

Disease-Specific Quality-of-Life Questionnaires in Rhinitis and Rhinosinusitis: Review and Evaluation

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Abstract Quality of life (QoL) measurements are the best approximation of the burden of disease for the patient. Patient-reported outcome measurements (PROMs) estimate health-related quality of life (HRQoL). PROMs can be generic or disease-specific. Generic PROMs allow comparisons between different diseases but can be relatively insensitive for measuring changes within a disease. Recommended QoL questionnaires in allergic rhinitis and rhinoconjunctivitis are the RQLQ (or adapted versions), in chronic rhinosinusitis, the SNOT-22 or RSOM-31, and in acute rhinosinusitis, the modified SNOT-16. PROMs can be used both for daily clinical work and for research. In daily practice, a quick evaluation of the questionnaire directly indicates how the patient is doing. It makes sure that symptoms important for the patient are not overlooked and, during the consultation, the physician can elaborate on specific aspects of the symptomatology. It is important, especially in research, to realize that disease-specific questionnaires are only validated for specific diseases and are not automatically valid for other diseases.

Keywords Rhinitis · Rhinosinusitis · Allergic rhinitis · Health-related quality of life · Quality of life · QoL · Patient reported outcome measurement · Questionnaire · Review · Evaluation

Introduction

The burden and relief of symptoms as perceived by the patient should play an essential role in the choice and

evaluation of treatment by the clinician in treating disease, especially chronic disease.

There are many possible ways to assess the burden of disease or to evaluate the success of initiated treatment, e.g. objective measures, such as imaging, medication use, provocation tests or the degree of symptoms [1]. In rhinology, it is well known that there is poor correlation between imaging and endoscopy and symptoms [2, 3]. Also, the use of medication does not provide complete insight into the patients' troubles, as is the case when measuring only the degree of symptoms. Recently, in rhinitis and rhinosinusitis, the concept of control as an important way to describe effectiveness of treatment on disease has also been proposed [4•, 5•]. Quality of life (QoL) measurements are the best approximation of the burden of disease for the patient. In rhinology, questionnaires are widely used both in clinical practice and in research, to assess the health-related quality of life (HRQoL). The burden of disease is defined by more than only nasal symptoms with HRQoL questionnaires, which also give insight into issues like sleep, daily activities or the emotional consequences of the disease. It must be emphasized that there is a major difference between symptom scores and HRQoL instruments, as the latter aim to provide a comprehensive physical, functional and psychosocial quality of life assessment.

PROMs

Patient-reported outcome measurements (PROMs) estimate HRQoL. These questionnaires have been developed to provide a standardized, quantified and summarized version of the patients' physical symptoms and the functional and psychosocial consequences of the disease and treatment. PROMs differ from symptom-scores in such a way that

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HRQoL instruments translate symptoms into broader concerns that are important to patients.

Generic Versus Disease-specific PROMs

Generic PROMs measure overall QoL. The most widely tested and used instrument for general health assessment is the Medical Outcomes Study Short-Form 36-Item Health Survey (SF-36). This instrument has been translated and validated in many languages.

Generic PROMs allow comparisons between conditions or treatments, and therefore can be used to determine not only the impact of different diseases on patient groups but also the relative cost-utility of different interventions and, thus, aid in commissioning decisions. However, generic instruments may be unresponsive to small, but important to the patient, changes in HRQoL. This makes generic instruments less suitable for measuring individual clinical outcomes.

Disease-specific QoL questionnaires for allergic rhinitis were first developed by Juniper in 1991 [6], and for rhinosinusitis in 1995 by Piccirillo [7]. In the following decade, many other questionnaires were designed for clinical and research use, each with a specific purpose [8–11]. With the development of rhinitis- and rhinosinusitis-specific HRQoL instruments, quality criteria were postulated regarding the psychometric properties of these questionnaires. Van Oene et al. [12] assessed the construction, description, feasibility, validation study and psychometric performance of QoL questionnaires concerning rhinitis and rhinosinusitis for adults (Table 1).

In this review, an update is provided on the quality assessment of the disease-specific QoL questionnaires for rhinitis and rhinosinusitis, including those developed since the publication by van Oene et al. [12].

Specific PROM for Which Disease?

In a well-designed instrument the generation of items is based on (1) research of the literature, (2) input of experienced clinicians, and (3) input from patients. This instrument is then validated for a specific illness. Therefore, HRQoL instruments cannot be used interchangeably between rhinitis, and acute and chronic rhinosinusitis.

In patients with allergic rhinitis and rhinoconjunctivitis, the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) [6, 10] is considered the gold standard in assessment of HRQoL. This instrument has been adapted in several forms: the standardized form of RQLQ, Nocturnal RQLQ (NRQLQ) for measurement of nocturnal rhinitis, and the mini-RQLQ, which utilizes only half of the 28

questions of the RQLQ. Although Juniper developed a questionnaire measuring perennial rhinitis in patients with allergic and non-allergic rhinitis [13] for pure non-allergic rhinitis (NAR), to date, there are no validated questionnaires available.

To measure the burden of nasal obstruction, the Nasal Obstruction Symptom Evaluation (NOSE) scale was developed by Stewart in 2004 [14]. However, this instrument has been validated solely in septoplasty patients, and therefore is not validated in rhinosinusitis patients.

The recent EPOS 2012 document [4••] has made recommendations for the use of specific instruments in rhinosinusitis. The assessment was based on several factors: (1) availability of a published psychometric validation, (2) time to complete an instrument for the patient, and (3) the number of studies utilizing each instrument (validation studies excluded) (Table 2).

Overview of Validated HRQoL Instruments

Based on the systematic review by van Oene [12], we give an overview of instruments that have high quality psychometric properties. Instruments validated after the publication by van Oene were graded by the authors, using the system proposed by van Oene.

Allergic Rhinitis

Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ)

The RQLQ was developed to measure QoL in rhinoconjunctivitis as a result of nose and eye symptoms [6]. It has 28 questions in seven domains (activity limitations, sleep problems, non-nose/eye symptoms, practical problems). This instrument has been translated into 16 languages and is used extensively throughout the world in both clinical studies and clinical practice.

Standardized Version of the RQLQ (RQLQ(S))

In the RQLQ, the patient can choose 3 activities that are bothered by his/her complaints. In the RQLQ(S), these 3 freely chosen activities have been replaced by generic activities (regular activities at home and at work, recreational activities and sleep), to create a more suitable instrument for large clinical trials and cross-sectional surveys [10].

MiniRQLQ

In order to create an instrument more suitable for large clinical trials, Juniper developed the MiniRQLQ containing only 14 questions [11].

Table 1 Characteristics and criteria for quality- assessment

Property	Part	Criterion	Points
A. Construction			
Measurement Goals	Targeted patient population	If provided	1
	Purpose: - discrimination and/or - evaluation	If provided	1
	For use in: - (clinical) trial or - clinical practice	Used for level of reliability	–
Item generation	Sources: - literature (incl. questionnaires) - clinician - patients	If all 3 sources are used	1
Item reduction	Approach: - conceptual - patient feedback - statistical analysis	If all 3 methods are used	1
	Scale construction: - conceptual - patient feedback - statistical analysis	If all 3 methods are used	1
	B. Description		
	Items, domains, response, score	If all 4 are provided	1
	Timeframe	If provided	1
C. Feasibility			
	Feedback of patients	If obtained	1
	Completion time	If provided	1
D. Validation Sstudy			
	Kind of patients	If representative of target patient population	1
	Number of patients	If ≥ 100	1
E. Psychometric properties			
Reliability	Internal reliability	At group level: Cronbach's $\alpha \geq 0.7$ or At individual level: Cronbach's $\alpha \geq 0.9$	1
	Test-retest	(significant T-test and Pearson/Spearman) or (ICC): At group level: correlation ≥ 0.7 or At individual level: correlation ≥ 0.9	1
Validity	Content validity	If confirmed (qualitative)	1
	Convergent validity	If correlation is between 0.4 – and 0.8	1
	Discriminant validity	If the purpose is: - evaluation: this item is NA - discrimination: p - value < 0.05	NA 1
Responsiveness		If the purpose is: - evaluation: p - value < 0.05 or responsiveness statistic is ≥ 0.5 - discrimination: this item is NA	1 NA
Clinically significant change		If the purpose is: - evaluation: used method and outcome provided - discrimination: this item is NA	1 NA

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Table 2 Recommended outcome tools based on current literature

Adult Allergic Rhinitis and Rhinoconjunctivitis – RQLQ (or adapted versions) [1–3]
Adult ARS – Modified SNOT-16 [4••]
Adult CRS – SNOT 22 [5] or RSOM-31 [6]
RQLQ – rhinoconjunctivitis quality of life questionnaire; ARS – acute rhinosinusitis; SNOT – sinonasal outcome test; CRS – chronic rhinosinusitis; RSOM – rhinosinusitis outcome measure; Based on: EPOS 2012 [7] and van Oene [8]

Nocturnal Rhinoconjunctivitis Quality of Life Questionnaire (NRQLQ)

The NRQLQ was designed to measure the functional problems that are most troublesome to patients with nocturnal allergic rhinitis. The instrument consists of 16 items over 4 domains (sleep problems, symptoms during sleep time, symptoms on waking and practical problems) [15].

Nasal Obstruction Symptom Evaluation (NOSE)

The NOSE scale is an instrument used to specifically assess the component of nasal obstruction. The instrument consists of 5 questions seeking to rate the burden of nasal obstruction during the past month. Strictly, it is not a disease-specific QOL questionnaire because it only evaluates one symptom. It is well validated and easy to use in epidemiologic studies [14].

Rhinosinusitis

Rhinosinusitis Outcome Measure-31 (RSOM-31)

The RSOM-31 contains 31 items divided into seven domains (nasal, eye, ear, sleep, general, functional and emotional problems). For each symptom, there are two response scales: severity and importance. The product of the magnitude and importance scores creates the symptom-impact score. The instrument is well validated and is widely used; however, the severity and importance scales make it somewhat difficult for the patient to fill out the questionnaire [7]. For this reason, it is often used as the SNOT questionnaire with only the severity scales [9, 16].

Sinonasal Outcome Test-20 (SNOT-20)

The SNOT-20 is a modification of the 31-item RSOM, containing 20 nose, sinus and general items. The importance scale was removed to make scoring easier. The SNOT-20 provides two main scores: (1) total score, which is the mean score for all 20 items, and (2) importance score, which is the mean score for the five items identified as important [16]. A

limitation of this questionnaire is that two critical questions are not included, ‘nasal obstruction’ and ‘loss of smell’ (see SNOT-22 below).

Sinonasal Outcome Test-22 (SNOT-22)

The SNOT-20 questionnaire, based on the RSOM-31, missed two critical questions: nasal obstruction and loss of smell. These were again included in the SNOT-22 questionnaire. In addition, the magnitude level was changed back to a five-category scale. In 2009, Hopkins et al. validated this instrument, and demonstrated its reliability and ease of use [9].

Sinonasal Outcome Test-16 Modified for Acute Rhinosinusitis (SNOT-16-ARS)

The SNOT-16 was modified to create an easy-to-use tool for primary care patients with clinically diagnosed acute rhinosinusitis. The instrument uses a 4-item response scale and patients select maximum of 5 items that they felt were most important from the list. The validation study is well described and the modified SNOT-16 is a valid and reliable instrument for primary care patients with ARS [17•].

Rhinosinusitis Quality of Life Survey (RhinoQoL)

The RhinoQoL is a 17-item instrument, which measures symptom frequency, bothersomeness and impact scales in patients with acute and chronic sinusitis [18].

Impact of Rhinitis on QoL

Adults and children with allergic and non-allergic rhinitis are bothered both by the nasal symptoms themselves as well as associated symptoms such as headache and fatigue. The combination can produce severe impairment of day-to-day physical, emotional, occupational, and social functioning and can cause emotional distress [19]. The importance is demonstrated by the WHO ARIA guidelines: rhinitis severity is now based on the impact of disease on QOL [20]. There is also ample evidence that AR and NAR are associated with an incremental adverse impact on the disease-specific QOL of patients with asthma and the level of asthma control [20, 21]. One of the aims of treating patients with rhinitis should be that all individual patient problems are recognized and treated appropriately.

Impact of ARS on QoL

ARS is thought to have a substantial impact on patients’ HRQoL and daily functioning, but this has not been well

documented. The EPOS 2012 document recommends assessing the severity of symptoms with the use of a 10-cm visual analogue scale (VAS), or at least asking the patient to rate their symptoms as absent, mild, moderate, or severe. It is advised to record the severity of symptoms in a fashion that is clinically meaningful.

Generic Measures of QoL in ARS

Rechtweg et al. [22]. used SF-36 questionnaires to measure possible differences in QoL outcomes in ARS patients treated with either Clarithromycin or Amoxicillin/Clavulanate. Regrettably, they only provide the *p* values of these differences and no SF-36 scores for comparison with other diseases.

Impact of CRS on QoL

Generic Measures of QoL in CRS

Van Agthoven measured SF-36 scores in patients with refractory CRS. All subscales were scored below the general population, and even lower than patients with hypertension, diabetes or angina [23]. Thus, it should come as no surprise that health care spending was significantly greater for sinusitis than for other chronic diseases, e.g., peptic ulcer disease, acute asthma and hay fever [24–26].

Disease-specific Measures of QoL in CRS

Measuring disease-specific quality of life involves asking patients a fixed set of questions regarding possible symptoms, and to rate these according to their perceived burden. The RSOM-31, SNOT-22 and RhinoQoL cover not only nasal symptoms but also symptoms of the ears or eyes. Furthermore, the instruments try to capture sleep disturbance and excessive tiredness. Emotional problems, such as irritability, frustration or depression, are also addressed.

Nasal obstruction is one of the most commonly reported symptoms of CRS. Comparing patients with CRSwNP and CRSsNP using the RSOM-31, the former more often score higher on nasal symptoms, such as decreased sense of taste/smell or rhinorrhoea, while the latter score higher on facial pain and ear pain [27].

When do you Use PROMs in Clinic and Research

PROMs can be used both for daily clinical work and for research. It seems intuitive that physicians would wish to measure whether they are successful in achieving their treatment aims.

For centuries, assessment of outcomes has involved simple dichotomous measurements, usually decided by the surgeons themselves, e.g., dead or alive, cure or residual disease, sometimes with some subtleties, e.g., better or worse. There has been a growing demand for greater transparency and publication of outcome data following treatment. Moreover, increasing emphasis has been placed on the patients' own evaluation of their HRQoL before and following medical or surgical interventions. Coupled with the explosion of evidence-based medicine, this has led to a significant refinement in the measurement of outcomes. The use of validated outcome measures helps physicians to evaluate their practice and improve management schemes. In many healthcare systems, measurements of outcomes have become an important assessment tool for the quality of patient care.

The Use of PROMs in the Daily Practice

In daily practice, measurements of patients' symptoms are performed with validated questionnaires. The patient fills out the questionnaire at home before the visit to the clinic or when sitting in the waiting room. Questionnaires for rhinitis (RQLQ), rhinosinusitis (RSOM-31), and asthma (asthma control test, ACT) are routinely used.

When the patient enters the consultation room, a quick evaluation of the questionnaire directly indicates how the patient is doing. Apart from the questions about nasal symptoms, these disease-specific questionnaires contain questions on the eye, sleep, ear, and general symptom domains. During the consultation, the physician can elaborate on specific aspects of the symptomatology and, in a very efficient semi-structured way, perform the consultation. This way of working is time saving and ensures that symptoms important for the patient are not overlooked. It also directly points to patients that will be difficult to treat, e.g., because of many symptoms not directly related to the disease or to another diagnosis: facial pain/headache without relevant nasal symptoms and not caused by a sinus problem. One has to realize, however, that standardized questionnaires derived from the population as a whole may restrict a patient's choice of symptoms to report, and may fail to capture those of importance to the individual. It is therefore important to always ask the patient whether other symptoms not in the questionnaire bother him or her. Finally, the questionnaire ensures that other important aspects like the lower airways or smoking are never forgotten.

Several publications have demonstrated the lack of correlation between patient-derived measures of symptom severity in chronic rhinosinusitis and objective measures, such as the radiological Lund–Mackay scoring [2]. Similarly, a recent systematic review has demonstrated no correlation

between sensation of nasal obstruction and measurements of cross-sectional airflow using rhinometry [28]. The absence of correlation does not suggest that either patient-rated or objective scores are invalid, but rather they are measuring different aspects of the disease process, and therefore are useful adjuncts in outcome measurement.

For the majority of rhinological symptoms (where reducing the impact of symptoms on the quality of life of the patient is the primary aim of treatment), patient-rated measures are usually more useful in guiding treatment. Clinician-rated measures may, however, provide more useful feedback to give an indication whether the aimed reduction in symptoms is feasible. When there are a lot of symptoms in the absence of significant disease as rated by the doctor, the chance of a favorable outcome is smaller.

In the clinical setting, repeated measures map the individual patient's well-being, and allow improvements or exacerbations to be readily identified. It also helps to identify, together with the patient, what the present aims of the treatment will be. Often, over time, the symptoms and therefore the desire for symptom relief change, and identifying these shifts is made easy with the use of structured questionnaire.

If used in other diseases, it is unclear whether they will reliably measure improvements or exacerbations. The amount of information derived from the questionnaire has to be balanced against the effort of the patient. For many practices, short questionnaires like the mini-RQLQ for rhinitis (14 questions), the Nasal Obstruction Symptom Evaluation (NOSE) questionnaire for nasal obstruction (5 questions), the SNOT-22 for CRS (22 questions) and the asthma control test in patients with asthma (5 questions) are useful and easy to use.

The Use of PROMs in Research

In research, the use of validated questionnaires is crucial for reliable interpretation of results, and some guidelines even recommend them to be the primary outcome of clinical trials [29]. Unfortunately, not all diseases have had PROMS developed and, in such a case, QoL questionnaires are often used that are not validated for the disease [22, 30]. The results of these studies should always be interpreted with some care.

Most importantly, PROMs can be used to assess the effect of a (new) treatment, or to compare the effects of two different treatments on the issues most important to the patient. However, it is important the proper PROMs are used in the proper population.

The first important question is whether the questionnaire has been validated in a population comparable to the research population. This concerns not only diagnosis but also patient characteristics and baseline HRQoL measurements.

To interpret the burden of initial disease, one has to know what score is 'normal'. This can be done by comparing the score of the affected population to a non-affected population. Picirillo [7] described a RSOM-31 mean symptom impact score of 1.85 (theoretical range RSOM-31: 0–20) in audiology patients, compared to a score of 5.81 in a pre-treatment CRS population. Atlas [18] described a symptom impact score of 97.8 in a group of control patients, compared to a symptom impact score of 47.6 in ARS and 55.3 in CRS patients, where lower scores indicate more severe symptoms (theoretical range RhinoQoL: 0–100). Hopkins [9] recruited healthy individuals from hospital staff and the local tennis club and found an average SNOT-22 score of 9.3 (mean: 0.42) in healthy individuals, compared to a SNOT-22 score of 42.0 (mean: 1.91) in the pre-operative CRS population (theoretical range SNOT-22: 0–110). Due to the difference in scales, the scores of the RSOM-31 and SNOT-22 cannot be directly compared with each other. The importance of knowing the symptom scores in a normal population is evident; clinicians treating patients with near-normal scores can expect little patient satisfaction and might need to revise their diagnosis.

To interpret the effect of treatment, the minimally important difference (MID) should be available for the instrument [31]. This defines a difference in score that is *clinically* significant, as opposed to *statistically* significant, which is more commonly reported. For example, the MID in the RQLQ is approximately 0.5, in the MiniRQLQ 0.70, in the RSOM-31 a 30 % change in total score, in the SNOT-16 (for ARS) 0.5, and in the SNOT-22 8.9 (mean approximately 0.5) [7, 9, 11, 17•].

Which Instrument to Choose Based on Quality?

Based on a thorough and valid assessment of the clinimetric quality, one can decide which instrument is most suitable for the specific research population. Also, the findings of a generic and a disease specific instrument can be combined.

For allergic rhinitis, the MiniRQLQ and the standardized RQLQ score well on the quality assessment.

For CRS, both the RSOM-31 and its product SNOT-22 score very well in the quality assessment, together with the RhinoQoL. The SNOT-22 score, however, is easier to calculate and interpret than the RSOM-31 score.

For ARS, only the RhinoQoL and the modified SNOT-16 have been validated. In both instruments, the validation process was well documented. The SNOT-16 might be somewhat easier for the patient to fill out, and the calculation of the score is less complicated.

When measuring HRQoL in rhinology patients, the asthma control test (ACT) or the RhinAsthma Patient Perspective

(RAPP) are helpful to identify patients with poorly controlled asthma [32, 33]. The RAPP is a simple eight-question questionnaire with good measurement properties and sensitivity to health changes, which will provide a valid, reliable and standardized HRQoL measurement in patients with asthma and comorbid allergic rhinitis in clinical practice.

Patient-reported Outcome Measures in the Lower Airways

Also, in asthma, there is a strong body of evidence regarding the relationship between HRQoL evaluated by PROMs and objective measures of lung function [34, 35]

Asthma appears to have a good lower airways correlation to the reactive diseases of the nose. Currently, several outcome measures are considered important in asthma: FEV₁, bronchial hyperreactivity, symptom scores, emergency department visits and hospitalizations, exhaled nitric oxide or other exhaled gases, beta-agonist use, exacerbations, and quality of life (QoL) [36]. However, the burden of the disease and the HRQoL are of primary concern for physicians.

Many of the asthma outcome measures do not correlate well with one another. Specifically, comparisons between lung function and daytime symptom scores or beta-agonist use reveal a poor correlation [35]. In a study of patients with persistent asthma treated with triamcinolone or switching to salmeterol, lung function was shown not to correlate with asthma exacerbations [37]. As there is no one parameter that can exclusively serve as a marker of asthma control, patient-derived information becomes critical in evaluating this disease.

Similar observations can be made in chronic obstructive pulmonary disease (COPD). Tsiligianni et al. performed a meta-analysis of factors influencing disease-specific QoL in COPD patients [34]. Most studies showed a non-significant or weak association between FEV₁ and health status, while others revealed a moderate association. Highest correlations (in modest range, 0.4–0.6) were found for 3 questionnaires (Quality of Well-Being Scale, Chronic Respiratory Questionnaire dyspnoea, and COPD Control Questionnaire) used in only 6 studies. The other health status measures, including the most frequently used St George's Respiratory Questionnaire, correlated weakly with FEV₁.

General Thoughts on the Philosophy of Using PROMs

The patient's perspective on the disease, which the PROMs try to capture, is neither the defining feature of disease nor

second to the objective findings. In 1995, Wilson and Cleary proposed a conceptual model of patient outcomes [38]. They are to be considered in the perspective of objective findings (biological and physiological variables, e.g., radiographic or endoscopic measures of sinusitis) in combination with characteristics of the individual (symptom amplification, personal motivation, values, and preferences) and their environment (psychological, social, and economic supports). These variables contribute to the formation of five levels of outcomes, moving from the cellular to individual to societal levels: *biological and physiological*, *symptom status*, *functional status*, *general health perceptions*, and *overall quality of life*. Even though HRQoL measures in rhinitis and rhinosinusitis combine, to a variety of degrees, measures from all five levels of this model, it is necessary to remember that physicians frequently focus on the level close to their understanding of disease (e.g., questions on nasal symptoms in case of rhinosinusitis). Specialists are more prone to treating the specific aspects of disease (*biological and physiological* and *symptom status* levels), while general practitioners are more inclined to also address the overall health of the individual (*functional* and *general health perceptions* levels).

What makes the continuous need for utilization of PROMs in health care critical is the fact that they capture aspects of the disease that are not easily recorded by static quantifiable parameters. They provide an opportunity to measure these variables not captured on the biological level. In addition, they allow for continuous measurement of the overall perception of health by the patient. Ultimately, it is the patient that we treat, and their symptoms are what brings them to our care.

Conclusions

PROMs measuring QOL are an essential part of instruments of the clinician interested in his patients and the researcher needing validated and reliable tools.

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- Of major importance

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