

Why generic and disease-specific quality-of-life instruments should be used together for the evaluation of patients with persistent allergic rhinitis

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Summary

Background The importance of assessing health-related quality of life (HRQL) of patients with allergic rhinitis (AR) has been well established, but the specific roles of rhinitis-specific or general health instruments have not been delineated.

Objective We analysed the psychometric properties of a disease-specific instrument, the Rhinoconjunctivitis Quality-of-Life Questionnaire (RQLQ) and the general health instrument, the Medical Outcome Short-Form 36 (SF-36) as they are employed in combination in patients with persistent AR in clinical practice.

Method We analysed the data collected from a prospective study of 43 newly diagnosed patients with persistent AR and 44 controls. We interviewed the patients four times, at baseline, weeks 4, 8 and 10.

Results The RQLQ and SF-36 have good discriminative property, internal consistency, and test-retest reliability. The RQLQ is superior to the SF-36 as an evaluative instrument because more of its domains respond to change, the magnitude of change was greater, and the response was faster. The SF-36 is more susceptible to floor and ceiling effects. Both instruments are unsuitable for mildly symptomatic patients based on Rasch model analysis. Each questionnaire assesses a distinct and significant portion of the total HRQL of persistent AR.

Conclusion The SF-36 and RQLQ are good for discriminating rhinitis patients from controls, but the former is poor for detecting changes in QOL. Both are inappropriate for mildly symptomatic patients. Each instrument measures non-overlapping halves of the measurable HRQL. For an assessment of the HRQL in persistent AR that is complete and responsive both instruments should be employed together.

Keywords factor analysis, Medical Outcome Short-Form 36, persistent allergic rhinitis, quality of life, Rasch modelling, Rhinoconjunctivitis Quality-of-Life Questionnaire, RQLQ, SF-36, symptom score
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Introduction

Allergic rhinitis (AR) exerts a heavy economic and social burden not only because it is highly prevalent in many parts of the world, but also because the symptoms interfere profoundly with many aspects of life. Indeed, the patient's subjective assessment of the effects of the illness and of its treatment, also known as health-related quality of life (HRQL), is considered to be very relevant for clinical practice, interventional trials, and outcome monitoring [1–3].

Individually, the disease-specific Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) and the generic SF-36 Health Survey (SF-36) have been employed to assess HRQL in AR in population studies as well as clinical trials. The

RQLQ and SF-36 have been used together but the rationale for this combined use has not been examined [4–8]. The indications for choosing one instrument over the other, or whether they should only be used together, are not known. Because these instruments are increasingly used as outcome measures in clinical trials, their scientific (reliability, validity, responsiveness) and clinical properties (feasibility, appropriateness) must be demonstrated [9].

The two aims of this study are to investigate the psychometric properties of the RQLQ and SF-36 employed prospectively in routine clinical practice, and to examine the rationale of employing them in combination.

Materials and methods

Subjects

We conducted a prospective interviewer-administered study on patients with persistent AR with approval from the Ethics

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Committee. Singapore is a tropical country without seasonal variation in the weather, so persistent AR is the main form of this disease. Informed consent was obtained from all patients and controls. We recruited patients from the outpatient clinic of the Department of Otorhinolaryngology, and the Nose Clinic, a combined clinic conducted by Otorhinolaryngologists and Allergists, at Tan Tock Seng Hospital, Singapore. Newly diagnosed patients were selected because they have the greatest capacity to experience a change in their health status. Inclusion criteria were:

- age 18 years and above;
- presence of one or more of the features of AR (clear nasal discharge, nasal congestion or nose itch, plus ear itch, eye itch or sneezing) for more than 4 days a week for 4 weeks or more [10];
- positive skin prick tests to at least one common perennial local aeroallergen, namely *Dermatophagoides pteronyssinus*, *D. farinae*, cockroach, cat and dog (Greer Laboratories Inc., Lenoir, NC, USA); and
- ability to understand English.

Patients were excluded if they had chronic sinusitis, nasal polyposis, nasopharyngeal carcinoma, pollen allergy, asthma uncontrolled with medications or recent life events that may interfere with HRQL evaluation.

The questionnaires were administered on four occasions, at baseline, weeks 4, 8 and 10. Patients did not see their previous responses. Doctors treated their patients according to their clinical judgement, which is generally consistent with the ARIA guidelines [10]. No patient was treated with immunotherapy. There was no run-in period because this was not a drug trial. An Allergy Nurse Educator counseled all patients about allergen avoidance. Volunteer controls, who were hospital staff, medical students and military personnel, completed one set of the questionnaire only. We assessed test–retest reliability utilizing the last two interviews rather than the first two because the patients' clinical status is more likely to be stable later in the course of treatment.

Questionnaires

We asked our patients to quantify the severity of sneezing, runny nose, blocked nose, itchy nose and itchy eyes in the preceding 1 week with a 10-centimetre visual analogue scale (VAS).

The RQLQ, designed specifically for AR, was published in 1991 and validated in a prospective two-arm therapeutic trial of seasonal AR [11, 12]. The RQLQ comprises 28 questions divided into seven sections, namely, sleep, non-rhinitis symptoms (e.g. fatigue and thirst), practical problems (e.g. the need to blow nose repeatedly), nasal symptoms, eye symptoms, activities and emotions. The items in the questionnaire were considered to be important and to occur frequently by the patients themselves. It can be self- or interviewer-administered and has been translated into German [13], Dutch [14], and other languages [15]. In addition, subjects are asked to nominate three activities in their lives that they think have been affected by rhinitis. A standardized version of the RQLQ (in which these activities are pre-selected) and an abridged version (in which certain items are removed) are also available [16, 17]. The RQLQ is fairly well

accepted and has been adopted as an outcome measure in clinical trials of seasonal AR [15, 18–20]. We have shown that it is valid for use in English-speaking patients with persistent AR in this country [21]. We used the standard interviewer-administered English version.

The Medical Outcome Short-Form 36 (SF-36) is a generic QOL instrument that has been used widely used to assess HRQL in many disease states [22–24]. The SF-36 has been used to study the QOL of AR in the United States [4, 5], France [25, 26], Italy [27], and Japan [28] and has been used as an outcome measure in clinical trials as well [29–32]. It has 36 questions categorized into nine functional domains. We used the Standard version of the SF-36 with a 4-week recall period [33].

Statistical analysis

The summary RQLQ score is taken as the mean of the scores of all 28 items, as per Juniper et al. [12], which is different from the mean of the average score of each domain as used by De Graaf-in't Veld et al. [14]. The SF-36 data were scored according to the manual [33]. We compared the symptoms, mean RQLQ and SF-36 scores of patients and controls with the two-tailed Mann–Whitney *U*-test, as we did not assume normal distribution.

The test–retest reliability of the questionnaires, determined using the responses of the patients in the third and fourth interviews, was assessed with intra-class correlation.

We determined the standard deviation of the difference in symptom score of the third and fourth visit (assuming that the clinical status and the symptom scores of these patients remained unchanged over this period), thereby deriving the intra-person (individual-level) variability. We defined 'unchanged' patients as those whose change in symptom score lie within two standard deviations [34]. In contrast to asking patients to rate their QOL at a particular visit compared with the previous one, this method allows us to determine if the patient's symptoms have changed over two or more visits.

To determine if the responsiveness of the instruments improved over time, we assessed 'early' change (the difference between first and second interviews) and net change (the difference between first and third interviews). There is no single best responsiveness statistic for assessing HRQL instruments [35], so we used a battery of five indices: Liang's relative efficacy [36] and standardized response mean [37], Kazis' effect size [38], Guyatt's responsiveness statistic [39], and Deyo's ROC curve [40].

We explored the construct validity of the two instruments by determining the intra-class correlation of their items with the symptom scores and of the items of each questionnaire with each other (correlation matrix).

For factor analysis, all the responses in the items of the RQLQ (Likert scale 0–6 best to worst) were transformed to reflect better health perception with higher scores (1–7 worst to best) by taking the difference of the raw score from 7. We made use of all the items of both questionnaires simultaneously for factor analysis, thereby gaining an understanding of the interrelation of the items and their proportional contribution to the total HRQL. The factors were extracted by principal component analysis and varimax rotation [41].

We investigated the difficulty of every item of the questionnaires with Rasch model analysis.

We analysed the data with the SPSS Professional Statistics 8.0. Rasch model analysis was carried out with BIGSTEPS, which is available at www.winsteps.com. All statistical tests were conducted at 5% level of significance.

Results

Subjects' characteristics

Eighty-four patients were screened. Forty-one patients were rejected: 22 because they did not fulfill the inclusion criteria and 19 because they did not complete all four sets of questionnaires.

The 43 patients who completed all the questionnaires and the 19 who did not were similar in terms of age ($P = 0.74$), race ($P = 0.44$), occupation ($P = 0.05$), education ($P = 0.052$), family income ($P = 0.78$), sneezing symptom score ($P = 0.69$), nose itch symptom score ($P = 0.52$), runny nose symptom score ($P = 0.23$) and eye symptom score ($P = 0.64$). However, the 19 patients who were omitted from the analysis were more likely to be married (10 out of 19 married vs. 10 out of 43, $P = 0.02$) and had milder nasal symptoms (63.4 vs. 76.7, $P = 0.025$). We feel that omitting these 19 patients should not materially alter our conclusions.

The 43 patients and 44 controls were comparable in terms of age, sex, marital status, occupation and family income but they had significantly different rhinitis symptom scores (Table 1).

Validity of the Rhinoconjunctivitis Quality-of-Life Questionnaire and Medical Outcome Short-Form 36

Discriminative property All but four items of the SF-36 were statistically significantly different between patients and controls (data not shown). These four exceptions were lifting or carrying groceries, climbing one flight of stairs, walking one hundred metres, and bathing or dressing oneself. These activities belong to the physical-functioning domain and are unlikely to be affected even in highly symptomatic rhinitic patients. In contrast, all 28 items of the RQLQ were statistically different between patients and controls (data not shown).

However, all the domain and summarized scores of the SF-36 and RQLQ were significantly different between patients and controls (Table 2), confirming their discriminative ability. This suggests that rhinitic patients have wide-ranging impairment in their quality of life that is not restricted to nasal symptoms. Because some domains of the SF-36 (especially role-physical and role-emotional) have very wide standard deviations, the questionnaire will have reduced sensitivity as an evaluative tool [42].

Floor and ceiling effect When patients perceive that they have improved or deteriorated beyond what a HRQL questionnaire can measure, the ceiling or floor effect, respectively, is said to occur. These inadequacies are often unreported and they are also difficult to eradicate. Table 3 shows the proportion of patients whose responses reached the maximum and minimum scores in the domains of each questionnaire;

Table 1. Subjects' characteristics

	Persistent allergic rhinitis	Controls	P-value
Number	43	44	–
Age (years)			
Range	18–64	19–44	–
Mean	26.6	27.66	0.064*
Sex, number (%)			
Females	16 (37.2)	19 (43.9)	0.663
Marital status, number (%)			
Married	10 (23.3)	12 (27.3)	0.540
Single	33 (76.7)	31 (70.5)	–
Widowed	0 (0)	1 (2.3)	–
Ethnicity, number (%)			
Chinese	38 (88.4)	32 (72.7)	0.104
Malay	2 (4.7)	3 (6.8)	–
Indian	2 (4.7)	9 (20.5)	–
Others	1 (2.3)	0 (0)	–
Occupation, number (%)			
Housewife	2 (4.7)	0 (0)	0.211
Student	8 (18.6)	10 (22.7)	–
Military service	20 (46.5)	12 (27.3)	–
Clerical	3 (7.0)	7 (15.9)	–
Technical	3 (7.0)	3 (6.8)	–
Professional	5 (11.6)	11 (25.0)	–
Others	2 (4.7)	1 (2.3)	–
Education level, number (%)			
Secondary	15 (34.9)	12 (27.7)	0.498
Technical	1 (2.3)	3 (6.8)	–
Tertiary	27 (62.8)	29 (65.9)	–
Family income, number (%)			
< \$1000	3 (7.0)	2 (4.7)	0.636
\$ 1000 to \$ 2499	16 (37.2)	11 (25.6)	–
\$ 2500 to \$ 4999	17 (39.5)	21 (48.8)	–
\$ 5000 to \$ 10 000	6 (14.0)	6 (14.0)	–
> \$ 10 000	1 (2.3)	3 (6.8)	–
Symptom, VAS scale mean $\pm$ standard deviation			
Sneezing,	69.42 $\pm$ 23.24	4.89 $\pm$ 9.58	<0.01*
Nose itch	56.16 $\pm$ 26.19	5.14 $\pm$ 10.46	<0.01*
Blocked nose	76.74 $\pm$ 19.66	4.48 $\pm$ 9.84	<0.01*
Runny nose	74.47 $\pm$ 23.22	3.66 $\pm$ 9.10	<0.01*
Eye symptoms	45.51 $\pm$ 32.98	4.80 $\pm$ 13.99	0.01*
Duration of illness (years)			
Median	8	–	–
Range	1–38	–	–

*Mann–Whitney U -test. All P -values from Pearson's χ^2 test, unless otherwise stated. A Singapore dollar is worth about 0.55 US dollars at the time of writing. VAS, visual analogue scale.

values above 20% are regarded as substantial [24]. Floor and ceiling effect was more obvious in the SF-36 than the RQLQ, especially in the domains of role-physical and role-emotional. The ceiling effect of the SF-36 came into play as the health status improves, rendering it incapable of tracking further improvement in patients with mild symptoms.

There was a prominent floor effect in the eye-symptoms score of the RQLQ, consistent with the low score in the eye symptom in the VAS scale. Our patients with persistent AR often report no conjunctival symptoms [21,43].

Rasch model analysis In Rasch model analysis, the item difficulty and patient ability measures are listed on both sides

Table 2. Discriminative property of RQLQ and SF-36 (lower scores indicate better perception of health in RQLQ and vice versa in SF-36)

Instrument	Domains or dimensions	Persistent allergic rhinitis, mean $\pm$ SD	Controls, mean $\pm$ SD	Mann-Whitney U-test (<i>P</i> -value)
Mean RQLQ scores	Activities	3.77 $\pm$ 1.03	0.08 $\pm$ 0.32	<0.001
	Sleep	2.85 $\pm$ 1.70	0.21 $\pm$ 0.74	<0.001
	Non-rhinitis symptom	3.24 $\pm$ 1.34	0.46 $\pm$ 1.11	<0.001
	Practical problems	3.78 $\pm$ 1.64	0.30 $\pm$ 0.70	<0.001
	Nasal symptom	4.03 $\pm$ 1.32	0.23 $\pm$ 0.70	<0.001
	Eye symptoms	1.98 $\pm$ 1.69	0.15 $\pm$ 0.52	<0.001
	Emotion	3.37 $\pm$ 1.49	0.17 $\pm$ 0.64	<0.001
	Summary score	3.26 $\pm$ 1.15	0.26 $\pm$ 0.57	<0.001
Mean SF-36	Physical functioning	80.12 $\pm$ 14.41	94.20 $\pm$ 10.83	<0.001
	Role-physical	44.19 $\pm$ 42.20	92.61 $\pm$ 19.87	<0.001
	Bodily pain	68.49 $\pm$ 25.04	90.16 $\pm$ 16.70	<0.001
	General health	51.28 $\pm$ 23.90	77.55 $\pm$ 15.14	<0.001
	Vitality	51.40 $\pm$ 17.71	72.16 $\pm$ 15.34	<0.001
	Social functioning	66.28 $\pm$ 24.33	92.61 $\pm$ 12.45	<0.001
	Role-emotional	48.06 $\pm$ 45.60	95.45 $\pm$ 18.46	<0.001
	Mental health	62.23 $\pm$ 14.77	79.09 $\pm$ 15.16	<0.001

RQLQ, Rhinoconjunctivitis Quality-of-Life Questionnaire; SF-36, Medical Outcome Short-Form 36; SD, standard deviation.

Table 3. Patients' responses attaining the maximum and minimum scores over the three encounters

Instrument	Domains or dimensions	First visit		Second visit		Third visit	
		Floor (%)	Ceiling (%)	Floor (%)	Ceiling (%)	Floor (%)	Ceiling (%)
Mean RQLQ scores	Activities score	2.3	0	0	7.0	0	11.7
	Sleep score	4.7	9.3	0	14.0	7.0	23.3
	Non-rhinitis symptom score	2.3	0	0	4.7	2.3	7.0
	Practical problems score	11.6	2.3	2.3	7.0	2.3	7.0
	Nasal symptom score	7.0	0	2.3	7.0	2.3	7.0
	Eye symptoms score	2.3	20.9	0	18.6	0	32.5
	Emotion score	9.4	2.3	2.3	11.6	0	16.3
	Summary score	0	0	0	2.3	0	4.7
Mean SF-36 domains	Physical functioning	0	11.6	0	18.6	0	23.3
	Role-physical	37.2	27.9	20.9	46.5	16.3	46.5
	Bodily pain	0	25.6	0	20.9	2.3	27.9
	General health	0	0	0	0	0	0
	Vitality	0	0	0	0	2.3	0
	Social functioning	0	18.6	0	23.3	2.3	25.6
	Role-emotional	41.9	37.2	30.2	51.2	30.2	55.8
	Mental health	0	0	0	0	0	2.3

The scores for the RQLQ have been reversed, so that the floor results indicate the worst health perception and the ceiling now indicate the best health perception for both questionnaires.

RQLQ, Rhinoconjunctivitis Quality-of-Life Questionnaire; SF-36, Medical Outcome Short-Form 36.

of a linear logit scale. The software automatically locates the item of mean difficulty and assigns it the value of zero. The item measure indicates how difficult that item is (Table 4). The five most difficult items in decreasing order were: need to blow nose repeatedly (RQLQ), embarrassment (RQLQ), need to rub nose/eyes (RQLQ), perception that the patient gets ill more easily than other people (SF-36) and better health rating compared to a year ago (SF-36). The five easiest items in increasing order were: walking more than a kilometre (SF-36), climbing one flight of stairs (SF-36), walking several hundred metres (SF-36), climbing several flights of stairs (SF-36) and walking one hundred metres (SF-36).

Nonetheless, the logit scores for the items in both questionnaires are too low for 23 of the patients, thus explaining the considerable ceiling effect. The mismatch of item difficulty and patient ability worsened as the patients improve over the follow-up period (data not shown).

Internal consistency Cronbach's α for the scales is shown in the Table 5. Most of the domains in both questionnaires were above 0.7, suggesting that both instruments have good internal consistency.

Test-retest reliability The 2-week test-retest reliability (in terms of the intra-class correlation) is shown in Table 5, in which the RQLQ and SF-36 performed fairly well. The

Table 4. Rasch analysis of the items of the SF-36 and RQLQ

Person measure	Item measure	Items	Infit mnsq	Infit zstd	Outfit mnsq	Outfit zstd	Corr
23 patients with scores from 0.49 to 0.1							
0.09	0.09	Practical problems (c)*	0.68	-1.9	0.65	-1.9	0.59
	0.08	Emotional (d)*	1.1	0.5	1.07	0.3	0.59
	0.08	Practical problems (b)*	0.59	-2.5	0.58	-2.4	0.63
	0.08	General Health (4)	1.26	1.2	1.26	1.1	0.51
0.07	0.07	Health transition	0.79	-1.2	0.76	-1.2	0.49
0.07	0.07	Nasal symptoms (a)*	0.69	-1.8	0.66	-1.8	0.56
0.07	0.07	Role-Emotional (1)	2.67	6	2.51	5.1	0.52
	0.07	Vitality (3)	0.45	-3.6	0.43	3.4	0.7
	0.07	Vitality (1)	0.57	-2.6	0.65	-1.9	0.51
	0.07	Practical problems (a)*	0.59	-2.5	0.56	-2.4	0.65
	0.07	Nasal symptoms (b)*	0.5	-3.2	0.49	-3	0.66
	0.07	Bodily pain (2)	1.37	1.7	1.36	1.5	0.39
0.06	0.06	Mental health (2)	0.72	-1.6	0.87	-0.6	0.44
0.06	0.06	Role-physical (1)	2.5	5.5	2.3	4.4	0.59
0.06	0.06	Role-physical (2)	2.24	4.7	2.07	3.8	0.69
	0.06	Role-emotional (2)	2.4	5.2	2.27	4.4	0.63
	0.06	Non-rhinitis symptom (c)*	0.51	-3.1	0.49	-3	0.69
	0.06	Mental health (5)	0.74	-1.5	0.83	-0.8	0.41
0.05	0.05	General health (2)	0.73	-1.5	0.82	-0.9	0.56
	0.05	General health (1)	0.91	-0.4	1.04	0.2	0.56
	0.05	Non-rhinitis symptom (d)*	0.44	-3.6	0.42	-3.4	0.76
	0.05	General health (5)	0.59	-2.5	0.68	-1.7	0.58
	0.05	Role-physical (3)	2.49	5.4	2.39	4.6	0.6
	0.05	Sleep (b)*	0.84	-0.8	0.84	-0.8	0.51
	0.05	Social functioning (2)	2.98	6.7	2.83	5.7	0.41
	0.05	Non-rhinitis symptom (a)*	0.56	-2.7	0.53	-2.6	0.63
0.04	0.04	Emotional (b)*	0.68	-1.8	0.65	-1.8	0.65
	0.04	Activities (b)*	0.51	-3	0.51	-2.8	0.69
	0.04	Vitality (2)	0.7	-1.7	0.64	-1.8	0.66
	0.04	Non-rhinitis symptom (g)*	0.87	-0.7	0.83	-0.8	0.61
	0.04	Sleep (c)*	0.49	-3.1	0.47	-3	0.68
0.03	0.03	Activities (a)*	0.65	-2	0.64	-1.8	0.52
0.03	0.03	Emotional (a)*	0.57	-2.5	0.56	-2.3	0.76
0.03	0.03	Eye symptoms (d)*	0.64	-2	0.6	-2	0.75
	0.03	Mental health (4)	0.9	-0.5	1.03	0.2	0.33
	0.03	Nasal symptoms (d)*	0.6	-2.3	0.56	-2.3	0.66
	0.03	Physical functioning (10)	2.67	5.7	2.43	4.5	0.55
0.02	0.02	Activities (c)*	0.7	-1.6	0.7	-1.5	0.55
	0.02	Non-rhinitis symptom (f)*	0.43	-3.5	0.42	-3.3	0.75
	0.02	Nasal symptoms (c)*	0.78	-1.1	0.75	-1.2	0.65
	0.01	Mental health (3)	0.68	-1.7	0.68	-1.5	0.53
	0.01	Bodily pain (1)	0.61	-2.1	0.67	-1.6	0.52
0	0	Role-emotional (3)	0.8	-1	0.96	-0.2	0.51
0	0	General health (3)	0.7	-1.6	0.82	-0.8	0.52
	0	Sleep (a)*	0.77	-1.2	0.72	-1.3	0.53
	0	Non-rhinitis symptom (b)*	0.37	-4	0.38	-3.4	0.74
	-0.01	Non-rhinitis symptom (e)*	0.52	-2.7	0.52	-2.4	0.66
-0.02	-0.02	Eye symptoms (a)*	0.68	-1.7	0.67	-1.5	0.61
-0.04	-0.04	Mental health (1)	0.68	-1.5	0.69	-1.3	0.59
	-0.05	Emotional (c)*	1.14	0.6	1.06	0.2	0.52
-0.06	-0.06	Physical functioning (3)	1.22	0.9	1.52	1.7	0.33
-0.06	-0.06	Social functioning (1)	0.58	-2	0.58	-1.8	0.61
	-0.07	Vitality (4)	0.51	-2.4	0.52	-2.1	0.8
	-0.08	Eye symptoms (b)*	1.01	0.1	0.88	-0.4	0.6
	-0.08	Physical functioning (1)	0.96	-0.2	1.08	0.3	0.42
	-0.08	Physical functioning (6)	1.52	1.8	1.75	2.1	0.41
	-0.11	Eye symptoms (c)*	1.07	0.2	0.9	-0.3	0.55
	-0.12	Role-physical (4)	0.94	-0.2	1.02	0.1	0.31
	-0.15	Physical functioning (2)	2.1	2.8	2.48	3	0.01

Table 4. (Contd.)

Person measure	Item measure	Items	Infit mnsq	Infit zstd	Outfit mnsq	Outfit zstd	Corr
– 0.17	– 0.17	Physical functioning (7)	1.31	0.9	1.19	0.5	0.57
	– 0.18	Physical functioning (5)	3.02	4	3.2	3.7	0.06
	– 0.25	Physical functioning (8)	1.35	0.8	1.58	1	0.4
	– 0.28	Physical functioning (4)	1.51	1	1.83	1.3	0.31
	– 0.28	Physical functioning (9)	1.84	1.5	2.05	1.6	0.14
	0		1.05	– 0.4	1.06	– 0.4	
	0.09		0.69	2.7	0.68	2.3	

Items with an asterisk are from the RQLQ.

fit mnsq, infit mean square; infit zstd, infit z-standard; outfit mnsq, outfit mean square; outfit zstd, outfit z-standard; corr, correlation; RQLQ, Rhinoconjunctivitis Quality-of-Life Questionnaire; SF-36, Medical Outcome Short-Form 36.

Table 5. Internal consistency and test–retest reliability of the RQLQ and SF-36

Instrument	Domains	Cronbach's α	Intra-class correlation coefficient
RQLQ	Activities	0.70	0.67
	Sleep	0.83	0.79
	Non-rhinitis symptom	0.88	0.90
	Practical problems	0.80	0.77
	Nasal symptom	0.79	0.78
	Eye symptoms	0.89	0.83
	Emotion	0.87	0.88
	Summary score	0.95	0.88
SF-36	Physical functioning	0.73	0.80
	Role-physical	0.87	0.77
	Bodily pain	0.86	0.91
	General health	0.88	0.95
	Vitality	0.80	0.88
	Social functioning	0.67	0.68
	Role-emotional	0.67	0.83
	Mental health	ND	0.80

RQLQ, Rhinoconjunctivitis Quality-of-Life Questionnaire; SF-36, Medical Outcome Short-Form 36.

domains of activity in the RQLQ and social functioning in the SF-36 had the lowest test–retest reliability.

Responsiveness to change We used five evaluative instruments in this study to assess this property of the RQLQ and SF-36 assessed at weeks 4 and 8 (Tables 6a and b, respectively) [40, 44]. The five did not produce consistent ranking of domain sensitivity. Compared with baseline, 10 patients improved at week 4 and 14 improved by week 8. Only seven of those who improved at week 4 remained so at week 8.

By 4 weeks, all the domains of the RQLQ registered a change in the patients who improved, verifying that it is sensitive enough to be used as an evaluative instrument in routine work and clinical trials. The 'activities' domain is one of the most sensitive, justifying the belief that the patients' ability to perform their own chosen activities best reflects their health status.

On the other hand, only two domains of the SF-36 (role-physical and vitality) recorded a change in this time frame. After 8 weeks, three more domains of the SF-36 (general health, role-emotional and mental health) showed a response in patients who improved. All the evaluative statistics show

that the scores of the RQLQ changed to a greater extent in improved patients compared with the SF-36. Significantly, the sensitivity of the SF-36 improves as the interval between assessments was extended.

Therefore, the RQLQ was superior to the SF-36 in detecting change in QOL of AR in three ways: more of its domains reflect that the HRQL has improved, their magnitude of change was greater, and its response was faster.

Combined use of Rhinoconjunctivitis Quality-of-Life Questionnaire and Medical Outcome Short-Form 36 in persistent allergic rhinitis

There are a few obvious differences between the RQLQ and the SF-36. The RQLQ probes for the symptoms closely associated with rhinitis (in the past 1 week) while the SF-36 interrogates for the secondary effects of the disease on the QOL (in the past 4 weeks in the version we used).

Factor analysis We analysed all the items of the SF-36 and RQLQ simultaneously (Table 7). They resolved into 17 components, almost none of which contained items from both questionnaires, indicating that each instrument addresses distinct and different aspects of the QOL. The first two components, with the highest variance, belong to the RQLQ. Together, they account for 86.1% of the total variance, 54% of which is contributed by the RQLQ and 46% by the SF-36. Therefore, a comprehensive measure of the HRQL in persistent AR is obtained only by using data from both questionnaires collected concurrently.

The 10 components of the SF-36 roughly corresponded to the domains except the items in Physical Function. The items of the 'sleep', 'practical problems' and 'eye symptoms' in the RQLQ fell into the same component. Otherwise, the components were quite consistent with the original domains of the RQLQ. The distribution of items in the eighth component demonstrates that the questions on 'fatigue', 'reduced productivity', 'tiredness' and 'worn out' are internally correlated and would be candidates for elimination in scale shortening [16, 45].

Correlation matrix To understand the inter-relationship of the questionnaires, we compared the correlation of their items with each other as well as with the symptom scores (Table 8). There was only weak correlation between the SF-36 and the

RQLQ, similar to the impression gathered from factor analysis. Nonetheless, there was some correlation between the general health domain (SF-36) with the RQLQ domains of non-rhinitis symptoms, practical problems and eye symptoms; role-emotional (SF-36) with eye symptoms (RQLQ); and vitality (SF-36) with non-rhinitis symptoms domain (RQLQ). The eye-symptom domain of the RQLQ correlated with the eye-symptom VAS, and the nasal-problem domain (RQLQ) with the sneezing VAS and runny nose VAS. There was no correlation between any domain in the SF-36 with any rhinoconjunctivitis symptom. Significantly, the emotion domain in the SF-36 clearly measured a different property from the same-named domain in RQLQ.

Discussion

We studied the validity of the RQLQ and SF-36 when they are used in the assessment of HRQL of patients with persistent AR treated with standard treatment in the outpatient clinic.

A fundamental quality of HRQL instruments, the discriminative property, has been demonstrated for the RQLQ and SF-36 in AR in this and previous studies [5, 25, 26]. The test-retest reliability of the questionnaires was reasonable, though the self-nominated activities of the RQLQ was poor in this respect. One simple way to improve test-retest reliability is to let patients see their previous responses [46].

If HRQL is to be used as an outcome measure in a clinical trial, the QOL instruments to assess it must be sufficiently responsive. There had been some controversy whether the RQLQ is a sufficiently sensitive instrument [8, 13]. Here, we showed that the RQLQ is more sensitive than the SF-36, consistent with the general finding that disease-specific measures are more sensitive than generic ones [47]. We identified the domains of the SF-36 that perform poorly and showed that this was because of their low signal-to-noise ratio (because of the wide variance). These findings are similar to those in a study of 39 patients with seasonal AR treated with topical budesonide. In that study, four out of five domains of the RQLQ registered a change (the emotion domain did not change significantly, while the activities and eye-symptom

Table 6a. Responsiveness (early) of the SF-36 and RQLQ (difference between first and second interviews)

Instrument	Domains	Patients	Liang's relative efficacy	Deyo's ROC curve	Liang's standardized response mean	Kazis' effect size	Guyatt's responsiveness statistic
SF-36	Physical functioning	Improved (10)	0.00	0.53	-0.06	-0.07	-0.06
		Unchanged (32)			0.21	0.24	0.224
	Role-physical	Improved	0.20	0.57	0.60	0.53	0.55
		Unchanged			0.39	0.35	0.36
	Bodily pain	Improved	0.02	0.38	-0.22	-0.21	-0.33
		Unchanged			0.42	0.42	0.66
	General health	Improved	0.07	0.56	0.39	0.23	0.47
		Unchanged			0.25	0.14	0.30
	Vitality	Improved	0.10	0.60	0.53	0.45	0.49
		Unchanged			0.17	0.14	0.15
	Social functioning	Improved	0.06	0.46	0.25	0.21	0.18
		Unchanged			0.54	0.45	0.40
	Role-emotional	Improved	0.12	0.55	0.39	0.37	0.45
		Unchanged			0.22	0.21	0.25
	Mental health	Improved	0.03	0.58	0.26	0.24	0.21
		Unchanged			0.02	0.02	0.01
RQLQ	Activities	Improved	0.88	0.77	1.82	2.32	1.50
		Unchanged			0.69	0.88	0.57
	Sleep	Improved	0.29	0.66	1.06	1.14	1.23
		Unchanged			0.21	0.22	0.24
	Non-rhinitis symptom	Improved	0.35	0.60	1.03	0.99	1.30
		Unchanged			0.70	0.68	0.88
	Practical problems	Improved	0.45	0.70	1.25	1.42	1.38
		Unchanged			0.46	0.52	0.50
	Nasal symptom	Improved	1	0.81	1.77	2.21	1.84
		Unchanged			0.59	0.73	0.61
	Eye symptoms	Improved	0.05	0.47	0.46	0.43	0.66
		Unchanged			0.26	0.24	0.37
	Emotion	Improved	0.62	0.67	1.37	1.22	1.50
		Unchanged			0.85	0.76	0.93
	Summary	Improved	0.58	0.70	1.52	1.60	1.80
		Unchanged			0.67	0.71	0.80

Liang's standardized response mean, Kazis' effect size and Guyatt's responsiveness statistic are calculated both for improved and unchanged patients, while Liang's relative efficacy and Deyo's ROC curve are composite scores derived from both groups. The domain of nasal symptoms of the RQLQ was used as the comparator in calculating Liang's relative efficacy.

RQLQ, Rhinoconjunctivitis Quality-of-Life Questionnaire; SF-36, Medical Outcome Short-Form 36.

Table 6b. Responsiveness (net) of the SF-36 and RQLQ (difference between first and third interviews)

Instrument	Domains	Patients	Liang's relative efficacy	Deyo's ROC curve	Liang's standardized response mean	Kazis' effect size	Guyatt's responsiveness statistic
SF-36	Physical functioning	Improved (14)	0.02	0.40	0.21	0.20	0.18
		Unchanged (39)			0.41	0.38	0.35
	Role-physical	Improved	0.09	0.54	0.57	0.59	0.61
		Unchanged			0.37	0.39	0.40
	Bodily pain	Improved	0.01	0.64	0.16	0.14	0.22
		Unchanged			-0.11	-0.09	-0.15
	General health	Improved	0.41	0.71	0.68	0.51	1.08
		Unchanged			-0.04	-0.03	-0.06
	Vitality	Improved	0.08	0.60	0.37	0.46	0.51
		Unchanged			0.03	0.04	0.04
	Social functioning	Improved	0.07	0.46	0.42	0.40	0.36
		Unchanged			0.50	0.48	0.42
	Role-emotional	Improved	0.08	0.58	0.46	0.63	0.77
		Unchanged			0.19	0.25	0.31
	Mental health	Improved	0.32	0.64	0.64	0.68	0.59
		Unchanged			0.28	0.30	0.26
RQLQ	Activities	Improved	1.04	0.87	1.62	2.77	1.78
		Unchanged			0.39	0.67	0.43
	Sleep	Improved	0.29	0.78	1.10	1.42	1.52
		Unchanged			0.02	0.02	0.02
	Non-rhinitis symptom	Improved	0.28	0.73	1.04	1.34	1.75
		Unchanged			0.30	0.38	0.50
	Practical problems	Improved	0.42	0.76	1.37	1.59	1.54
		Unchanged			0.31	0.36	0.35
	Nasal symptom	Improved	1.00	0.85	1.58	2.28	1.90
		Unchanged			0.39	0.57	0.47
	Eye symptoms	Improved	0.07	0.54	0.71	0.67	1.03
		Unchanged			0.21	0.19	0.30
	Emotion	Improved	0.38	0.70	1.30	1.31	1.60
		Unchanged			0.65	0.65	0.80
	Summary	Improved	0.49	0.79	1.48	1.89	2.13
		Unchanged			0.38	0.49	0.55

The domain of nasal symptoms of the RQLQ was used as the comparator in calculating Liang's relative efficacy.

RQLQ, Rhinoconjunctivitis Quality-of-Life Questionnaire; SF-36, Medical Outcome Short-Form 36.

domains were omitted) compared with five out of eight SF-36 items. Also, the scores in the RQLQ varied to a larger extent than those in the SF-36 [20].

Remarkably, in this study, we also showed that the evaluative property of these instruments may improve over time. The existence of this variation has been postulated but has not been observed until now [47]. The reason for this is unclear but could include actual improvement in clinical status or patient's increasing familiarity with the instrument. The domains that do not change with improvement in the patient's status could also represent those areas in the QOL that are resistant to therapy.

The floor-and-ceiling effect was a major problem with the SF-36 when applied to AR. Even though this is less of a problem for the RQLQ, Rasch analysis showed that the items in both questionnaires do not match well our patients' capabilities as 23 of 43 patients demonstrated logit measures above the instruments' range.

Using factor analysis and the correlation matrix, we showed that the disease-specific and the general health instrument each covered a different half the total measurable HRQL. This was also demonstrated, using a different

technique, in a study of QOL of knee pain [48]. Therefore, using the RQLQ and the SF-36 in combination affords a more comprehensive picture of the QOL in rhinitis and ameliorates the ceiling/floor limitations when only one questionnaire is used. Using them together enables the former to act as a safeguard that the impact on QOL stems from rhinitis and not other conditions, and the SF-36 allows comparison of QOL among different diseases [26].

There are a few shortcomings in this study. The responsiveness of the SF-36 could have been improved if the 4-week recall rather than 1-week recall version of the instrument was used. Our data, which was obtained through interviews, may not be comparable with that derived from self-administered questionnaires. The design of this study does not allow us to derive the minimal clinically important difference of either questionnaire.

We may hereby define the roles of the SF-36 and RQLQ in the assessment of HRQL in persistent AR. The RQLQ is useful for detecting early and small changes in the HRQL, while the SF-36 adds supplementary QOL data indirectly related to rhinitis and allows comparison with other diseases. Both of them contribute significant and non-overlapping information on the total measurable HRQL.

Table 7. Factor analysis performed with all the items of the RQLQ and SF-36

Factor	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Activities (a)													0.518				
Activities (b)													0.791				
Activities (c)															0.767		
Sleep (a)	0.755																
Sleep (b)	0.763																
Sleep (c)	0.730																
Non-rhinitis symptom (a)	0.537							0.559									
Non-rhinitis symptom (b)								0.822									
Non-rhinitis symptom (c)																	
Non-rhinitis symptom (d)								0.538									
Non-rhinitis symptom (e)		0.698															
Non-rhinitis symptom (f)			-0.713														
Non-rhinitis symptom (g)																	
Practical problems (a)											-0.546						
Practical problems (b)	0.604																
Practical problems (c)		0.667															
Nasal symptoms (a)		0.697															
Nasal symptoms (b)		0.762															
Nasal symptoms (c)		0.788															
Nasal symptoms (d)		0.547															
Eye symptoms (a)	0.612																
Eye symptoms (b)	0.624																
Eye symptoms (c)	0.649																
Eye symptoms (d)	0.819																
Emotional (a)																	
Emotional (b)		0.548															
Emotional (c)		0.726															
Emotional (d)																0.623	
Physical functioning (1)										0.808							
Physical functioning (2)									0.839								
Physical functioning (3)									0.735								
Physical functioning (4)																	0.513
Physical functioning (5)												0.822					
Physical functioning (6)																	
Physical functioning (7)																	
Physical functioning (8)						0.817											
Physical functioning (9)						0.856											
Physical functioning (10)						0.553											
Role-physical (1)					0.688												
Role-physical (2)					0.758												
Role-physical (3)					0.853												
Role-physical (4)					0.681												
Bodily pain (1)						0.552						0.522					
Bodily pain (2)												0.740					
General health (1)			0.729														
General health (2)			0.742														
General health (3)			0.826														
General health (4)																	
General health (5)			0.779														
Vitality (1)							0.530										
Vitality (2)																	
Vitality (3)																	0.672
Vitality (4)										0.569							
Social functioning (1)				0.766													
Social functioning (2)																	
Role-emotional (1)				0.750													
Role-emotional (2)				0.754													
Role-emotional (3)				0.720													
Mental health (1)																	
Mental health (2)							0.692										
Mental health (3)							0.577										

Table 7. (Contd.)

Factor	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Mental health (4)								0.820									
Mental health (5)																	
Health transition														0.713			
Variance (%)	28.49	9.66	6.43	6.07	5.25	4.29	3.62	3.19	2.92	2.93	2.42	2.11	1.99	1.86	1.78	1.69	1.62
Cumulative variance	28.49	38.15	44.58	50.65	55.89	60.18	63.80	66.99	69.91	72.64	75.06	77.17	79.16	81.02	82.79	84.48	86.10

The distribution of items in the factors do not overlap, indicating that the two questionnaires address distinct aspects of the quality of life.

RQLQ, Rhinoconjunctivitis Quality-of-Life Questionnaire; SF-36, Medical Outcome Short-Form 36.

Table 8. Correlation matrix of RQLQ, SF-36 and symptom scores in persistent allergic rhinitis

Instrument	Domains	RQLQ							Symptom scores				
		Activities	Sleep	Non-rhinitis symptom	Practical problems	Nasal symptom	Eye symptoms	Emotion	Sneezing	Nose itch	Blocked nose	Runny nose	Eye symptoms
SF-36	Physical functioning	-0.11	0.09	0.26	0.12	0.02	0.16	0.00	0.11	-0.12	-0.28	-0.03	0.06
	Role-physical	0.22	0.28	0.31	0.39	0.23	0.45	0.36	0.34	0.20	0.28	0.18	0.33
	Bodily pain	0.16	0.16	0.43	0.45	0.25	0.33	0.30	0.17	0.04	0.03	-0.05	-0.03
	General health	0.34	0.39	0.62	0.56	0.28	0.50	0.40	0.02	0.18	0.07	-0.04	0.15
	Vitality	0.36	0.25	0.53	0.37	0.30	0.37	0.44	0.14	0.10	0.13	0.09	0.17
	Social functioning	0.10	0.13	0.46	0.33	0.24	0.40	0.47	0.32	0.21	-0.03	0.28	0.31
	Role-emotional	0.09	0.23	0.40	0.34	0.18	0.52	0.37	0.16	0.12	-0.03	0.18	0.49
	Mental health	0.16	0.08	0.36	0.12	0.25	0.14	0.23	0.13	0.01	-0.07	0.12	0.12
Symptom scores	Sneezing	0.20	0.27	0.17	0.32	0.52	0.36	0.36					
	Nose itch	0.16	0.08	0.06	0.12	-0.03	0.14	0.25					
	Blocked nose	0.41	0.37	0.15	0.32	0.39	0.39	0.47					
	Runny nose	0.06	0.31	0.16	0.27	0.57	0.18	0.35					
	Eye symptoms	0.29	0.40	0.33	0.29	-0.05	0.68	0.27					

RQLQ, Rhinoconjunctivitis Quality-of-Life Questionnaire; SF-36, Medical Outcome Short-Form 36.

Conclusions

Both the RQLQ and SF-36 can be used to assess the quality of life of patients with persistent AR. They discriminate between patients and controls, they are sensitive to change in the symptoms, they show internal consistency and they have reasonable test-retest reliability.

The SF-36 is less sensitive to change than the RQLQ. It also has lower test-retest reliability and was more prone to floor and ceiling effects. Because of the ceiling effect, the SF-36 is not suitable for patients with minimal symptoms. Each instrument measures non-overlapping aspects of the HRQL. The SF-36 allows comparison of QOL of rhinitis patients with that of sufferers of other diseases.

By using both questionnaires together, we exploit the strengths of each instrument and thereby obtain a complete, responsive and portable assessment of the QOL in persistent AR.

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