

A questionnaire to measure quality of life in adults with nocturnal allergic rhinoconjunctivitis

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Background: Many patients with rhinoconjunctivitis experience symptoms at night and these interfere with getting a good night's sleep.

Objective: The aim of this study was to develop the Nocturnal Rhinoconjunctivitis Quality of Life Questionnaire (NRQLQ) to measure the functional problems that are most troublesome to patients with nocturnal allergic rhinoconjunctivitis (NAR).

Methods: After generating a list of 256 potentially important items, 132 patients with NAR identified the items that were most troublesome. The top scoring 16 items are included in the NRQLQ in four domains (sleep problems, symptoms during sleep time, symptoms on waking and practical problems). The NRQLQ asks patients to recall their experiences during the previous week and score each item on a 7-point scale.

Results: One hundred and six patients with NAR participated in a 3 week validation study. This showed the NRQLQ to have good reliability (ICC = 0.87) and responsiveness (responsiveness index = 0.93). For both cross-sectional and longitudinal construct validity correlations between the NRQLQ and other measures of health status were close to a priori predictions.

Conclusions: The NRQLQ has strong evaluative and discriminative measurement properties and can be used with confidence in both clinical practice and clinical trials to measure the functional impairments that are most troublesome to patients with nocturnal allergic rhinoconjunctivitis. (*J Allergy Clin Immunol* 2003;111:484-90.)

Key words: Quality of life, rhinitis, rhinoconjunctivitis, nocturnal, questionnaire, measurement, health status

Most clinicians now recognize the importance of incorporating an assessment of health-related quality of life (HRQL) into their clinical studies and clinical practice. Conventional measures of disease severity provide valuable information about the status of the organ system, but they tell very little about the functional impair-

Abbreviations used

AQLQ:	Asthma Quality of Life Questionnaire
HRQL:	Health-related quality of life
ICC:	Intraclass correlation coefficient
MOSSM:	Medical Outcomes Study Sleep Module
NAR:	Nocturnal allergic rhinoconjunctivitis
NRQLQ:	Nocturnal Rhinoconjunctivitis Quality of Life Questionnaire
PRQLQ:	Paediatric Rhinoconjunctivitis Quality of Life Questionnaire
RQLQ:	Rhinoconjunctivitis Quality of Life Questionnaire
RQLQ(S):	Standardized version of the Rhinoconjunctivitis Quality of Life Questionnaire
SF-36:	Medical Outcomes Survey Short Form 36

ments (physical, emotional, occupational, and social) that are important to patients in their everyday lives. Patients with rhinoconjunctivitis are bothered by their symptoms, but the overall impact of rhinoconjunctivitis on their day-to-day lives cannot be estimated from the severity of these symptoms.¹⁻³ Therefore, both for clinical practice and for research, it is important to have valid instruments that evaluate the overall impact of the rhinoconjunctivitis on patients' day-to-day lives.

In patients with allergic rhinitis, the severity of sneezing, blocked nose, and rhinorrhea tends to peak during the night and in the early morning.⁴ This is worse in some patients than others, and there has been a concern that the resultant impairments to HRQL might be different in these patients compared with patients whose problems are mainly during the day. In addition, patients whose HRQL impairment is associated with these nocturnal symptoms might require a treatment plan that specifically addresses these problems.

In this study, we evaluated the HRQL problems of patients with nocturnal allergic rhinoconjunctivitis (NAR) and developed a disease-specific, quality of life questionnaire to measure these impairments, the Nocturnal Rhinoconjunctivitis Quality of Life Questionnaire (NRQLQ). The methods we have used are those used to develop and validate more than a dozen disease-specific quality of life questionnaires,⁵ including the Rhinoconjunctivitis Quality of Life Questionnaire² and the Paediatric Rhinoconjunctivitis Quality of Life Questionnaire.⁶

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QUESTIONNAIRE DEVELOPMENT

Specifications

We identified the construct (concept) that we wished to measure and the measurement characteristics required of the NRQLQ:

1. Include all problems that are most important to adults with predominantly NAR with related sleep interruptions.
2. Summary scores for each domain should be amenable to statistical analysis.
3. Reliable (ie, gives reproducible results in patients who are stable and able to discriminate between patients of different levels of impairment).
4. Responsive (ie, sensitive to clinically important changes even if the changes are small).
5. Valid (ie, measures the functional impairments associated with nocturnal allergic rhinoconjunctivitis).
6. In both interviewer and self-administered formats.
7. Short and easily understood by patients.

Item generation phase

The first step was to develop a list of the functional impairments of patients with NAR. We used a range of resources, which included focus group discussions with patients, a review of the literature and other HRQL instruments, discussions with clinicians who look after adults with rhinoconjunctivitis, and our previous experience in developing HRQL instruments. Two hundred fifty-seven potentially important items were identified.

Item reduction phase

One hundred three adults with NAR were asked to identify which of the 257 items they had experienced as a result of their rhinoconjunctivitis and to score each positively identified item for importance (1 = not very important, 4 = very important). The 16 items that were identified most frequently and that scored the highest in importance were included in the NRQLQ (Fig 1). None of these 16 items had item-item correlations greater than $r = 0.8$ (ie, they were not synonyms of the same problem). The items were placed in 4 domains according to clinical sensibility^{7,8}: problems with sleep (4 items), symptoms during sleep time (5 items), symptoms on waking in the morning (4 items), and practical problems (3 items). In the NRQLQ, patients are asked to recall their experiences during the previous week and to respond to each item on a 7-point scale (0 = no impairment; 6 = maximum impairment). The self-administered version of the NRQLQ was tested in 10 patients with current symptoms of NAR to check for ease and accuracy of understanding.

VALIDATION STUDY

Testing the measurement properties

HRQL measurement instruments might have one or more purposes. A discriminative instrument is designed to distinguish between people at a single point in time. For instance, we may wish to differentiate between

patients with mild, moderate, and severe impairment of quality of life as the result of their NAR so that patients with more severe impairment can be enrolled in a clinical trial. Discriminative instruments require good reliability (high ratio of variance between patients to variance within patients) and cross-sectional construct validity (appropriate correlations between established rating scales and the instrument being tested).⁹

An evaluative instrument is designed to measure longitudinal change in an individual or group of patients. For instance, we might wish to determine whether a group of patients with NAR receiving an experimental intervention improves more than a group of patients receiving a control treatment. Evaluative instruments require good responsiveness (the ability to detect important within-patient changes, even if they are small) and longitudinal construct validity (appropriate correlations between changes in the new questionnaire and changes in other measures of health status).⁷

METHODS

Subjects

One hundred fifteen adults 18 years of age or older were enrolled from 4 clinics in the United States. All patients were required to have current symptoms of NAR with impaired sleep quality. Symptoms were required to be sufficiently troublesome to require additional medication and to score 1.0 or more in the symptom domain of the Standardized Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ(S)) (0 = no impairment, 6 = maximum impairment).¹⁰ Patients were not permitted to have nasal or sinus infections requiring treatment with antibiotics or to have any illness, other than rhinoconjunctivitis, that had an effect on HRQL. They were required to understand the study instructions and to be able to complete a daily symptom diary. All patients signed an informed consent. The study was approved by a central institutional review board.

Study design

The study was a 3-week, unblinded, observational study with subjects assessed in the clinic at baseline and after 1 and 3 weeks. The NRQLQ, the RQLQ(S),¹⁰ the Medical Outcomes Study Sleep Module (MOSSM),¹¹ and the Medical Outcomes Survey Short Form 36 (SF-36)¹² were completed at each visit. For 1 week before each follow-up visit, patients recorded rhinoconjunctivitis symptoms in a diary.

Treatment

At enrollment, patients were not taking any medication for their NAR and were asked to tolerate 1 week without any additional medications so that we could make an estimate of the reliability (reproducibility) of the instrument while the patients were in a stable clinical state. Those who refused were permitted to increase their usual rhinoconjunctivitis medication as prescribed by their clinician. After 1 week, all patients were given additional triamcinolone acetonide aqueous nasal spray (Nasacort AQ, Aventis Pharmaceuticals) to be taken as two sprays (55 µg/spray) in each nostril once per day for 2 weeks (ie, until the end of the study). Patients could supplement this treatment with their own rhinoconjunctivitis medications if relief was not obtained with triamcinolone.

Outcome measures

Nocturnal Rhinoconjunctivitis Quality of Life Questionnaire. The self-administered version of this questionnaire was the first questionnaire completed by all patients at every clinic visit (Fig 1).

**NOCTURNAL RHINOCONJUNCTIVITIS
QUALITY OF LIFE QUESTIONNAIRE©
SELF-ADMINISTERED**PATIENT ID: _____
DATE: _____

Page 1 of 2

Please complete all questions by circling the number that best describes how **troubled** you have been during the last week as a result of your nose/eye symptoms?

	Not troubled	Hardly troubled at all	Some- what troubled	Mod- erately troubled	Quite a bit troubled	Very Troubled	Extremely troubled
SLEEP PROBLEMS							
1. Difficulty getting to sleep	0	1	2	3	4	5	6
2. Unable to get a good night's sleep or wake up during the night	0	1	2	3	4	5	6
3. Restless (tossing and turning)	0	1	2	3	4	5	6
4. Having to get up because of stuffy nose or to blow nose	0	1	2	3	4	5	6
SLEEP TIME PROBLEMS							
5. Nasal congestion or stuffy nose	0	1	2	3	4	5	6
6. Sinus pressure or pain	0	1	2	3	4	5	6
7. Runny nose	0	1	2	3	4	5	6
8. Post-nasal drip (drainage down back of nose/throat)	0	1	2	3	4	5	6
9. Headache	0	1	2	3	4	5	6

FIG 1. Nocturnal rhinoconjunctivitis quality of life questionnaire. Figure continued on following page.

**NOCTURNAL RHINCONJUNCTIVITIS
QUALITY OF LIFE QUESTIONNAIRE
SELF-ADMINISTERED**

PATIENT ID: _____
DATE: _____

Page 2 of 2

How troubled have you been during the last week as a result of your nose/eye symptoms?

Not troubled	Hardly troubled at all	Some- what troubled	Mod- erately troubled	Quite a bit troubled	Very Troubled	Extremely troubled
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SYMPTOMS ON WAKING IN THE MORNING
(during the first hour after waking)

10. Feel tired and unrefreshed	0	1	2	3	4	5	6
11. Nasal congestion or stuffy nose	0	1	2	3	4	5	6
12. Congestion in sinuses	0	1	2	3	4	5	6
13. Takes time to clear nighttime drainage after waking up	0	1	2	3	4	5	6

PRACTICAL PROBLEMS

(during waking hours)

14. Have to avoid symptom triggers (such as dust, cigarette smoke, strong smells and perfumes)	0	1	2	3	4	5	6
15. Need to rub nose or eyes	0	1	2	3	4	5	6
16. Have to take medication	0	1	2	3	4	5	6

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FIG 1. Continued.

Asthma, rhinitis,
other respiratory
diseases

TABLE I. Patient baseline demographics

Characteristic	
Number	106
Sex (M/F)	37/69
Age (mean: SD)	35.6: 11.7
NRQLQ overall score (mean: SD)	3.17: 1.07
RQLQ overall score (mean: SD)	2.8: 1.10
Symptom diary overall score (mean: SD)	1.91: 1.01

Standardized Rhinoconjunctivitis Quality of Life Questionnaire.

This self-administered questionnaire was developed to measure the functional impairments that are most troublesome to adults with rhinoconjunctivitis irrespective of whether it is predominantly troublesome during the day or at night. There are 28 questions in domains: activity limitation (3 items), sleep problems (3 items), non-nasal/eye symptoms (7 items), practical problems (3 items), nasal symptoms (4 items), eye symptoms (4 items), and emotional function (4 items).

The Medical Outcomes Study Sleep Module. This validated questionnaire¹¹ contains 12 items that assess the following constructs of sleep function: initiation (2 items), maintenance (2 items), respiratory problems (2 items), quality (1 item), perceived adequacy (1 item), and somnolence (3 items).

Medical Outcomes Study Short Form 36. This is a generic health profile,¹² which provides summary scores in two domains, physical health and mental health. It has been well validated for use in patients with rhinitis.³

Symptom Diary. For 1 week before each follow-up clinic visit, patients completed a diary of their symptoms.¹³ Each morning and each evening they scored the severity (0 = nil, 1 = mild, 2 = moderate, 3 = severe) and frequency (0 = nil, 1 = a few short episodes, 2 = frequent episodes, 3 = continuous) of sneezing, stuffy nose, runny nose, itchy nose, and eye symptoms. Results are expressed as mean scores for nose and eye symptoms (0 = asymptomatic, 3 = very symptomatic).

Statistical analysis

Discriminative properties. Reliability of the NRQLQ was determined from patients who remained in a stable clinical state between the baseline visit and the end of the first week. Classification of stability was based on whether patients had changed by <0.5 (the minimal important difference) on the overall score of the RQLQ(S). Reproducibility was expressed as the within-subject variance. Reliability was expressed as an intraclass correlation coefficient (ICC), which is the ratio of the between-subject variance to the total variance.

Cross-sectional construct validity was evaluated by correlating NRQLQ scores with the scores from the other measures of health status. Before the analysis, a group of clinicians made a priori predictions concerning the level of correlation that should be expected between the NRQLQ and these other health status measures if the NRQLQ is truly measuring NAR-specific quality of life.

Evaluative properties

Responsiveness of the NRQLQ was assessed in three ways. First, we determined the ability of the questionnaire to detect within-subject changes in patients whose clinical status changed between weeks 1 and 3 (Δ overall RQLQ(S) ≥ 0.5) by using a paired *t* test. Second, we examined the ability of the questionnaire to distinguish between patients who remained stable between weeks 1 and 3 (Δ overall RQLQ(S) < 0.5) and those who changed (Δ overall RQLQ(S) ≥ 0.5) by using an unpaired *t* test. Third, we calculated the responsiveness index of questionnaire (Δ /sd Δ).¹⁴ Longitudinal construct validity was evaluated by correlating change in each domain of the NRQLQ with change in other measures of health sta-

tus. Like the cross-sectional correlations, a priori predictions were made for the expected longitudinal correlations.

RESULTS

The characteristics of the 106 patients who completed the study and were included in the analysis are shown in Table I.

Eighty patients were in a stable clinical state between weeks 0 and 1 (Δ overall RQLQ(S) $< \pm 0.5$) and provided data for the reliability analysis. The ICC for the overall score was 0.87, with slightly lower values for each of the domains (0.74 to 0.83) (Table II). Cross-sectional correlations between the NRQLQ and other measures of health status were close to the a priori predictions (Table III).

Seventy-seven patients showed clinically important improvements or deteriorations in their health status between weeks 1 and 3 (Δ overall RQLQ(S) $\geq \pm 0.5$), whereas the other 29 patients remained clinically stable (Δ overall RQLQ(S) $< \pm 0.5$). In the patients who changed, the NRQLQ was able to detect changes both in overall score and in each domain with a high degree of significance (Table IV). Similarly, the NRQLQ was able to detect the difference between these two groups of patients (Table IV). The responsiveness index for the overall NRQLQ was 0.93. Correlations between change in NRQLQ scores between weeks 1 and 3 and change in other measures of health status were close to the a priori predictions in Table V.

DISCUSSION

This study has identified the functional impairments that are most troublesome to patients with allergic rhinoconjunctivitis who have problematic nocturnal symptoms with sleep disturbance. As might be expected, patients identified that they had most of their HRQL impairments during the night and early morning. These included troublesome local symptoms such as stuffy nose and sinus congestion as well as systemic symptoms such as headache. In addition, these patients had a wide range of sleep-associated problems. Only 3 daytime problems were considered sufficiently troublesome to be included in the final NRQLQ. This is in contrast to the less circadian-focused patients, who as well as not being able to sleep well at night are also bothered by daytime symptoms, limited daily activities (physical, social, and occupational), poor concentration, reduced productivity, and emotional problems such as irritability and frustration.²

There is no evidence to suggest that patients with NAR have a condition different from those whose rhinoconjunctivitis is more troublesome during the day. Therefore, the reason why some patients should be particularly bothered at night is not clear. It may be that some patients are very sound sleepers and have minimal problems getting to sleep and staying asleep even when their symptoms are severe. In contrast, light sleepers may be much more bothered during the night and less able to cope in the early morning. Alternatively, it may be that different types of nasal symptoms are more likely to interfere with sleep. For

TABLE II. Reliability (n = 80), weeks 0 to 1

Instrument	Domain	Within-subject variance	Between-subject variance	ICC*
NRQLQ	Overall	0.19	1.29	0.87
	Problems with sleep	0.34	1.62	0.79
	Symptoms during sleep time	0.30	1.48	0.81
	Symptoms on waking in the morning	0.36	1.98	0.83
	Practical problems	0.56	1.96	

*0.74

TABLE III. Cross-sectional validity (Pearson correlation coefficients) (n = 106), week 1

Instrument	Domain	NRQLQ			
		Sleep	Symptoms during sleep	Symptoms on waking	Practical problems
RQLQ(S)	Overall	0.76	0.82	0.77	0.71
	Activity limitation	0.57	0.63*	0.66*	0.59**
	Sleep disturbance	0.91***	0.70	0.64	0.55
	Non-nasal/eye symptoms	0.64*	0.67**	0.62**	0.57
	Practical problems	0.51	0.60	0.63*	0.64***
	Nasal symptoms	0.59	0.80**	0.79**	0.61
	Eye symptoms	0.46	0.59**	0.48**	0.51
	Emotional function	0.59*	0.61	0.56	0.55*
Diary	Nasal symptoms AM	0.39	0.56***	0.49***	0.29*
	Eye symptoms AM	0.36	0.38	0.34***	0.21
	All symptoms AM	0.40	0.50***	0.46***	0.27*
	Nose symptoms PM	0.44	0.54	0.46*	0.31*
	Eye symptoms PM	0.42	0.42	0.31	0.27
	All symptoms PM	0.47	0.52*	0.42**	0.31*
	Overall	-0.68***	-0.54	-0.50	-0.52
MOSSM	Overall	-0.68***	-0.54	-0.50	-0.52
SF-36	Physical function	-0.06	-0.11	-0.09*	-0.04
	Mental function	-0.06*	-0.01	0.03	-0.06

A priori predictions of Pearson correlation coefficients (if no asterisk, then no prediction was made): *0 < r < 0.4; **0.4 < r < 0.6; ***r > 0.6.

TABLE IV. Responsiveness—mean change in score between weeks 1 and 3

Domain	Stable patients* Mean (SD) (n = 29)	Patients who changed Mean (SD) (n = 77)	Difference (P value)†
Overall	-0.19 (0.64)	1.60 (0.96)‡	<.0001
Problems with sleep	-0.21 (0.79)	1.45 (1.07)‡	<.0001
Symptoms during sleep time	-0.07 (0.78)	1.55 (1.09)‡	<.0001
Symptoms on waking in the morning	-0.23 (1.08)	1.93 (1.22)‡	<.0001
Practical problems	-0.21 (0.89)	1.66 (1.25)‡	<.0001

*Stable is defined as a change of -0.5 to 0.5 on the Overall RQLQ(S) between weeks 1 and 3.

†Unpaired t test.

‡P < .01.

instance, nasal stuffiness, blockage, and congestion as well as rhinorrhea were troublesome to these patients and interfered with sleep, whereas itchiness or sneezing appeared much less important. Furthermore, the acute early phase allergic reactions, which result mainly in sneezing, itchiness, and runny nose after exposure to pollen and animal dander during the day, may be followed at night by the late-phase problems of persistent inflammation (stuffiness, blockage, and congestion). Thus, there may be real subsets of patients with allergic rhinoconjunctivitis who vary in

their HRQL impairments according to whether they have predominantly early or late-phase allergic reactions.

Categorizing patients into “stayed the same” or “changed” is always a difficult methodologic problem. The categorizing instrument needs to be valid and to measure a construct similar to the one being measured by the new instrument and to have a moderate to strong correlation with the new instrument. In the past, we have used transition ratings.^{2,5} However, recent research has shown that these ratings can be inaccurate because patient

TABLE V. Longitudinal validity (Pearson correlation coefficients) (n = 106), weeks 1-3

Instrument	Domain	NRQLQ			
		ΔSleep	ΔSymptoms during sleep	ΔSymptoms on waking	ΔPractical problems
RQLQ(S)	ΔOverall	0.68	0.77	0.72	0.68
	ΔActivity limitation	0.40	0.57*	0.51*	0.48**
	ΔSleep disturbance	0.71***	0.64	0.63	0.56
	ΔNon-nasal/eye symptoms	0.60*	0.53**	0.56**	0.47
	ΔPractical problems	0.52	0.64	0.61*	0.61***
	ΔNasal symptoms	0.54	0.77**	0.64**	0.60
	ΔEye symptoms	0.44	0.55**	0.45**	0.52
	ΔEmotional function	0.48*	0.57	0.54	0.53*
Diary	ΔNasal symptoms AM	0.27	0.45***	0.46***	0.23*
	ΔEye symptoms AM	0.31	0.33	0.35***	0.15
	ΔAll symptoms AM	0.32	0.44***	0.46***	0.21*
	ΔNose symptoms PM	0.48	0.55	0.48*	0.38*
	ΔEye symptoms PM	0.38	0.36	0.27	0.22
	ΔAll symptoms PM	0.51	0.54	0.45**	0.36*
MOSSM	ΔOverall	-0.63***	-0.46	-0.48	-0.48
SF-36	ΔPhysical function	0.04	-0.10	0.01*	-0.12
	ΔMental function	-0.04*	0.06	-0.05	0.02

A priori predictions of Pearson correlation coefficients (if no asterisk, then no prediction was made): * $0 < r < 0.4$; ** $0.4 < r < 0.6$; *** $r > 0.6$.

responses tend to correlate much more closely with follow-up values than with baseline values.¹⁵ Therefore, categorization was based on the minimal important difference of the RQLQ(S), which had acceptable correlations with the NRQLQ ($r = 0.69$ to 0.81) (Table II). To minimize confounding (ie, completing one questionnaire would affect how patients completed the other questionnaire), the NRQLQ was always completed at the beginning of each visit and the RQLQ(S) was completed at the end.

This study identified the functional problems that are most troublesome to patients with NAR and showed that they are distinct and cannot be fully or accurately assessed by using existing instruments such as the RQLQ(S). The validation study analysis has shown that the NRQLQ has strong discriminative and evaluative measurement properties. This indicates that the NRQLQ can be used with confidence to determine problems of patients with NAR and the severity of this impairment. In addition, it can be used both in clinical practice and in clinical trials to evaluate the effectiveness of interventions.

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