Allergy 2005: 60: 1073–1078

Copyright © Blackwell Munksgaard 2005

ALLERGY
DOI: 10.1111/j.1398-9995.2005.00833.x

Original article

A new tool to evaluate the impact of chronic urticaria on quality of life: chronic urticaria quality of life questionnaire (CU-Q_2oL)

Background: Health-related quality of Life in patients with chronic urticaria is evaluated by mean of generic instruments or questionnaire designed for skin diseases. No disease-specific tool is now available for the assessment of chronic urticaria impact from patients' viewpoint.
Objective: The aim of our study is to develop and validate a new questionnaire specifically designed for the assessment of quality of life in chronic urticaria (Chronic Urticaria Quality of Life Questionnaire – CU-Q_2oL)
Methods: In the development phase of CU-Q_2oL an initial list of items of 37 items was compiled and given to 80 patients with chronic urticaria; the 23 most significant items were selected and converted into questions evaluating the answers on a Likert scale of five steps. The validation procedure involved 125 patients (86 F and 39 M) (age 42.17 ± 9.24 years).
Results: Following a statistical analysis, CU-Q_2oL showed a six-dimensional structure and good levels of internal consistency for the extracted factors: Pruritus (0.79), Swelling (0.65), Impact on life activities (0.83), Sleep problems (0.77), Looks (0.83) and Limits (0.74). In stable conditions CU-Q_2oL showed a good reliability, ranged between 0.64 and 0.92. Responsiveness to clinical changes was accomplished.
Discussion: These results provide evidence that CU-Q_2oL has specificity enough for being a valid tool for detecting the relative burden of CU on subjective wellbeing, and for obtaining a global evaluation both of CU impact and of treatments, taking into account the patient's point of view. The CU-Q_2oL was easily and quickly filled up and well accepted by the patients.

I. Baiardini[1,4], M. Pasquali[1], F. Braido[1], F. Fumagalli[1], L. Guerra[1], E. Compalati[1], M. Braga[2], C. Lombardi[3], O. Fassio[4], G. W. Canonica[1]

[1]Allergy and Respiratory Diseases, Department of Internal Medicine, University of Genoa, Genoa, Italy; [2]Unit of Allergology, Clinical Immunology and Reumatology, Spedali Civili, Brescia, Italy; [3]Pneumoallergy Unit Department of Internal Medicine S. Orsola Hospital Brescia, Brescia, Italy; [4]Psychology Department, University of Turin, Turin, Italy

Key words: disease specific questionnaire; quality of life; urticaria; validation.

Prof. G. W. Canonica
Allergy and Respiratory Diseases
DIMI
Pad. Maragliano
L.go R. Benzi 10
16132 Genoa
Italy

Accepted for publication 27 January 2005

Chronic Urticaria (CU) is a skin disorder characterized by erithematous wheals, intense itch, with or without angioedema, daily for at least 6–8 weeks and can persists for years (1, 2). It remains a big problem in terms of aetiology, pathogenetic mechanism and pharmacologic treatment. A critical aspect in the management of CU is its burden on patient's well-being and quality of life.

The expression quality of life, and more specifically health-related quality of life (HRQoL), has been introduced to refer the impact of an illness and its therapy upon a patient, as perceived by the patient himself (3). With rising frequency HRQoL assessment is included in outcome research, providing data about the consequences of disease and treatment from the patient's perspective. Accordingly a large number of instruments have been validated, both generic and disease specific. Generic questionnaire has been developed to assess HRQoL in all health conditions. Specific questionnaires, whilst evaluating the multiple aspects of HRQoL, comprise content specific to the health problem in question, making them more sensitive and potentially more responsive to changes following clinical intervention.

Although CU can be a problem that interferes with subjective well-being and daily life, usually its evaluation has focused on clinical endpoints. While numerous studies are now available about HRQL in other dermatological conditions, only few reports on this topic in patients with CU have been found in the literature search. Using the generic Nottingham Health Profile, O'Donnel et al. (4) showed that adult patients with CU report QoL scores comparable with those of patients suffering from coronary artery disease. Health status and subjective satisfaction in CU have been recently assessed by mean of two generic tools, SF-36 and SAT-P (5); the presence of CU seems to have a substantial burden on both physical and emotional components of health status, with a consequent negative influence on subjective satisfaction. Poon and colleagues evaluated the nature of disability caused in CU patients using a speciality-specific measure, and highlighted the degree of

social and work restrictions in different chronic forms of urticaria (6). To date, HRQoL in adults with CU has been measured using generic questionnaires or questionnaires addressed to dermatologic diseases (4–6). Whilst generic instruments have the advantage of permitting comparison across different diseases, they are less suitable for assessment within a specific disease.

The available questionnaires aimed at assessing HRQoL in skin diseases (the Dermatology Quality of Life Index and the SKINDEX) (7, 8) permit a comparison between different dermatological conditions, but are not specifically developed to CU patients: in fact they have been used with patients suffering from clinical conditions really different from urticaria such as eczema, lypodistrophy, skin cancer, ichthyosis, psoriasis, melasma, iperhidrosis and acne (9–16).

The need of a new tool to evaluate HRQoL in CU seems to be justified for several reasons:

1. a specific questionnaire that includes all relevant aspects of HRQoL in CU does not exist;
2. use of both generic and specific tools in patient-based outcome assessment is recommended (17);
3. use of one single generic instrument seems insufficient in capturing subtle changes of HRQoL.

On the basis of these premises, the aim of our study was to develop and assess the psychometric properties of a questionnaire that evaluate the CU burden from the patient's perspective.

Our goal was to develop an instrument (1) able to capture physical, psychosocial and practical aspect of HRQoL of particular relevance for patients with CU; (2) generated and tested following procedures well established and applied to other similar questionnaires; (3) designed for use by the patient himself; simple to administer and score.

Methods

The development and validation of the new questionnaire occurred in two separate phases (development process and validation process) involving different groups of patients. The method used for the two steps is described in detail below.

Patients

All adult patients recruited in the development and validation of the new questionnaire had consistent clinical history, at least 6 weeks in duration, of intermittent or daily symptoms of urticaria (wheal, itching, swelling, etc.). Patients with other dermatological and other chronic diseases were excluded.

Development procedure

In order to make certain that the questionnaire included items appropriate and relevant for CU patients, items' generation and selection were conducted on the basis of current guidelines.

Item generation. An initial list of problems was generated on the basis of the following sources:

1. A panel of clinical and research experts in immunology, dermatology and allergy was requested to identify the symptoms and problems troublesome for CU patients; as result 28 relevant items were indicated.
2. An exploratory semi-structured interview was carried out with 60 patients affected by CU: patients were asked to describe the areas of their life that were impaired by the presence of CU; an initial list of 31 expressions/items was recognized, maintaining, whenever possible, the patient's expressions.

The items generation phase resulted in a total of 59 items. A qualitative selection was performed by eliminating those items resulted redundant, ambiguous, difficult to understand, expressed in negative form.

Item reduction. The resulted list contained 37 items that were administered to patients who had to indicate: (a) which of the items they have experienced (the response options were yes/no); (b) the importance of each selected item on a four-point scale (1: not at all; 4: very much).

In this first phase a sample of 80 consecutive outpatients' with CU was accrued during a three-month period. On the basis of collected data we subsequently calculated: (a) the percentage of patients who indicated each item as a consequence of their disease (frequency range: 0–100); (b) the importance (mean value) attributed from the patient to each item indicated as a problem (range: 0–4); (c) the overall importance score of the item, defined as the product of the frequency and the mean importance divided by 100 (range: 0–4). The result of this first phase generated a 23-item questionnaire, where patients had to indicate, on a Likert scale with multiple options (1: not at all; 5: very much), how much they were been troubled by each problem. The questionnaire was then administered to a different patients' population for validation.

Validation procedure

The validation process was performed in accordance with published guidelines (17). In addition to CU-Q_2oL, participants completed the SF-36 health survey, a generic, widely used questionnaire that provides an evaluation of the health status (18). It is composed of 36 items corresponding to eight domains: Physical Function, Role Limitation (Physical), Bodily Pain, General Health, Vitality, Social Function, Role Limitation (Emotional) and Mental Health. In addition, SF-36 provides two composite scores, Physical (PCS) and Mental (MCS) Component Summary that compute the physical and mental aggregate scores (19).

The SF-36 has been used extensively as an indicator of HRQoL also in dermatologic diseases (5, 20–22).

The aim of the validation phase was to evaluate the following properties of the new instrument:

1. Validity. It assesses whether an instrument actually measures that which it was designed to measure. Two validation analyses were designed. Factorial analysis was performed on CU-Q_2oL scores in order to identify potential subscales in accordance to our hypotheses; the principal component method with Varimax rotation was adopted. By mean of Pearson correlation coefficients, we also assessed the relationship between the new questionnaire and the SF-36, in order to evaluate the convergent validity.

2. Internal consistency. It measures the homogeneity of a scale. It was computed using Chronbach's correlation coefficient on the extracted factors. Measures with reliability of 0.50–0.70 or greater have been recommended for the purpose of comparing group.
3. Reliability. It refers to the degree to which an instrument yields stable scores over a short period of time, assuming there is no clinical change. Reliability was assessed by administering CU-Q_2oL to 22 untreated stable patients at baseline and after 1 week. Inter class coefficient (ICC) was calculated. An ICC of >0.75 indicates excellent reproducibility while an ICC between 0.4 and 0.75 indicates a good reproducibility (23).
4. Responsiveness. It measures the ability of the questionnaire to detect significant differences over time in patients whose status has changed. Responsiveness was assessed indirectly, based on the repeated measurements performed at baseline and after 2/3 weeks. We selected a group of 31 patients treated with second generation antihistamines, reporting diminished symptoms as well an improvement on the SF-36. CU-Q_2oL scores were compared by using a nonparametric test (Wilcoxon).

Item and scale scores were oriented so that higher scores indicate worse HRQoL. In order to make scores more meaningful and to permit comparisons between different populations of patients, linear transformations of raw scores indicating the percent of maximum possible score were performed. Thus the minimum possible score is defined as 0 and the maximum possible score is defined as 100.

The statistically significant cut-off value was set at $P < 0.05$. The whole statistical analysis was conducted by using SPSS10.0 (SPSS Inc., Chicago, IL, USA).

Results

CU-Q_2oL development procedure

Out of 80 patients, 76 completed the preliminary questionnaire. As reported in Table 1 the majority of patients were female; the mean age was 48.9 ± 7.8 with range of 18–81. On the basis of patients' answers, items included in the questionnaire were those that scored highest in impact. Where an arbitrary cut-off value of 1.5 was used for impact, 14 items were excluded. Table 2 summarizes the results of this first phase, indicating the items removed due to the low total importance.

Table 1. Development procedure: sample characteristics ($n = 76$)

	n (%)
Gender	
Male	29 (38.16)
Female	47 (61.84)
Age, years mean (SD)	48.9 (7.82)
Marital status	
Single	23 (30.26)
Married	53 (69.74)
Years of education	
0–5	4 (5.2)
6–8	33 (43.42)
9–13	26 (34.21)
>13	13 (17.10)
Employment status	
Employed	47 (61.84)
Unemployed	2 (2.63)
Housewife	13 (17.10)
Retired	8 (10.53)
Student	6 (7.89)
Duration of urticaria, months mean (SD)	21.15 (27.32)

CU-Q_2oL validation procedure

Out of 130 patients, 125 filled in both CU-Q_2oL and SF-36. The assessment of data missing from completed questionnaire was very small (1.85%). Table 3 summarizes sample's demographic and clinic characteristics.

1. Validity. Factor analysis revealed a six-dimensional structure, which explained up to 59.97 of the total variance (Table 4). This solution was deemed appropriate on the basis of eigenvalues. Association between CU-Q_2oL and SF-36 scores were all in the expected direction: as showed in Table 5 conceptually similar domains had higher correlations than conceptually unrelated domains. For example, statistically significant correlations were found between the factor *Impact on life activities* of CU-Q_2oL and all SF-36 domains indicating, as expected, that the daily life burden of CU is associate to a general heath status worsening; on the contrary, the factor *Looks* of CU-Q_2oL, that evaluates an area of relevance for CU patients (physical appearance), correlated only with the domains Role Physical, Social Functioning and Role Emotional of SF-36. Both the strength and direction of correlations observed between the CO-Q_2oL, and the SF-36 reflected our expectations.
2. Internal consistency. Internal-consistency reliability for the extracted factors exceeded the minimum reliability standard of 0.50–0.70 recommended for group comparison. In fact all the dimensions showed satisfactory Chronbach's alpha values: Pruritus (0.79), Swelling (0.65) Impact on life activities (0.83), Sleep problems (0.77), Limits (0.74), Looks (0.83). No substantial damage was caused by removal of any items.
3. Reliability. Inter Class Coefficients (ICCs) are good (>0.40 and <0.75) for the following items: '*Physical Activity*', '*Social Relationship*', '*Do you have difficulties in falling asleep?*', '*Do you feel in a bad mood?*'. ICCs were greater or equal to 0.75 for the others items.
4. Responsiveness. Among the group of patients who reported a significant diminished symptoms as well an improvement on the SF-36, a statistically significant difference was recorded in 18 out of 23 items. Results of responsiveness to clinical change of CU-Q_2oL, shown in Table 6, suggest that the questionnaire is responsive to expected changes in severity of symptoms.

Table 2. Development procedure: results of item reduction

Item	Frequency (%)	Mean importance	Overall impact
Urticaria interfere with my eating behaviour	69.74	3.01	2.10
I can't participate in the activities I enjoy	**23.68**	**1.75**	**0.42**
Eyes swelling	63.16	2.84	2.23
Urticaria interferes with my social relationship	67.11	2.59	1.74
Loss of working days	**27.63**	**1.99**	**0.54**
Urticaria interferes with my spare time	80.26	2.02	1.62
I feel helpless	**21.05**	**2.39**	**0.50**
Difficulties in falling asleep	78.95	2.12	1.67
I feel embarrassed by urticaria signs on my body	84.21	2.73	2.29
I think I'll succeed in controlling symptoms with drugs	**50.00**	**1.15**	**0.57**
Difficulties in being concentrate	61.84	2.53	1.56
I have to limit my physical activity due to urticaria	57.89	2.88	1.67
Pruritus	96.05	3.61	3.46
Urticaria interferes with my sexual life	**31.58**	**2.44**	**0.77**
Urticaria interferes with my work	69.74	2.73	1.90
I feel ill	**43.42**	**2.19**	**0.95**
Urticaria interferes with my sleep	71.10	2.98	2.12
I feel nervous	76.31	2.95	2.25
Urticaria interferes with my sport activities	57.89	3.06	1.77
I wake up during the night	61.84	2.83	1.75
Wheals	90.79	2.62	2.37
I think my doctor'll control urticaria symptoms	**30.26**	**1.52**	**0.46**
I'm troubled because I have to take drugs everyday	**26.32**	**1.39**	**0.36**
I have to put some limit in choosing my food	69.42	2.37	1.65
I think I'll succeed in controlling urticaria symptoms with drugs	**40.79**	**2.06**	**0.84**
I'm in a bad mood	71.05	2.54	1.80
I have some problems in using cosmetics	55.26	2.77	1.53
I'm worried that there is no effective treatment for urticaria	**44.73**	**1.21**	**0.54**
I feel tired during the day because of my bad night sleep	60.53	2.70	1.57
I feel anxious about my health condition	**38.15**	**3.12**	**1.19**
I'm embarrassed in going to public places	72.37	2.94	2.13
I'm troubled by the sudden appearance of symptoms	**42.10**	**1.76**	**0.74**
I'm troubled by drugs' side effects	71.05	2.19	1.55
I'm annoyed by frequent medical controls	**30.26**	**1.94**	**0.59**
I've some limits in choosing clothes material	51.31	2.97	1.52
Lips swelling	61.84	3.15	1.95
Drug expenses are too high	**48.68**	**1.31**	**0.63**

Bold faces indicate low important items (overall impact <1.5).

Discussion

The presence of a chronic condition results in physical, emotional and social problems that may impact patients' referred HRQoL. Only few published studies have described this topic in CU patients, highlighting, by mean of generic tools, a significant reduction of health status, well-being and personal satisfaction. The choice of a generic questionnaire, because of a specific one is not available, does not result the gold standard: when only a generic HRQoL instrument is used, the relative burden of a disease may not be accurately captured. In fact some dimensions of generic questionnaires have little relevance for people with CU, while important aspects affecting this group of patients are omitted. For example the physical appearance is an area not investigated by generic instruments like SF-36 and NHP, but one of importance for people with CU. In contrast, physical functioning and mobility, covered by both SF-36 and NHP, result aspects of less concern for the majority of CU patients.

The purpose of this study was to design and validate a new specific tool for evaluate HRQoL in patients with CU, by adhering to established methodological guidelines and by following a recognized framework of questionnaire design.

The psychometric testing of the CU-Q_2oL provides evidence that the new questionnaire appropriately reflects HRQoL in CU patients. In fact, as described in the development procedure, it includes items that have been determined by the patients and are consequently meaningful to them. Furthermore, the validation process shows that the questionnaire met the standards for validity with good validity, internal consistency, reliability and responsiveness. These psychometric characteristics make the CU-Q_2oL useful to evaluate the specific burden of CU on HRQL and to detect the changes induced by effective

Table 3. Validation procedure: sample characteristics ($n = 125$)

	n (%)
Gender	
Male	46 (36.8)
Female	79 (63.2)
Age, years mean (SD)	53.69 ± 11.7
Marital status	
Single	41 (32.8)
Married	84 (67.2)
Years of education	
0–5	10 (8)
5–8	42 (33.6)
8–13	51 (40.8)
>13	22 (17.6)
Employment status	
Employed	83 (66.4)
Unemployed	2 (1.6)
Housewife	16 (12.8)
Retired	15 (12)
Student	9 (7.2)
Duration of urticaria, months mean (SD)	25.81 (31.71)

Table 4. Chronbach alpha correlation coefficient on factorial scores

Factor	Items	Alpha coefficient
Pruritus	Pruritus	0.881
	Wheals	0.841
Swelling	Eyes swelling	0.906
	Lip swelling	0.895
Impact on life activities	Urticaria interferes with my work	0.828
	Urticaria interferes with my physical activities	0.794
	Urticaria interferes with my sleep	0.661
	Urticaria interferes with my spare time	0.780
	Urticaria interferes with my social relationship	0.832
	Urticaria interferes with my eating behavior	0.514
Sleep problems	Do you have difficulties in falling asleep?	0.795
	Do you wake up during the night?	0.764
	Do you feel tired during the day because of your bad night sleep?	0.808
	Do you have difficulties in keeping concentration?	0.684
	Do you feel nervous?	0.529
Limits	Do you feel in a bad mood?	0.575
	Do you have to put some limit in choosing your food?	0.681
	Does urticaria limits your sport activities?	0.627
Looks	Are you troubled by drugs' side effects?	0.7322
	Are you embarrassed due to urticaria symptoms?	0.7444
	Are you embarrassed in going to public places?	0.7720
	Do you have any problems in using cosmetics?	0.7208
	Do you have any limits in choosing clothes material?	0.7421

Table 6. CU-Q_2oL items with a significant difference in patients who reported significant diminished symptoms and better SF-36 scores

Item	*P*-value
Pruritus	0.0001
Wheals	0.003
Eyes swelling	0.01
Urticaria interferes with my work	0.002
Urticaria interferes with my sleep	0.01
Urticaria interferes with my spare time	0.004
Urticaria interferes with my social relationship	0.04
Do you have difficulties in falling asleep?	0.005
Do you wake up during the night?	0.02
Do you feel tired during the day because of your bad night sleep?	0.03
Do you feel in a bad mood?	0.004
Do you have to put some limit in choosing your food?	0.0001
Do you have to limit your physical activity?	0.02
Are you troubled by drugs' side effects?	0.04
Are you embarrassed due to urticaria signs?	0.003
Are you embarrassed in going to public places?	0.01
Do you have any problems in using cosmetics?	0.002
I've some limits in choosing clothes material	0.0001

interventions, but also appears to be the first validated questionnaire specific for the assessment of HRQoL in CU.

The CU-Q_2oL is simple to administer and results well accepted by the responding patients. In average it requires 5 minutes to complete and can be filled without assistance. The new questionnaire is also easily evaluated by mean of a software that permits to obtain a score about the six dimensions extracted and in addition reports the critical items (items in which patient reported the higher score).

CU-Q_2oL questionnaire:

1. captures the impact of CU on patients' HRQoL;
2. can be a complement of clinical measures (i.e. analysing the global impact of a drugs on patient' well-being);
3. can aid treatment decision-making (i.e. tailoring the treatment not only on the symptoms by also on the QoL more influenced parameters);
4. can be useful in urticaria treatment assessment (i.e. evaluation or comparison of symptomatic treatments on CU patient quality of life).

In conclusion, based on the findings of this study, the CU-Q_2oL is a valid instrument for the assessment of

Table 5. Correlation (*r*) of the CU-Q2oL with SF-36

	PF	RF	BP	GH	VY	SF	RE	MH	PCS	MCS
Pruritus	−0.184*	−0.375***	−0.153	−0.137	−0.205*	−0.345***	−0.263**	−0.296***	−0.219*	−0.299***
Swelling	0.002	−0.053	0.051	−0.286***	−0.240**	−0.195*	−0.152	−0.174	−0.009	−0.237**
Impact on life activities	−0.344***	−0.483***	−0.331***	−0.313***	−0.316***	−0.383***	−0.395***	−0.425***	−0.398***	−0.389***
Sleep problems	−0.170	−0.238**	−0.301***	−0.315***	−0.341***	−0.348***	−0.364***	−0.331***	−0.241**	−0.390***
Limitations	−0.257**	−0.362***	−0.357***	−0.484***	−0.462***	−0.401***	−0.236**	−0.439***	−0.426***	−0.380***
Looks	−0.152	−0.217*	−0.045	−0.026	−0.044	−0.203*	−0.195*	−0.134	−0.096	−0.158

*, **, ***Significant at $P = 0.05$, 0.01 and 0.001, respectively.

HRQoL in clinical management of CU and for the evaluation of treatment outcomes. The future application on large population should be useful for a global approach to this dermatological condition.

Acknowledgments

This study has been partially supported by: ARMIA (Associazione Ricerca Malattie Immunologiche e Allergiche), GA[2] LEN, MIUR. (unrestricted Educational Grant).

References

1. Greaves M. Chronic urticaria. J Allergy Clin Immunol 2000;**105**:664–672.
2. Zuberbier T. Urticaria. Allergy 2003;**58**:1224–1234.
3. Schipper H, Clinch J, Olweny CLM. Quality of life studies: definitions and conceptual issues. In: Spilker B, editors. Quality of life and pharmacoeconomics in cinical trials. Philadelphia: Lippincot-Raven Press, 1990:11–23.
4. O'Donnel BF, Lawlor F, Simpson J, Morgan M, Greaves MW. The impact of chronic urticaria on the quality of life. Br J Dermatol 1997;**136**:197–201.
5. Baiardini I, Giardini A, Pasquali M, Dignetti P, Guerra L, Specchia C et al. Quality of life and patients' satisfaction in Chronic urticaria and respiratory allergy. Allergy 2003;**58**:621–623.
6. Poon E, Seed PT, Greaves MW, Kobza-Black A. The extent and nature of disability on different urticarial conditions. Br J Dermatol 1999;**140**:667–671.
7. Finlay A, Khan GK. Dermatology life quality index (DLQI) – a simple practical measure for routine in clinical use. Clin Exp Dermatol 1994;**19**:210–216.
8. Chren MM, Lasek RJ, Flocke SA, Zyzansky SJ. Improved discriminative and evaluative capability of a refined version of Skindex, a quality-of-life instrumet for patients with skin diseases. Arch Dermatol 1997;**133**:1433–1440.
9. Wallenhammar LM, Nyfiall M, Lindberg M, Meding B. Health-related quality of life and hand-eczema-a comparison of two instruments, including factor analysis. J Invest Dermatol 2004;**122**:1381–1389.
10. Blanch J, Rousand A, Martinez E, De Lazzari E, Milinkovic A, Peri JM et al. Factors associated with severe impact of lipodystrophy on the quality of life of patients infected with HIV-1. Clin Infect Dis 2004;**38**:1464–1470.
11. Rhee JS, Matthews BA, Neuburg M, Smith TL, Burzynsky M, Nattinger AB. Skin cancer and quality of life: assessment with the dermatology life quality index. Dermatol Surg 2004;**30**:525–529.
12. Genemo A, Sjoden PO, Johansson E, Vahlquist A, Lindberg M. Health-related quality of life among patients with ichthyosis. Eur J Dermatol 2004;**14**: 61–66.
13. Bergstrom KG, Arambula K, Kimball AB. Medication formulation affects quality of life: a randomized single-blind study of clobetasol propionate foam 0.05% compared with combined program of clobetasol cream 0.05% for the treatment of psoriasis. Cutis 2003;**72**:407–411.
14. Balkrishnan R, Mcmichael AJ, Camacho FT, Saltzberg F, Housman TS, Grummer S et al. Developmen and validation of a health-related quality of life instrument for women with melasma. Br J Dermatol 2003;**149**:572–577.
15. Campanati A, Penna L, Guzzo T, Menotta L, Silvestri B, Lagalla G et al. Quality-of-life assessment in patients with hyperhidrosis before and after treatment with botulinum toxin: results of an open-label study. Clin Ther 2003;**25**:298–308.
16. Newton JN, Mallon E, Klassen A, Ryan TJ, Finlay AY. The effectiveness of acne treatment: an assessment by patients of the outcome of therapy. Br J Dermatol 1997;**137**:563–567.
17. Testa MA, Simonson DC. Assessment of quality-of-life outcomes. N Eng J Med 1996;**334**:835–840.
18. Ware JE, Snow KK, Kosinski M et al. SF-36 Health survey. Manual and interpretation guide. Boston: The Health Institute, New England Medical Center, 1993.
19. Ware JE, Kosinski M, Keller SD. SF-36 Physical and mental health summary scales: a user's manual. Boston: Health Assessment Lab, New England Medical Center, 1994.
20. Bingefors K, Lindberg M, Isacson D. Self-reported dermatological problems and use of prescribed topical drugs correlate with decreased quality of life: and epidemiological survey. Br J Dermatol 2002;**147**:285–290.
21. Heydendael VM, de Borgie CA, Spuls PI, Bossuyt PM, Bos JD, de Rie MA. The burden of psoriasis is not determined by disease severity only. J Invest Dermatol Symp Proc 2004;**9**:131–135.
22. Terreehorst I, Duivenvoorden HJ, Tempeles-Pavlica Z, Oosting AJ, Monchy JG, Bruijnzeel-Koomen CA et al. The unfavourable effects of concomitant asthma and sleeplessness due to the atopic-eczema/dermatitis syndrome (AEDS) on quality of life in subjects allergic to house-dust mites. Allergy 2002;**57**:919–925.
23. Rosner B. Foundamentals of biostatistics. Belmont, CA: Duxbury Press, 1995:519.