distress in patients with cutaneous lymphoma. Br J Dermatol 2009; 160: 815–822.
6. Ghodsi SZ, Chams-Davatchi C, Daneshpazhooh M, Valikhani M, Esmaili N. Quality of life and psychological status of patients with pemphigus vulgaris using Dermatology Life Quality Index and General Health Questionnaires. J Dermatol 2012; 39: 141–144.
7. Tabolli S, Pagliarello C, Paradisi A, Cianchini G, Giannantoni P, Abeni D. Burden of disease during quiescent periods in patients with pemphigus. Br J Dermatol 2014; 170: 1087–1091.
8. Paradisi A, Sampogna F, Di Pietro C, Cianchini G, Didona B, Ferri R, et al. Quality-of-life assessment in patients with pemphigus using a minimum set of evaluation tools. J Am Acad Dermatol 2009; 60: 261–269.
9. Klaassen KM, van de Kerkhof PC, Pasch MC. Nail psoriasis, the unknown burden of disease. J Eur Acad Dermatol Venereol 2014; 28: 1690–1695.
10. Tabolli S, Alessandroni L, Gaido J, Sampogna F, Di Pietro C, Abeni D. Health-related quality of life and nail disorders. Acta Derm Venereol 2007; 87: 255–259.
11. Al-Mutairi N, Eldin ON. Clinical profile and impact on quality of life: seven years experience with patients of alopecia areata. Indian J Dermatol Venereol Leprol 2011; 77: 489–493.
12. Sampogna F, Spagnoli A, Di Pietro C, Pagliarello C, Paradisi A, Tabolli S, et al. Field performance of the Skindex-17 quality of life questionnaire: a comparison with the Skindex-29 in a large sample of dermatological outpatients. J Invest Dermatol 2013; 133: 104–109.
13. Nijsten TE, Sampogna F, Chren MM, Abeni DD. Testing and reducing Skindex-29 using Rasch analysis: Skindex-17. J Invest Dermatol 2006; 126: 1244–1250.
14. Chren MM, Lasek RJ, Quinn LM, Covinsky KE. Convergent and discriminant validity of a generic and a disease-specific instrument to measure quality of life in patients with skin disease. J Invest Dermatol 1997; 108: 103–107.
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. Arch Dermatol 1997; 133: 1433–1440.
16. Abeni D, Picardi A, Puddu P, Pasquini P, Chren MM. [Construction and validation of the Italian version of Skindex-29, a new instrument to measure quality of life in dermatology.] G Ital Dermatol Venereol 2001; 136: 73–76 (in Italian).
17. Abeni D, Picardi A, Pasquini P, Melchi CF, Chren MM. Further evidence of the validity and reliability of the Skindex-29: an Italian study on 2,242 dermatological outpatients. Dermatology 2002; 204: 43–49.
18. Szklo M, Nieto F. Epidemiology: beyond the basics. 2nd edn. Sudbury, MA, USA: Jones and Bartlett Publishers, 2007: p. 84.
19. Greenland S, Robins JM. Conceptual problems in the definition and interpretation of attributable fractions. Am J Epidemiol 1988; 128: 1185–1197.
20. Testa MA, Simonson DC. Assesment of quality-of-life outcomes. N Engl J Med 1996; 334: 835–840.
21. Sampogna F, Sera F, Abeni D. Measures of clinical severity, quality of life, and psychological distress in patients with psoriasis: a cluster analysis. J Invest Dermatol 2004; 122: 602–607.
22. Chrostowska-Plak D, Reich A, Szepietowski JC. Relationship between itch and psychological status of patients with atopic dermatitis. J Eur Acad Dermatol Venereol 2013; 27: e239–242.
23. Reich A, Hrehorow E, Szepietowski JC. Pruritus is an important factor negatively influencing the well-being of psoriatic patients. Acta Derm Venereol 2010; 90: 257–263.