

Review article

Chronic rhinosinusitis and nasal polyps: the role of generic and specific questionnaires on assessing its impact on patient's quality of life

Chronic rhinosinusitis (CRS) including nasal polyps is a chronic inflammatory disease of the nasal and paranasal sinus mucosa that, despite differing hypotheses of its cause, remains poorly understood. Primary symptoms are nasal blockage, loss of smell, rhinorrhea, and facial pain or pressure. Chronic rhinosinusitis causes significant physical symptoms, has a negative impact on quality of life (QoL), and can substantially impair daily functioning. A global evaluation of patients must include, together with nasal symptoms, nasal endoscopy, and CT scan, the measurement of QoL. To assess QoL in CRS, specific and generic questionnaires may be used. Chronic rhinosinusitis has a considerable impact on a patient's QoL but comorbidities, such as asthma and atopy, have an accumulative negative effect. Both medical and surgical treatments lead to a similar improvement on the QoL of CRS and nasal polyp patients.

I. Alobid^{1,2}, M. Bernal-Sprekelsen¹, J. Mullol^{1,3}

¹Rhinology Unit and Smell Clinic, Department of Otorhinolaryngology, Hospital Clínic i Universitari;

²Department of Otorhinolaryngology, Hospital Municipal de Badalona; ³Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Barcelona, Spain

Key words: chronic rhinosinusitis; medical treatment; nasal polyposis; quality of life; surgical treatment.

J. Mullol
Rhinology Unit and Smell Clinic
Department of Otorhinolaryngology
Hospital Clínic i Universitari
c/Villarroel, 170
Barcelona 08036
Spain

Accepted for publication 17 May 2008

Chronic rhinosinusitis (CRS) is a significant health problem, which seems to mirror the increasing frequency of allergic rhinitis and resulting in a large financial burden on general population (1). Recent data have demonstrated that CRS is among the most common chronic conditions, affecting around 5%–15% of the urban community in Europe (2) and the USA (3). In the European guidelines (EPOS) (4, 5), CRS has been defined as nasal congestion in combination with nasal discharge, $\pm$ facial pain/pressure, $\pm$ reduction or loss of smell more than 12 weeks, and either endoscopic signs of polyps and/or mucopurulent discharge and/or; edema/mucosal obstruction in middle meatus, and/or CT changes within the ostiomeatal complex and/or sinuses (Fig. 1). Chronic rhinosinusitis and nasal polyposis (NP) are frequently associated with asthma and other pulmonary disorders such as bronchiectasis, cystic fibrosis (CF), and aspirin sensitivity (6, 7). Because CRS is a pathology with rising prevalence and costs that affects a significant portion of the population, the outcome evaluation and verification of therapy effectiveness are essential (3).

For a complete and thorough assessment of CRS morbidity and the evaluation of treatment, it is imperative that the physical, social, and emotional problems associated with this condition are measured in a valid way. Because critical questions about its cause, pathophysiology, and optimal treatment remain unanswered, CRS still generates significant healthcare costs and affects the quality of life (QoL). Although CRS is not a life-threatening disease, it can significantly decrease patient's QoL (8–10). Quality of life is a very important outcome in the evaluation of CRS severity and its measurements reflect the effect that symptoms and disease have on the patient's daily life (11). However, it is of interest that the presence and/or severity of nasal symptoms do not always correlate with QoL questionnaires (12). The concept of the minimal important difference (MID) refers to the smallest difference in a score that is considered to be worthwhile or important (13). Juniper et al. (14) define an MID as 'the smallest difference in a score...which patients perceive as beneficial and which would mandate, in the absence of troublesome side-effects and excessive cost, a change in the patient's management'.

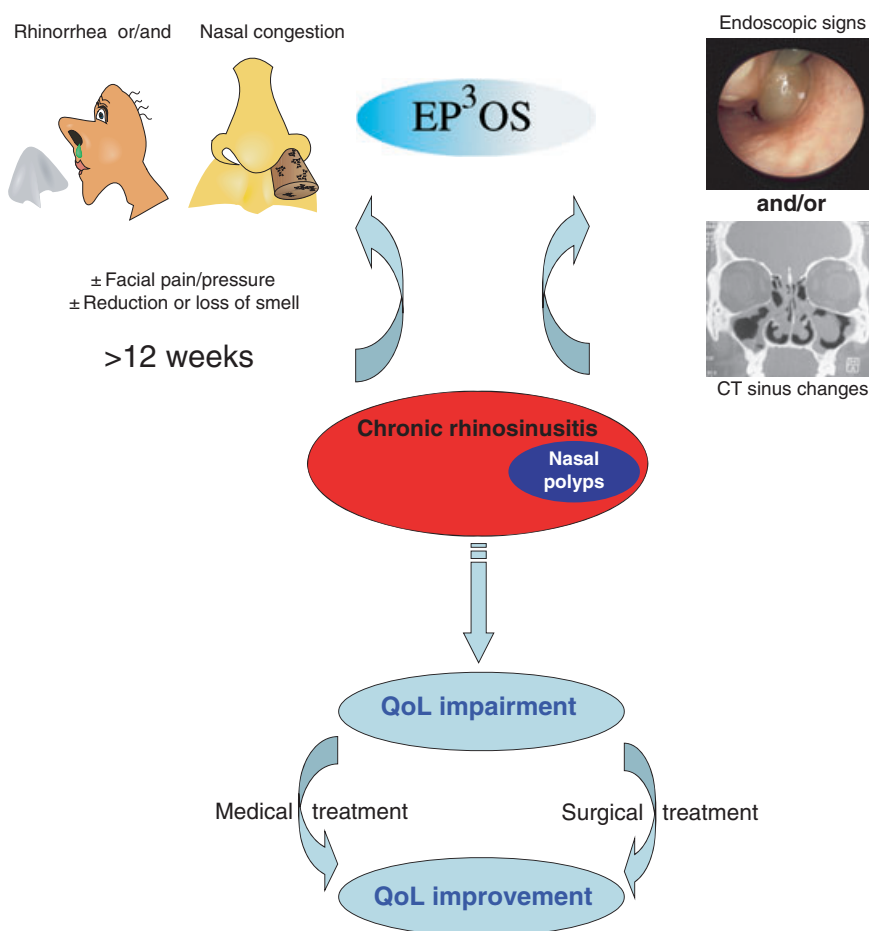


Figure 1. Scheme of the chronic rhinosinusitis definition in the European Position Paper on Rhinosinusitis and Nasal Polyps (EP³OS 2007). Chronic rhinosinusitis, including nasal polyps, has an important negative impact on patients' quality of life which is improved by both medical and surgical treatment.

The quality of life concept

Medicine has traditionally relied on the assessment of change using laboratory, imaging, or clinical tests. However, the assessment of QoL is increasingly being recognized as an important alternative outcome measure. In the past decade, a psychometric theory has been applied to the development of patient-oriented health assessments of health. These health measures focus on multiple health domains in an effort to present a complete picture of health and disease. Patient-perceived subjective outcome is an integral part in reporting results of health care (15). Specifically, QoL has been characterized as the functional effects of an illness and its consequent therapy upon a patient as perceived by the patient (16). Juniper has commented that the last sentence is particularly important because it emphasizes that these are the impairments that the patients consider to be important (17).

Quality of life is a general term integrating several aspects of life such as physical, psychological, social, economical, emotional, cognitional, and sexual dimen-

sions. A disturbance in any one of these aspects will in turn affect the other domains and influence the overall QoL. The measures of QoL have evolved as the emphasis on medical care has shifted from symptom scores and objective test results to an assessment of patient-centered effect of disease and response to treatment. The QoL instruments have proved to be very useful providing comparative data with other medical conditions, which could be regarded as more serious.

The assessment of patient-reported outcomes is important in clinical trials, and in some cases symptomatic outcome should be the primary treatment outcome. Therefore, a need exists for validated instruments to assess patient-based outcomes (18). However, there are many pitfalls in the reporting of QoL information (19). These problems include the use of unfamiliar scales, failure to describe the minimally clinically important differences, failure to explain the clinical importance of the instrument, failure to differentiate between inferences for individuals and for individuals *vs* groups, identifying sample size requirements and statistical power, and

whether the data are analyzed according to an original plan (20).

Psychometric requirements of quality of life questionnaire

The QoL instrument should be easy to administer, acceptable to both patients and healthcare professionals, and resource efficient (21). Psychometric properties of clinical outcome measures for CRS, including nasal polyps, are:

Validity

The instrument should measure what it is intended to measure (22). Different types of validity should be taken into account:

- Convergent validity is demonstrated when scores of the test being examined are highly correlated to scores of a test thought to measure similar or related concepts.
- Discriminant validity is demonstrated when scores of the test being examined are not correlated to scores of a test meant to measure a very different construct.

Reliability

The instrument should have a high intra- and inter-examiner or test–retest reliability. There are several types of reliability that should be analyzed.

- *Internal consistency reliability*: In this estimation, a single measurement instrument is administered to a group of people on one occasion to estimate reliability. In effect, the reliability of the instrument is evaluated by estimating how well the items that reflect the same construct yield similar results. We are looking at how consistent the results are for different items using the same construct within the measure. There are a wide variety of internal consistency measures that can be used. Internal consistency is usually estimated by calculating Cronbach's α (range 0–1). If a scale has an alpha of at least 0.7, the scale is considered to be reliable for group level comparison and a value of 0.9 or more for assessment at the individual level (23).
- *Test–retest reliability*: In the estimation of test–retest reliability, the same test is administered to the same sample on two different occasions. This approach assumes that there is no substantial change in the construct being measured between the two occasions. The amount of time existing between measures is critical. It is well known that the same item is measured twice; the correlation between the two observations will depend in part by how much time elapses between the two measurements.

Responsiveness

The measure should be sensitive to clinical change over a relative short period of time (24). Two types of responsiveness have been identified.

- Internal responsiveness is defined as the ability of a measurement to change during a prespecified time frame. It is often assessed by administering a measure before and after a treatment with known efficacy.
- External responsiveness reflects the extent to which changes in a measure relate to changes in other measures of health status.

Quality of life questionnaires

Generally, there are two major types of QoL instruments used in clinical trials: generic and specific. Generic measures allow comparison across different disorders, severities of disease, and interventions, whereas disease-specific scales contain items most relevant to the condition under study and that most likely will change with effective therapy (Table 1).

Generic questionnaires

Generic instruments are applicable to all health conditions and they allow a comparison of the impact of different diseases in QoL as well as healthy and diseased subjects. Short form-36 health survey (SF-36), short form-12 (SF-12), McGill pain questionnaire (MPQ), EuroQol 5D (EQ-5D), the Glasgow benefit inventory (GBI), and child health questionnaire (CHQ) are the most used generic instruments in CRS.

Short form-36 health survey. The SF-36 has been extensively used to provide information concerning the functional well-being of individuals with chronic diseases. It is one of the most widely used generic questionnaires (25). In 1991, the International Quality of Life Assessment (IQOLA) project was initiated to translate, adapt, and validate SF-36 for use in some 15 countries, showing good reproducibility and validity (26). The SF-36 questionnaire contains 36 items and measures health status in eight domains, covering both physical and mental health. The physical component summary includes four domains: physical functioning (10 questions), role physical functioning (four questions), bodily pain (two questions), and general health (five questions). The mental component summary includes four domains: vitality (four questions), role emotional functioning (three questions), social functioning (two questions), and mental health (five questions). The sum of the score is calculated for each domain and transformed to a percentage of the total possible score. Scores range from 0 to 100, with a higher score representing better functioning.

Table 1. Generic and specific quality of life questionnaires

Questionnaire	Number of items	Number of domains	Time fill-in	Type	Original language	Scoring
SF-36 (25)	36	8	10–20 min	Self-report	English	0–100
SF-12 (27)	12	8	5–10 min	Self-report	English	0–100
MPQ (28)	78	20	10–20 min	Interviewer	English	5-point scale
EQ-5D (30)	15	5	5–10 min	Self-report	Dutch, English, Finnish, Norwegian, Swedish	0–100
GBI (31)	18	3	5–10 min	Self-report	English	5-point scale
CHQ-PF50 (32)	50	14	15–20 min	Self-administered by parent	English	0–100
RSDI (35)	30	3	<5 min	Self-report	English	5-point scale
RSOM (35)	31	7	15–20 min	Self-report	English	6-point magnitude scale; 4-point importance scale
SNOT-20 (36)	20	–	<5 min	Self-report	English	6-point scale
SNOT-16 (37)	16	–	<5 min	Self-report	English	4-point scale
CSS (38)	6	2	<5 min	Self-report	English	5-point scale
RhinoQoL (39)	17	3	5–10 min	Self-report	English	5-point scale
SN-5 (40)	5	–	<5 min	Self-report	English	7-point scale
SOQ (41)	26	5	5–10 min	Self-report	English	5-point scale
RQLQ (42)	28	7	10–15 min	Self-report/ interviewer-administered	English	5-point scale

CSS, chronic sinusitis survey; CHQ-PF50, child health questionnaire parent form 50; EQ-5D, EuroQol 5D; GBI, Glasgow benefit inventory; MPQ, McGill pain questionnaire; RQLQ, rhinoconjunctivitis quality of life questionnaire; RhinoQoL, rhinosinusitis quality of life; RSDI, rhinosinusitis disability index; RSOM, rhinosinusitis outcome measure; SN-5, sinonasal-5; SNOT-16, sinonasal outcome test 16; SNOT-20, sinonasal outcome test 20; SF-36, short form-36 health survey; SF-12, short form-12 health survey; SOQ, sinusitis outcomes questionnaire.

Short form-12 health survey. The SF-12 is a shorter version of the SF-36 health survey designed to reproduce the physical and the mental component summary scores. It includes 12 questions from the SF-36 health survey: two questions concerning physical functioning, two questions on role limitations because of physical health problems, one question on bodily pain, one question on general health perceptions, one question on vitality (energy/fatigue), one question on social functioning, two questions on role limitations because of emotional problems, and two questions on general mental health. The scoring of individual items is identical to the SF-36 health survey (27).

McGill pain questionnaire. McGill pain questionnaire was designed to provide a quantitative profile of three psychological dimensions of pain. It primarily consists of three major classes of word descriptors: sensory, affective, and evaluative, those are used by patients to specify subjective pain experience. The MPQ contains an intensity scale and other items to determine the properties of patient's pain experience that can be treated statistically (28). The MPQ consists of 20 categories of words describing qualities of pain and patients indicate which words apply in their disease situation. At least six different pain variables can be calculated from the instrument. While relatively well studied in terms of validity and reliability, the MPQ may present some practical difficulties in clinical practice because it should be administered by an interviewer. The short form of the MPQ11 pain questionnaire (SF-MPQ) contains 11 ques-

tions referring to the sensory dimension of the pain experience and four questions related to the affective dimension. Each descriptor is ranked in a 4-point intensity scale (0 = none, 1 = mild, 2 = moderate, and 3 = severe). The pain rating index of the standard MPQ is also included as well as a visual analog scale (VAS) (29).

EuroQol 5D. It is a standardized instrument to be used as a measure of health outcome. The EQ-5D provides a simple descriptive profile and a single index value for health status that can be used in the clinical and economic evaluation of health care as well as in population-based health surveys. It is applicable to a wide range of health conditions and treatments. It is designed for self-completion by patients, being ideally suited for use in postal surveys, in clinics, and face-to-face interviews. It is cognitively simple and takes only a few minutes to be completed. The EQ-5D descriptive system comprises five dimensions of health: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension comprises three levels: no problems, some/moderate problems, and extreme problems. The EQ VAS records the self-rated health status on a vertically graduated (0–100) VAS (30).

Glasgow benefit inventory. It is defined as the general perception of well-being, including psychological, social, and physical well-being. The GBI is a validated questionnaire, which is sensitive to the change in health status after a specific event such as a surgical procedure. The

GBI has 18 questions; the response to each of them is based on a 5-point Likert scale ranging from a large deterioration in health status to a large improvement. To help control for response bias, half of the questions have the answers ranging from a large improvement to a large deterioration, whereas the other half range the other way. The GBI also has three subscales built into the format of the questionnaire, which measures general benefit (12 questions), the amount of social support (three questions), and changes in overall physical health status (three questions) of the patients (31).

Child health questionnaire. Various child health assessment instruments have been developed. The main pitfall frequently addressed in using this instrument is whether the parent or the child is the most appropriate respondent. Parents often serve as proxy reporters for targeted children, because they may have a better understanding of the health issues being investigated and a better comprehension of the instrument. The CHQ offers a 50-item parent proxy reported form known as the CHQ-parent form (CHQ-P50) and an 87-item child self-report form known as CHQ-child form (CHQ-CF87). These scales include physical functioning, role/social-physical, general health, bodily pain, family activities, role/social-emotional, role/social-behavioral, parental impact-time, parental impact-emotional, self-esteem, mental health, general behavior, family cohesion, and change in health. These 14 concepts can be summarized into two summary component scales representative of physical and psychosocial health. The CHQ-CF87 is analogous to the CHQ-PF50 in that it is self-administered or given by interview depending on the age of the child. Its 12 components are identical to those of the CHQ-PF50 with the exceptions that there are no parental impact-time and parental impact-emotional scales and there are no available physical and psychosocial summary scales (32). Cunningham et al. demonstrated significant decrements in the health-related QoL of children who undergo surgical treatment for recurrent CRS compared both with normative populations and other pediatric chronic illness groups. These results underscore the severity of this chronic recurrent disease process (33).

Specific questionnaires

Rhinosinusitis disability index. Rhinosinusitis disability index (RSDI) is a disease-specific health-related QoL instrument developed by physical, functional, and emotional impact of CRS. In this 30-item validated questionnaire, patients with CRS are asked to relate nasal and sinus symptoms to specific limitations on daily functioning. The RSDI is a valid measuring instrument for patients with sinus disease, and test-retest validity reveals reliability over time. The 30 items of the RSDI have been validated through Cronbach's alpha coefficient and Spearman's correlation (34).

Rhinosinusitis outcome measure. Rhinosinusitis outcome measure (RSOM) contains 31 items classified into seven domains and has been well validated and allowing the measurement of symptom severity and their importance to the patient (nasal, eye, ear, sleep, general, emotional, and functional problems). The RSOM-31 requires approximately 20 min to complete and has documented response to clinical change. For each item, there are two response scales: magnitude and importance. The magnitude scale has a 6-category response score, whereas the importance scale has a 4-category response score. The product of the magnitude and importance scores creates the symptom-impact score, a unique patient-specific score. The severity and importance scales, however, make it somewhat difficult for the patient to fill the questionnaire (35).

Sinonasal outcome test 20. The sinonasal outcome test 20 (SNOT-20) is a modification of the 31-item RSOM, containing 20 nose, sinus, and general items. It was derived from the RSOM through the elimination of 11 items. The importance scale was revised to make scoring easier. Two main scores are derived: (i) total score, which is the mean score for all 20 items and (ii) importance score, which is the mean score for the items identified as important. To complete the instrument, patients indicate how much they are affected in each area and identify the five most important items (36). The SNOT-20 was validated and demonstrated to be sensitive to change. Items identified as important had higher scores, on average, and showed greater change scores after treatment than items not identified as important. However, SNOT-20 does not contain questions on nasal obstruction and loss of smell and taste. These questions are however included in the SNOT-22 questionnaire, which is not validated.

Sinonasal outcome test 16. The sinonasal outcome test 16 (SNOT-16) asks patients to rate the severity of their symptoms and the social/emotional consequences of their rhinosinusitis. A higher SNOT-16 score indicates worse QoL and functional status. The SNOT-16 is a validated 16-item instrument designed for longitudinal measurement of CRS-specific symptoms. Items are scored on a 4-point scale, and the composite score is calculated as the mean of the answered responses. A maximum value of 3 means the most severe symptoms, and a score of 0 means no symptoms. Anderson et al. concluded that the SNOT-16 is a reliable, valid, and responsive instrument for measuring rhinosinusitis-specific health-related QoL (37).

Chronic sinusitis survey. Chronic sinusitis survey (CSS) is a valid, disease-specific measure for evaluating the health status and treatment effectiveness of adults with CRS. The CSS has been used to identify QoL consequences of CRS such as sinus-related symptoms and medical resource utilization associated with CRS. The CSS is a

6-item, duration-based monitor of CRS-specific outcomes. The symptom-based section contains pain or pressure, nasal congestion or difficulty to breathe through the nose, and rhinorrhea or postnasal drip. The medication-based section contains: antibiotics, prescription nasal sprays, and sinus medications in pill form. The severity of symptoms is scored 0 (none) to 4 (severe), and a total score is calculated from 0 (worst) to 100 (best) (38).

Rhinosinusitis quality of life survey. Rhinosinusitis QoL survey (RhinoQoL) is a specific instrument, which measures symptom frequency, bothersomeness, and impact scales. Atlas et al. developed and validated a new sinusitis-specific QoL questionnaire with 17 items. The three scales of the measurement were shown to be reliable and valid compared with a previously validated disease-specific instrument and a generic QoL measure (39).

Sinonasal-5 quality of life survey. The sinonasal-5 QoL survey (SN-5) comprises five domains: sinus infection, nasal obstruction, allergy symptoms, emotional distress, and activity limitations. Each domain consists of a number of symptom clusters. A point scale is used that ranges from 1 (none of the time) to 7 (all of the time) to grade the relative severity of each symptom cluster to give a mean domain score. A single QoL item is also included in the survey. This item asks caregivers to grade their child's QoL with a VAS that ranged from 0 (worst possible QoL) to 10 (best possible QoL). The survey has adequate test-retest reliability, is internally consistent, and correlates with related external constructs. Validation of the SN-5 survey provides clinicians and researchers with a simple and useful evaluative tool (40).

Sinusitis outcomes questionnaire. The sinusitis outcomes questionnaire (SOQ) survey consists of five sections. The first section assesses global symptoms and the next three evaluate specific symptoms of the nose and sinuses, eyes, and chest. Each of the 26 symptom questions is scored on a Likert scale from 0 to 5, indicating the severity of symptoms with a possible total symptom score between 0 and 130. The higher the score, the more symptomatic the patient. The fifth section explores the economic burden of their disease by assessing lost of work or school days; emergency department visits; hospitalization; nose, ear, or sinus surgery; antibiotics for sinusitis; bronchitis and otitis; and daily medications, including nasal sprays, inhalers, eye drops, and pills. The questionnaire was designed to be completed in 5 min or less (41).

Rhinoconjunctivitis quality of life questionnaire. The rhinoconjunctivitis quality of life questionnaire (RQLQ) was developed to measure QoL in rhinoconjunctivitis, both atopic and nonatopic, as a result of their nose and eye

symptoms. It has 28 questions in seven domains (activity limitations, sleep problems, nonnose/eye symptoms, practical problems, nose symptoms, eye symptoms, and emotional function) (42). Although it is optimal to use patient-specific activities, Juniper et al. have developed a version of the RQLQ in which the three activities are standardized for all patients with rhinoconjunctivitis. The RQLQ(S) has been fully validated and shows strong measurement properties.

QoL questionnaires in chronic rhinosinusitis

Generic and specific questionnaires were used to study the impact of CRS on QoL.

Generic questionnaires

There are many generic QoL questionnaires available for CRS studies. These measurements enable the comparison of patients suffering from CRS with other patients suffering from other diseases (Table 2).

Short form-36 health survey. Among generic instruments, the SF-36 is by far the most widely used and well validated and has been used for both pre- and postoperative studies in CRS. Compared with general population, many studies have demonstrated that CRS has a considerable impact on all SF-36 domains except for physical functioning (43–47). Patients with CRS ($n = 158$) and no prior surgery underwent cross-sectional evaluation using the SF-36. Significant differences were seen in several domains, including bodily pain, general health, vitality, and social functioning, compared with the eight subscales of general health assessment with similarly derived data for the American general population (48). Comparisons with other chronic diseases revealed increase bodily pain and worse social functioning for CRS patients than in patients with congestive heart failure, angina, chronic obstructive pulmonary disease, and back pain. These findings suggest that the national health impact of CRS is far greater than is currently appreciated.

The effect of surgical treatment was also studied with generic questionnaires pre- and postoperatively. Winstead and Barnett (44) showed a significant improvement in patients with CRS ($n = 125$) at 6 and 12 months following endoscopic sinus surgery (ESS) for all SF-36 domains and, at follow-up, QoL scores did not significantly differ from those of the American general population. Gliklich and Metson found that patients with CRS ($n = 108$) presented a significant improvement after sinus surgery in six SF-36 domains reaching near-normative levels (43). Comparing patients with CRS ($n = 123$) with the norm-based scores, both women's and men's SF-36 scores reached normal levels in seven domains after 3 months endonasal sinus surgery (47).

Table 2. Generic quality of life (QoL) questionnaires in chronic rhinosinusitis with and without nasal polyposis

Study	Disease	Patients number	Treatment	Time of treatment	QoL questionnaire	Impact on QoL	Level of evidence
Gliklich and Metson (38)	CRS†	158	Not defined‡	Not applicable	SF-36	Decreased levels	III
Gliklich and Metson (43)	CRS†	108	Surgery	12 months	SF-36	Decrease preop, improve postop	IIb
Winstead and Barnett (44)	CRS†	125	Surgery	6, 12 months	SF-36	Decrease preop, improve postop	IIb
Radenne et al. (10)	CRS + NP	49	Steroids vs surgery	6, 12 months	SF-36	Decrease pretreatment, improve posttreatment	IIa
Cunningham et al. (33)	CRS†	21	Surgery	Not applicable	CHQ	Decreased levels	III
van Agthoven et al. (55)	CRS†	56	Filgrastim	6 months	EQ-5D, SF-36, MPQ	Decrease pretreatment, improve after treatment	Ib
Salhab et al. (56)	CRS†	121	Surgery	6 months	GBI	Decrease preop, improve postop	IIb
Baumann and Blumenstock (47)	CRS†	123	Surgery	3 months	SF-36, EQ-5D	Decrease preop, improve postop	III
Alobid et al. (9)	CRS + NP	109	Steroids vs surgery	6, 12 months	SF-36	Decrease preop, improve postop	Ib
Alobid et al. (8)	CRS + NP	130	Not defined‡	Not applicable	SF-36	Negative impact of asthma and atopy	III
Atlas et al. (53)	CRS†	50	Surgery	3 months	SF-12	Decrease preop, improve post-op	IIb
Videler et al. (54)	CRS†	23	Surgery	12, 24 months	SF-36, MPQ	Decrease preop, improve postop	IIb
Alobid et al. (49)	CRS + NP	78	Oral and intranasal steroids	3, 6, 12 months	SF-36	Decrease pretreatment, improve after treatment	Ib
Newton et al. (57)	CRS†	50	Surgery	6, 12, 24 months	GBI	Decrease preop, improvements in total and general scores	IIb

CHQ, child health questionnaire; CRS, chronic rhinosinusitis; EQ-5D, EuroQol 5D; GBI, Glasgow benefit inventory; MPQ, McGill pain questionnaire; NP, nasal polyposis; QoL, quality of life; SF-36, short form-36 health survey; SF-12, short form-12.

†Studies including patients with and without nasal polyposis.

‡Studies containing both treated and nontreated patients.

Until recently, there was a lack of evaluable data on NP and QoL, with no adequate randomized trials. Only a few studies have provided some information about the effect of treatment of nasal polyps. Radenne et al. (10) investigated the impact of nasal polyps on QoL in patients ($n = 49$), in which the SF-36 questionnaire showed a high internal validity and reliability and that NP impaired QoL to a greater degree than perennial allergic rhinitis. More recently, Alobid et al. (49) demonstrated that QoL was impaired in patients with NP ($n = 109$) compared with the general population. Impairment was observed in all SF-36 domains except for physical functioning, which the impact on mental health was higher than on physical health. No correlation was found between QoL and age, gender, nasal symptoms, CT scan, and polyp size (49). Patients with nasal polyps had lower scores in all SF-36 domains except for physical functioning and general health than those reported for patients with chronic obstructive pulmonary disease (50), coronary artery disease (51), and asthma (52). In patients with NP ($n = 130$), asthma and atopy had an additional negative impact on QoL scores in role physical, bodily pain, vitality, and mental health, whereas aspirin sensitivity had no additional impact on QoL (8). Alobid et al. demonstrated a significant improvement in patients with NP ($n = 109$) on all SF-36 domains after both medical (oral steroids during 2 weeks and intranasal steroids during 12 months) and surgical (ESS followed by intranasal steroids during 12 months) treatment reaching the QoL level of the general population (9). One of the limitations of these studies using oral

steroids is the absence of specific instruments. It is difficult to know if the improvement of QoL is due to improvement of general state or nasosinusual symptom.

Short form-12 health survey. Using SF-12, Atlas et al. (53) studied the impact of CRS on QoL in comparison with RhinoQoL questionnaire in patients with CRS ($n = 50$). In this study, the SF-12 physical component score strongly correlated with the symptom impact score, whereas the SF-12 mental component score showed a low correlation with the disease-specific measures but correlating with symptoms (54).

McGill pain questionnaire. In patients who underwent Denker's procedure for refractory CRS ($n = 23$), QoL and pain were evaluated before surgery and after 12 months and 2 years of surgery with MPQ. A significant improvement in pain and most of the subscores after surgery was observed (55).

EuroQol 5D. Van Agthoven et al. investigated the influence of filgrastim administration on the QoL of refractory CRS patients ($n = 56$) who did not respond to regular treatments (55). The QoL was assessed with EuroQol, SF-36, and MPQ after 24 weeks. The QoL scores were reduced to the normative levels of general population and to the scores of patients with CRS undergoing sinus surgery. Although none of the differences were statistically significant, QoL scores of the filgrastim group suggested a better QoL than the placebo group. In addition, Baumann and Blumenstock demonstrated that, compared with male patients, female patients with CRS

($n = 123$) scored significantly worse in all SF-36 and in one domain of EQ-5D (47).

Glasgow benefit inventory. The GBI scores were mainly positive after functional ESS, indicating a benefit from the surgery. On comparing CRS patients with and without NP ($n = 121$), the difference in the total GBI and general subscale scores indicated a greater benefit for patients with nasal polyps (56). Newton et al. studied consecutive CRS patients with and without NP ($n = 50$). The patients were divided into three groups according to the time period elapsed since surgery (i.e., 6 months, 12 months, or up to 2 years). The GBI scores indicated a benefit from the procedure. Overall, surgery led to statistically significant improvements in both total and general GBI scores (57).

Child health questionnaire. Using CHQ, Cunningham et al. (33) demonstrated significant decrements in the general health of 21 children with recurrent CRS compared with a normative sample for both child- and parent-reported data, particularly in the physical domains. Children with CRS were perceived by their parents to have significantly more bodily pain and to

be more limited in their physical activities than children with asthma, juvenile rheumatoid arthritis, and other chronic disorders. Parent-child perceptions varied with parents reporting more pain and general behavioral effects relative to their children's reports in these areas (33).

Specific questionnaires

Several specific questionnaires for patients with CRS have been developed. In these questionnaires, specific symptoms for rhinosinusitis such as nasal blockage, loss of smell, rhinorrhea, headache, facial pain, and sneezing are included. They are usually more sensitive than general health status instruments. However, no validated disease-specific instruments were available to assess patient-oriented QoL in patients with NP. In addition, there were insufficient data to assess the effect of gender, duration of therapy, or comorbidity with asthma or aspirin sensitivity on QoL (Table 3).

Rhinosinusitis disability index. The RSDI has been used to evaluate patients with a variety of nasal disorders, sinus disorders, or both and to compare the impact of

Table 3. Specific quality of life (QoL) questionnaires in chronic rhinosinusitis with and without nasal polyposis

Study	Disease	Patients number	Treatment	Time of treatment	QoL questionnaire	Impact on QoL	Level of evidence
Gliklich and Metson (38)	CRS†	104	Surgery	6 months	CSS	Decrease preop, improve post-op	IIb
Anderson et al. (37)	CRS†	47	Local steroids vs surgery	6, 12 weeks	SNOT-16, SF-36	Decrease at baseline, improvement after medical and surgical treatment	IIb
Senior et al. (58)	CRS†	292	Not defined‡	Not applicable	RSDI	Greatest level of disability	III
Birch et al. (60)	CRS†	53	Not defined‡	Not applicable	RSDI	Decreased levels	III
Piccirillo et al. (36)	CRS†	102	Local steroids	6, 12 months	SNOT-20	Decrease at baseline, improvement after treatment	IIb
Kay and Rosenfeld (40)	CRS	85	Not defined‡	Not applicable	SN-5	Decreased levels	IIb
Ragab et al. (65)	CRS†	90	Local steroids vs surgery	6, 12 months	SNOT-20, SF-36	Decrease at baseline, improvement after medical and surgical treatment	Ib
Nathan et al. (41)	CRS	114	Immunotherapy + antibiotics	12 months	SOQ	Decrease at baseline, improvement after treatment	IIb
Briggs et al. (67)	CRS†	82	Surgery	Average of 52 months	SNOT-16	Decrease at baseline; smoking is associated with worse outcomes	IIb
Atlas et al. (53)	CRS	50	Surgery	3 months	RhinoQoL	Decrease preop, improve post-op	IIb
Javer and Genoway (61)	CRS†	95	Surgery	6, 12, 36 months	RSOM-31	Decrease preop, improve post-op	Ib
Ebbens et al. (62)	CRS†	116	Amphotericin nasal lavage	13 weeks	RSOM-31, SF-36	Decrease at baseline, no improvement after treatment	Ib (-)
Hissaria et al. (63)	CRS + NP	40	Oral steroids	2 weeks	RSOM-31	Decrease at baseline, improvement after treatment	Ib
Friedman et al. (69)	CRS	42	Nasal irrigation	1, 4 weeks	RQLQ	Decrease at baseline, improve only Dead Sea salt solution group	Ib
Wallwork et al. (64)	CRS†	64	Roxithromycin	3 months	SNOT-20	Decrease at baseline, improvement after treatment	Ib
Robinson et al. (59)	CRS†	123	Surgery	18 months	RSDI, CSS	Decrease preop, improve postop	III
Rudnick and Mitchell (68)	CRS	22	Surgery	6, 24 months	SN-5	Decrease preop, improve postop	Ib

CRS, chronic rhinosinusitis; NP, nasal polyposis; QoL, quality of life; RhinoQoL, rhinosinusitis quality of life survey; RQLQ, rhinoconjunctivitis quality of life questionnaire; RSDI, rhinosinusitis disability index; RSOM-31, rhinosinusitis outcome measure 31; SNOT-16, sinonasal outcome test 16; SNOT-20, sinonasal outcome test 20; SN-5, sinonasal 5 survey; SOQ, sinusitis outcomes questionnaire.

†Studies including patients with and without nasal polyposis.

‡Studies containing both treated and nontreated patients, (-) study with negative outcome.

these disorders on the physical, functional, and emotional QoL domains. Senior et al. have found that individuals with rhinologic disease in general have lower physical scores, followed by functional scores and emotional scores. Patients with CRS and allergic rhinitis ($n = 292$) had the greatest level of disability, whereas those with aspirin triad were the least affected (58). Using RSDI, similar proportions of ASA-tolerant ($n = 19$) and ASA-intolerant patients ($n = 104$) with CRS showed improvement on QoL measures after ESS (18 months) (59). Birch et al. (60) studied patients with CRS ($n = 53$) and demonstrated no correlation between the endoscopic score and either the patient's self-rated symptom score or RSDI score. However, there was a significant correlation between the self-rated symptom score and total QoL score (60).

Rhinosinusitis outcome measure. Javer and Genoway studied patients with CRS ($n = 95$) and demonstrated that QoL restrictions in patients with CRS were greatest for the RSOM-31 in the areas of nasal symptoms and sleep deprivation, which were significantly improved by ESS (61). Ebbens et al. studied the effect of intranasal treatment with amphotericin B compared with placebo in patients with CRS with and without NP ($n = 116$). The authors demonstrated that QoL measured by RSOM-31 were similar in both treatment groups at the time of randomization, and no significant differences were observed after 12 weeks of treatment (62). Hissaria et al. (63) studied the effect of a short course of oral prednisolone in ameliorating symptoms and improving QoL of patients with sinonasal polyposis ($n = 20$) compared with placebo. The RSOM-31 improved in both groups, but the prednisolone-treated group had a significantly greater improvement than the placebo group. However, the subset of nasal-specific RSOM scores (six parameters) showed a significant improvement only in the prednisolone group (63).

Sinonasal outcome test 20. The SNOT-20 is a valid outcome measure for patients with rhinosinusitis, describes the health burden, and is sensitive to clinical change (36). Wallwork et al. found a significant improvement in SNOT-20 score after 3 months of macrolide treatment (150 mg roxithromycin daily) in patients with CRS ($n = 64$) (64). In a randomized study, Ragab et al. (65) compared the medical (erythromycin 500 mg twice daily for 2 weeks, followed by 250 mg twice daily for 10 weeks) and surgical treatment of CRS using subjective and objective parameters including QoL. The authors administered SNOT-20 to patients with CRS ($n = 90$) before starting the treatment, after 6 months, and, finally, after 12 months. They concluded that both the medical and surgical treatment significantly improved QoL (65). Using SNOT-22, nasal polypectomy with additional surgery

seems to have no benefit over simple polypectomy in terms of health-related QoL improvement for patients with NP (66).

Sinonasal outcome test 16. Patients with CRS ($n = 47$) demonstrated excellent discriminant validity, and mean total SNOT-16 scores being significantly correlated with patient-reported overall health and bother at 6 and 12 weeks (37). Briggs et al. (67) studied patients with CRS ($n = 82$) and investigated whether smoking patients have poorer outcomes after ESS based on a reliable validated rhinosinusitis-specific QoL outcome test. They concluded that smoking is statistically associated with worse outcomes after ESS based on average SNOT-16 scores (67).

Chronic sinusitis survey. Gliklich and Metson investigated the symptom-based surveys in a prospective manner in patients with CRS ($n = 104$) before sinus surgery. They demonstrated that CSS is an efficient and reliable method to measure health status and health-related QoL outcomes in patients with CRS (38).

Rhinosinusitis quality of life survey. It can be used for acute and chronic sinusitis. Atlas et al. (39) investigated the validity and responsiveness of the RhinoQoL questionnaire. Patients with acute sinusitis ($n = 47$) and patients with CRS ($n = 50$) were compared with patients with allergic rhinitis ($n = 18$) and patients without nasal symptoms ($n = 60$). Patients with CRS undergoing ESS were assessed for symptoms and QoL, at baseline and 3 months postsurgery. Internal consistency was high for the symptom impact scale. The symptom frequency and, in particular, bothersomeness scales had lower internal consistency. The RhinoQoL demonstrated excellent responsiveness to change over time associated with surgery (39).

SN-5 quality of life survey. Kay and Rosenfeld try to validate the SN-5 survey as a measure of longitudinal change in health-related QoL for children aged 2–12 years with CRS symptoms ($n = 85$) (40). Children caregivers completed the SN-5 survey at entry and at least 4 weeks later. The survey included five symptom-cluster items covering the domains of sinus infection, nasal obstruction, allergy symptoms, emotional distress, and activity limitations. The authors concluded that the SN-5 was a valid, reliable, and responsive measure of QoL for children with persistent sinonasal symptoms, suitable for use in outcomes studies and routine clinical care (40). To study changes in QoL in children with CRS after surgical therapy, Rudnick and Mitchell demonstrated that CRS severely impacts QoL in children ($n = 22$) as documented by caregivers using the SN-5 questionnaire. After 24 months, either adenoidectomy or ESS, caregivers report a dramatic improvement in children's QoL (68).

Sinusitis outcomes questionnaire. The SOQ is a high-quality, user-friendly outcome instrument that can be inexpensively used. The SOQ data collected by Nathan et al. (41) support immunotherapy as an effective method for treating allergic rhinitis patients with CRS ($n = 114$) documented by history and imaging. Immunotherapy was associated not only with a reduction in symptoms, but also with a decrease in the use of more expensive healthcare resources, including antibiotics and sinus surgical procedures. Immunotherapy also improved QoL and overall health as evidenced by a decrease in absenteeism from work or school (41).

Rhinoconjunctivitis quality of life questionnaire. Friedman et al. (69) presented a short-term study providing evidence on the superiority of hypertonic Dead Sea salt solution over saline nasal irrigation for treatment of CRS patients with and without allergic rhinitis ($n = 42$). Patients were reassessed weekly and at 1 month. Both groups of treatment had similar symptoms and RQLQ scores at baseline and showed a significant improvement after treatment. The CRS patients treated with Dead Sea salt solution showed a better relief of symptoms compared with the CRS patients treated with saline nasal irrigation, and only the former group showed improved RQLQ scores (69).

Bronchiectasis and quality of life

Bronchiectasis consists of a permanent and irreversible destruction and dilatation of bronchi and bronchioles because of retained secretions and recurrent infections that cause inflammation, obstruction, and damage of the lower airway. Guilemany et al. (70) investigated the impact of bronchiectasis on QoL in patients with and without NP using SF-36 questionnaire. The three most disabling symptoms were anterior rhinorrhea, posterior rhinorrhea, and nasal obstruction. Patients with bronchiectasis and mild-moderate nasal polyps showed no further negative impact on QoL. Patients with bronchiectasis and nasal polyps had a higher nasal obstruction and loss of sense of smell that provoked no significant differences on QoL compared with patients without NP (70). This study provides additional evidence that the degree of abnormality of nasal symptoms is not associated with impairment of QoL measured by SF-36.

Cystic fibrosis and quality of life

Cystic fibrosis is the most common fatal, autosomal recessive disorder in Caucasian populations. The incidence is 1 in 3400 live births in the USA, and it is estimated that approximately 10 million individuals worldwide are carriers of the recessive gene (71). Cystic fibrosis is a complex, progressive disease that affects the exocrine glands of major organs, including those of the

respiratory, digestive, pancreas, liver, kidney, and reproductive systems. Treatment of the disease involves a multicomponent regimen, including airway clearance techniques, aerosol medications, inhalers, pancreatic enzymes, increased calorie intake, and antibiotics. There are many CF questionnaires (CFQ) to measure QoL for adolescents and adults with CF (72, 73).

Cystic fibrosis questionnaire-child version. Cystic fibrosis-specific QoL was measured using the CFQ-child version (CFQ-C). This measure is administered directly to children aged 6–13 years and consists of 36 items. These items assess the following seven QoL generic and disease-specific domains: physical functioning (eight items), energy and well-being (six items), emotional state (five items), social limitations (four items), body image (three items), eating disturbances (three items), and treatment constraints (two items). Two additional symptom scales, respiratory (four items) and digestive (one item), are also included. Two practice questions are used with colored rating cards to train the child on both types of response choices. The cards are used as reminders during administration of the questionnaire.

Cystic fibrosis questionnaire-parent version. Parents' report of their child's disease-specific QoL was measured using the CFQ-parent version (CFQ-P), a self-report measure consisting of 44 items. These items assess the following seven QoL domains: physical functioning (nine items), energy and well-being (six items), emotional state (four items), performance at school (four items), body image (three items), eating disturbances (two items), and treatment constraints (two items). Three symptom scales, respiratory (seven items), digestive (two items), and weight (one item), and an overall health perception scale (four items) are also included. This measure takes approximately 15–20 min to be completed.

Cystic fibrosis questionnaire-14+. An adolescent/adult form of the CFQ was developed to measure perceptions of QoL for teens and young adults with CF. This self-report measure consists of 48 items. In this version, however, nine QoL dimensions are assessed: physical functioning (eight items), energy and well-being (four items), emotional state (five items), social limitations (four items), role limitations (three items), body image (three items), eating disturbances (two items), treatment constraints (two items), and embarrassment (three items). Three symptom scales, respiratory (seven items), digestive (two items), and weight (one item), and an overall health perception scale (four items) are also included. The CFQ-14+ takes 15–20 min to be completed. The CF severity has an impact on QoL in adolescents and adults with CF. Some differences emerged between males and females, with females generally reporting poorer QoL. Evidence indicated that males and females perceived their health status

differently, with females having a more accurate perception of objective clinical health status (74).

Friedman and Stewart (75) studied the influence of status of the sinuses on the status of the lungs in patients with CF using SNOT-16 scores compared with FEV1. The severity of sinus disease correlated with the severity of lung disease in patients with CF under the age of 12.

Conclusions

- Quality of life has been defined as 'the functional effects of an illness and its consequent therapy upon a patient as perceived by the patient'.
- Specific QoL questionnaires are usually focused on one particular area such as a disease state, a selected population, or a certain function or problem.

References

- Polzehl D, Moeller P, Riechelmann H, Perner S. Distinct features of chronic rhinosinusitis with and without nasal polyps. *Allergy* 2006;**61**:1275–1279.
- Melen I. Chronic sinusitis: clinical and pathophysiological aspects. *Acta Otolaryngol* 1994;**515**:45–48.
- Kaliner MA, Osguthorpe JD, Fireman P, Anon J, Georgitis J, Davis ML et al. Sinusitis: bench to bedside – current findings, future directions. *J Allergy Clin Immunol* 1997;**99**:S829–S848.
- Fokkens W, Lund V, Mullol J, on behalf of the European Position Paper on Rhinosinusitis and Nasal Polyps Group. EP3OS 2007: European position paper on rhinosinusitis and nasal polyps 2007. A summary for otorhinolaryngologists. *Rhinology* 2007;**45**:97–101.
- Fokkens W, Lund V, Bachert C, Clement P, Hellings P, Holmstrom M et al. EAACI position paper on rhinosinusitis and nasal polyps executive summary. *Allergy* 2005;**60**:583–601.
- Settipane GA. Epidemiology of nasal polyps. *Allergy Asthma Proc* 1996;**17**:231–236.
- Demoly P, Crampette L, Daures JP. National survey on the management of rhinopathies in asthma patients by French pulmonologists in everyday practice. *Allergy* 2003;**58**:233–238.
- Alobid I, Benitez P, Bernal-Sprekelsen M, Guilemany JM, Picado C, Mullol J. The impact of asthma and aspirin sensitivity on quality of life of patients with nasal polyposis. *Qual Life Res* 2005;**14**:789–793.
- Alobid I, Benitez P, Bernal-Sprekelsen M, Roca J, Alonso J, Picado C et al. Nasal polyposis and its impact on quality of life. Comparison between the effects of medical and surgical treatments. *Allergy* 2005;**125**:215–219.
- Radenne F, Lamblin C, Vandezande LM, Tillie-Leblond I, Darras J, Tonnel AB et al. Quality of life in nasal polyposis. *J Allergy Clin Immunol* 1999;**104**:79–84.
- Tahamiler R, Canakcioglu S, Ogreden S, Acioglu E. The accuracy of symptom-based definition of chronic rhinosinusitis. *Allergy* 2007;**62**:1029–1032.
- Wabnitz DA, Nair S, Wormald PJ. Correlation between preoperative symptom scores, quality-of-life questionnaires, and staging with computed tomography in patients with chronic rhinosinusitis. *Am J Rhinol* 2005;**19**:91–96.
- Sloan JA, Symonds T, Vargas-Chanes D, Friedly B. Practical guidelines for assessing the clinical significance of health related quality of life changes within clinical trials. *Drug Inf J* 2003;**37**:23–31.
- Juniper EF, Guyatt GH, Willan A, Griffith LE. Determining a minimal important change in a disease-specific quality of life questionnaire. *J Clin Epidemiol* 1994;**47**:81–87.
- Tarlov AR, Ware JE Jr, Greenfield S, Nelson EC, Perrin E, Zubkoff M. The Medical Outcomes Study. An application of methods for monitoring the results of medical care. *JAMA* 1989;**262**:925–930.
- Schipper HCJ, Powell V. Definitions and conceptual issues. In: Spilker B, editor. *Quality of life assessment in clinical trials*. New York: Raven Press, 1990:11–24.
- Juniper EF. Measuring health-related quality of life in rhinitis. *J Allergy Clin Immunol* 1997;**99**:742–749.
- Lund VJ. Health related quality of life in sinonasal disease. *Rhinology* 2001;**39**:182–186.
- Yueh B, Feinstein AR. Abstruse comparisons: the problems of numerical contrasts of two groups. *J Clin Epidemiol* 1999;**52**:13–18.
- Meltzer EO, Hamilos DL, Hadley JA, Lanza DC, Marple BF, Nicklas RA et al. Rhinosinusitis: establishing definitions for clinical research and patient care. *J Allergy Clin Immunol* 2004;**114**:155–212.
- van Oene CM, van Reij EJ, Sprangers MA, Fokkens W. Quality-assessment of disease-specific quality of life questionnaires for rhinitis and rhinosinusitis: a systematic review. *Allergy* 2007;**62**:1359–1371.
- Muldoon MF, Barger SD, Flory JD, Manuck SB. What are quality of life measurements measuring? *BMJ* 1998;**316**:542–545.
- Bland JM, Altman DG. Cronbach's alpha. *BMJ* 1997;**314**:572.
- Husted JA, Cook RJ, Farewell VT, Gladman DD. Methods for assessing responsiveness: a critical review and recommendations. *J Clin Epidemiol* 2000;**53**:459–468.

25. Ware JE, Sherbourne CD. The MOS 36-item short form health survey. I. Conceptual framework and item selection. *Med Care* 1992;**30**:473–483.
26. Aaronson NK, Acquadro C, Alonso J, Apolone G, Bucquet D, Bullinger M et al. International Quality of Life Assessment (IQOLA) Project. *Qual Life Res* 1992;**1**:349–351.
27. Ware JE Jr, Kosinski M, Keller SD. A 12 Item Short Form Health Survey: Construction of scales and preliminary tests of reliability and validity. *Med Care* 1996;**34**:220–233.
28. Melzack R. The McGill Pain Questionnaire: major properties and scoring methods. *Pain* 1975;**1**:277–299.
29. Melzack R. The short-form McGill Pain Questionnaire. *Pain* 1987;**30**:191–197.
30. The EuroQol Group. EuroQol: A new facility for the measurement of health-related quality of life. *Health Policy* 1990;**16**:199–208.
31. Robinson K, Gatehouse S, Browning GG. Measuring patient benefit from otorhinolaryngological surgery and therapy. *Ann Otol Rhinol Laryngol* 1996;**105**:415–422.
32. Landgraf JM, Abetz L, Ware JE. The CHQ User's Manual. 1st ed. Boston, Mass: The Health Institute, New England Medical Center; 1996.
33. Cunningham JM, Chiu EJ, Landgraf JM, Gliklich RE. The health impact of chronic recurrent rhinosinusitis in children. *Arch Otolaryngol Head Neck Surg* 2000;**126**:1363–1368.
34. Benninger MS, Senior BA. The development of the Rhinosinusitis Disability Index. *Arch Otolaryngol Head Neck Surg* 1997;**123**:1175–1179.
35. Piccirillo JF ED, Haiduk A. Psychometric and clinimetric validity of the 3-item rhinosinusitis outcome measure (RSOM-31). *Am J Rhinol* 1995;**9**:297–306.
36. Piccirillo JF, Merritt MG Jr, Richards ML. Psychometric and clinimetric validity of the 20-item Sino-Nasal Outcome Test (SNOT-20). *Otolaryngol Head Neck Surg* 2002;**126**:41–47.
37. Anderson ER, Murphy MP, Weymuller EA Jr. Clinimetric evaluation of the Sinonasal Outcome Test-16. Student Research Award 1998. *Otolaryngol Head Neck Surg* 1999;**121**:702–707.
38. Gliklich RE, Metson R. Techniques for outcomes research in chronic sinusitis. *Laryngoscope* 1995;**105**:387–390.
39. Atlas SJ, Gallagher PM, Wu YA, Singer DE, Gliklich RE, Metson RB et al. Development and validation of a new health-related quality of life instrument for patients with sinusitis. *Qual Life Res* 2005;**14**:1375–1386.
40. Kay DJ, Rosenfeld RM. Quality of life for children with persistent sinonasal symptoms. *Otolaryngol Head Neck Surg* 2003;**128**:17–26.
41. Nathan RA, Santilli J, Rockwell W, Glassheim J. Effectiveness of immunotherapy for recurring sinusitis associated with allergic rhinitis as assessed by the Sinusitis Outcomes Questionnaire. *Ann Allergy Asthma Immunol* 2004;**92**:668–672.
42. Juniper EF, Guyatt GH. Development and testing of a new measure of health status for clinical trials in rhinoconjunctivitis. *Clin Exp Allergy* 1991;**21**:77–83.
43. Gliklich RE, Metson R. Effect of sinus surgery on quality of life. *Otolaryngol Head Neck Surg* 1997;**117**:12–17.
44. Winstead W, Barnett S. Impact of endoscopic sinus surgery on global health perception: an outcomes study. *Otolaryngol Head Neck Surg* 1998;**119**:486–491.
45. Durr DG, Desrosiers MY, Dassa C. Quality of life in patients with rhinosinusitis. *J Otolaryngol* 1999;**28**:108–111.
46. Wang PC, Tai CJ, Lin MS, Chu CC, Liang SC. Quality of life in Taiwanese adults with chronic rhino-sinusitis. *Qual Life Res* 2003;**12**:443–448.
47. Baumann I, Blumenstock G. Impact of gender on general health-related quality of life in patients with chronic sinusitis. *Am J Rhinol* 2005;**19**:282–287.
48. Gliklich RE, Metson R. The health impact of chronic sinusitis in patients seeking otolaryngologic care. *Otolaryngol Head Neck Surg* 1995;**113**:104–109.
49. Alobid I, Benítez P, Valero A, Berenguer J, Bernal-Sprekelsen M, Picado C et al. The impact of atopy, sinus opacification, and nasal patency on quality of life in patients with severe nasal polyposis. *Otolaryngol Head Neck Surg* 2006;**134**:609–612.
50. Alonso J, Prieto L, Ferrer M, Vilagut G, Broquetas JM, Roca J et al. Testing the measurement properties of the Spanish version of the SF-36 Health Survey among male patients with chronic obstructive pulmonary disease. Quality of life in COPD study group. *J Clin Epidemiol* 1998;**51**:1087–1094.
51. Failde I, Ramos I. Validity and reliability of the SF-36 health survey questionnaire in patients with coronary artery disease. *J Clin Epidemiol* 2000;**53**:359–365.
52. Espinosa De Los Monteros MJ, Alonso J, Ancochea J, Gonzalez A. Quality of life in asthma: reliability and validity of the short form generic questionnaire (SF-36) applied to the population of asthmatics in a public health area. *Arch Bronconeumol* 2002;**38**:4–9.
53. Atlas SJ, Metson RB, Singer DE, Wu YA, Gliklich RE. Validity of a new health-related quality of life instrument for patients with chronic sinusitis. *Laryngoscope* 2005;**115**:846–854.
54. Videler WJ, van Drunen CM, van der Meulen FW, Fokkens WJ. Radical surgery: effect on quality of life and pain in chronic rhinosinusitis. *Otolaryngol Head Neck Surg* 2007;**136**:261–267.
55. van Agthoven M, Fokkens WJ, van de Merwe JP, Marijke van Bolhuis E, Uyl-de Groot CA, Busschbach JJ. Quality of life of patients with refractory chronic rhinosinusitis: effects of filgrastim treatment. *Am J Rhinol* 2001;**15**:231–237.
56. Salhab M, Matai V, Salam MA. The impact of functional endoscopic sinus surgery on health status. *Rhinology* 2004;**42**:98–102.
57. Newton JR, Shakeel M, Ram B. Evaluation of endoscopic sinus surgery by Glasgow benefit inventory. *J Laryngol Otol* 2007;**25**:1–4.
58. Senior BA, Glaze C, Benninger MS. Use of the Rhinosinusitis Disability Index (RSDI) in rhinologic disease. *Am J Rhinol* 2001;**15**:15–20.
59. Robinson JL, Griest S, James KE, Smith TL. Impact of aspirin intolerance on outcomes of sinus surgery. *Laryngoscope* 2007;**117**:825–830.
60. Birch DS, Saleh HA, Wodehouse T, Simpson IN, Mackay IS. Assessing the quality of life for patients with chronic rhinosinusitis using the 'Rhinosinusitis Disability Index'. *Rhinology* 2001;**39**:191–196.
61. Javer AR, Genoway KA. Patient quality of life improvements with and without computer assistance in sinus surgery: outcomes study. *J Otolaryngol* 2006;**35**:373–379.
62. Ebbens FA, Scadding GK, Badia L, Hellings PW, Jorissen M, Mullol J et al. Amphotericin B nasal lavages: not a solution for patients with chronic rhinosinusitis. *J Allergy Clin Immunol* 2006;**118**:1149–1156.
63. Hissaria P, Smith W, Wormald PJ, Taylor J, Vadas M, Gillis D et al. Short course of systemic corticosteroids in sinonasal polyposis: a double-blind, randomized, placebo-controlled trial with evaluation of outcome measures. *J Allergy Clin Immunol* 2006;**118**:128–133.
64. Wallwork B, Coman W, Mackay-Sim A, Greiff L, Cervin A. A double-blind, randomized, placebo-controlled trial of macrolide in the treatment of chronic rhinosinusitis. *Laryngoscope* 2006;**116**:189–193.

65. Ragab SM, Lund VJ, Scadding G. Evaluation of the medical and surgical treatment of chronic rhinosinusitis: a prospective, randomised, controlled trial. *Laryngoscope* 2004;**114**:923–930.
66. Browne JP, Hopkins C, Slack R, Topham J, Reeves B, Lund V et al. Health-related quality of life after polypectomy with and without additional surgery. *Laryngoscope* 2006; **116**:297–302.
67. Briggs RD, Wright ST, Cordes S, Calhoun KH. Smoking in chronic rhinosinusitis: a predictor of poor long-term outcome after endoscopic sinus surgery. *Laryngoscope* 2004;**114**:126–128.
68. Rudnick EF, Mitchell RB. Long-term improvements in quality-of-life after surgical therapy for pediatric sinonasal disease. *Otolaryngol Head Neck Surg* 2007;**137**:873–877.
69. Friedman M, Vidyasagar R, Joseph N. A randomized, prospective, double-blind study on the efficacy of Dead Sea salt nasal irrigations. *Laryngoscope* 2006;**116**:878–882.
70. Guilemany JM, Alobid I, Angrill J, Ballesteros F, Bernal-Sprekelsen M, Picado C et al. The impact of bronchiectasis associated to sinonasal disease on quality of life. *Respir Med* 2006;**100**: 1997–2003.
71. Kosorok MR, Wei WH, Farrell PM. The incidence of cystic fibrosis. *Stat Med* 1996;**15**:449–462.
72. Henry B, Aussage P, Grosskopf C, Goehrs JM. Development of the Cystic Fibrosis Questionnaire (CFQ) for assessing quality of life in pediatric and adult patients. *Qual Life Res* 2003;**12**:63–76.
73. Quittner AL, Sweeny S, Watrous M, Munzenberger P, Bearss K, Gibson Nitza A et al. Translation and linguistic validation of a disease-specific quality of life measure for cystic fibrosis. *J Pediatr Psychol* 2000;**25**:403–414.
74. Gee L, Abbott J, Conway SP, Etherington C, Webb AK. Quality of life in cystic fibrosis: the impact of gender, general health perceptions and disease severity. *J Cyst Fibros* 2003;**2**: 206–213.
75. Friedman EM, Stewart M. An assessment of sinus quality of life and pulmonary function in children with cystic fibrosis. *Am J Rhinol* 2006;**20**:568–572.