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Quality of life in allergic rhinitis

Tunis Ozdoganoglu, Murat Songu and Hasan Mete Inancli

Abstract: Allergic rhinitis is a global health problem that causes major illness and disability worldwide. Although nasal and nonnasal symptoms are directly attributable to inflammation in the upper respiratory tract, individuals also experience generalized symptoms that include fatigue, mood changes, depression, anxiety and impairments of work and school performance, and cognitive function. Health-related quality of life focuses on patients' perceptions of their disease and measures impairments that have a significant impact on the patient. The burden of disease, as the patient perceives it, forms the basic motivation to seek medical aid or to undergo therapy. Adherence to therapy requires changes in health, perceived by patients as relevant and outweighing eventual disadvantages of intervention. Because so many factors are involved in health-related quality of life, there are multiple ways in which it can be measured. A variety of validated and standardized questionnaires have been developed including assessments of school performance, work performance, productivity, and other parameters that quantify the impact of allergic rhinitis and its treatment on quality of life. The aim of this review is to highlight the impact of allergic rhinitis on the quality of life and to analyze the most commonly used health-related quality of life instruments.

Keywords: generic questionnaires, health-related quality of life, intermittent allergic rhinitis, perennial allergic rhinitis, persistent allergic rhinitis, quality of life, seasonal allergic rhinitis, specific questionnaires

Introduction

Allergic rhinitis (AR) is a symptomatic disorder of the nose induced after allergen exposure by an immunoglobulin E (IgE)-mediated inflammation of the membranes lining the nose [Bousquet *et al.* 2008]. AR is a global health problem that causes major illness and disability worldwide. Patients from all countries, all ethnic groups and of all ages suffer from AR. Prevalence studies suggest that the prevalence of AR varies somewhat by country, but generally affects over 20% of both the adult and the pediatric population [Cingi *et al.* 2010]. In some countries, over 50% of adolescents are reporting symptoms of AR [Sears *et al.* 1993]. Using a conservative estimate, AR occurs in over 500 million people around the world. The prevalence of AR is increasing in most countries of the world, and particularly in areas with low or medium levels of prevalence.

AR is generally classified by expression of a cluster of four common nasal symptoms: sneezing, nasal itching, rhinorrhea, and nasal congestion

[Lierl, 1995]. In addition to these nasal symptoms, patients also complain of local, nonnasal symptoms, including tearing, itching of the eyes and palate, and conjunctival irritation and erythema. Although these nasal and nonnasal symptoms are directly attributable to inflammation in the upper respiratory tract, individuals often also experience generalized symptoms that include fatigue and mood changes, as well as impairment of cognitive function, depression and anxiety. Impairments on work and school performance are common in patients with moderate to severe symptoms.

The definition of quality of life (QOL) is offered by the World Health Organization: 'QOL includes psychological and social functioning as well as physical functioning and incorporates positive aspects of well-being as well as negative aspects of disease or infirmity'. This definition of QOL has a common basis with the definition of health given by the WHO in 1948: 'Health is a state of complete physical, mental, and social

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well-being and not merely the absence of disease'. Health-related quality of life (HRQOL) is a broad concept which can be defined as the patient's subjective perception of the impact of their disease and its treatment(s) on their daily life, physical, psychological and social functioning and well-being. HRQOL focuses on the part of QOL that is influenced by a disease: the functional effects of an illness and effects of its treatment on a patient, as perceived by the patient [Schipper and Powell, 1990]. Only one domain such as fatigue or psychological aspects cannot be considered as a measure of HRQOL, it is a multi-dimensional notion that describes the state of QOL. Also HRQOL should be clearly differentiated from the core symptoms of a disease (e.g. pain, migraine, pyrosis, etc.) assessed by the patient himself which are well-accepted primary and secondary efficacy endpoints in registration trials [EMA, 2007]. During the last three decades the focus on HRQOL has been increased in clinical research studies. Numerous questionnaires to measure the impact of a given disease have been developed and validated in recent years, and more and more attention is currently paid to this aspect in clinical trials.

The impact of allergic rhinitis on social life

The socio-economic impact of allergic rhinitis

Studies examining the economic impact of AR provide convincing evidence of its significant impact [Gupta *et al.* 2004]. The costs of AR can be divided into those associated with medical-care treatments (direct costs) and those resulting from nonmedical losses as a consequence (indirect costs). The most recent estimates of the annual cost of AR range from US\$2 billion to US\$5 billion [Reed *et al.* 2004]. The National Health Interview Survey (NHIS) was used to obtain information on the days lost from work and on lost productivity due to AR [Crystal-Peters *et al.* 2000]. Productivity losses associated with a diagnosis of AR in the 1995 were estimated at US\$601 million. When additional survey information was considered regarding the use of sedating over-the-counter allergy medications, as well as workers' self-assessments of their reduction in at-work productivity due to AR, the estimated productivity loss increased dramatically. At-work productivity losses were estimated to range from US\$2.4 billion to US\$4.6 billion. The cost of seasonal AR was studied in Germany and the average annual cost was 1089 Euros per child/adolescent and

1543 Euros per adult [Schramm *et al.* 2003]. In Japanese, the total costs for AR were US\$1.15 billion including direct and indirect costs as well as over-the-counter costs [Okuda, 1998].

Work impairment

It is generally accepted that AR impairs work performance by inducing work absenteeism as well as reducing work productivity that is correlated with the severity of AR [Bousquet *et al.* 2005; Shedden, 2005; Blanc *et al.* 2001]. The Work Productivity and Activity Impairment-Allergy Specific Questionnaire has been developed and validated to measure the effect of AR on work productivity (among adults), classroom activity (among students), and regular activities. It assesses function-related end points, providing a measure of the economic impact of AR and the potential of therapeutic interventions. The medical treatment of AR was found to improve work productivity in persistent AR [Bousquet *et al.* 2005], although treatment with sedative oral H₁-antihistamines was shown to reduce work productivity [Cockburn *et al.* 1999; Fireman, 1997].

Sleep disturbance

All dimensions of sleep are impaired by AR. Poorly controlled symptoms may contribute to sleep loss or disturbance [Santos *et al.* 2006; McNicholas *et al.* 1982; Lavie *et al.* 1981]. Moreover, sedation in patients with AR may be increased by using sedative treatments [Casale *et al.* 2003]. It has been shown that patients with moderate–severe symptoms of intermittent or persistent AR suffer from impaired sleep in comparison with normal subjects and patients with mild rhinitis. Also, seasonal AR leads to increased daytime sleepiness [Stuck *et al.* 2004]. The impact of the severity of rhinitis on QOL, including sleep, daily activities, and work performance, was shown to be stronger than the duration of rhinitis [Bousquet *et al.* 2006]. Over 80% of the patients with moderate–severe rhinitis reported impaired activities compared with only 40% of patients with mild rhinitis. A national controlled cross-sectional epidemiological study involving 260 French otorhinolaryngologists and allergologists and 591 patients with AR of at least 1 year's duration assessed sleep disorders, quality of sleep, and AR using validated tools [Léger *et al.* 2006]. The impact of the severity of rhinitis, but not its frequency, was significant for insomnia, severe insomnia, hypersomnia, respiratory arrest, observed apnea, sleepiness,

and regular use of sedatives. Léger and colleagues revealed that 43.7% of AR patients reported a feeling of fatigue on awakening despite a normal night's sleep [Léger *et al.* 2006]. Headache on awakening, anxiety, and depression as 'sleep blockers', and daytime somnolence were significantly more frequently reported by patients with AR than by controls. The severity of AR significantly influenced the mean duration of nocturnal sleep, the frequency of daytime sleepiness, and sleep latency.

Learning disability

HRQOL impairments associated with AR may also significantly impact learning ability. Allergic and control subjects were tested with respect to speed of cognitive processing, psychomotor speed, ability to sustain attention, verbal learning and memory, and mood. Only atopic subjects had significant decreases in verbal learning, decision-making speed, psychomotor speed, reaction time tests, and positive affect scores during the allergy season [Marshall and Colon, 1993]. These results indicate that AR does have a significant impact on many aspects of cognitive function and affect. Furthermore, children with AR may have school problems including absences and poor performance caused by distraction, fatigue, or irritability [Blaiss, 2004]. Seasonal AR may be associated with a reduced ability to learn and to be successful in examinations [Sundberg *et al.* 2007; Walker *et al.* 2007]. Treatment with sedating oral H₁-antihistamines will aggravate these problems, whereas treatment with nonsedating oral antihistamines will only partially reverse the limitations in learning [Vuurman *et al.* 1993].

Quality of life in allergic rhinitis

QOL is a concept including a large set of physical and psychological characteristics assessing problems in the social context of the lifestyle by the patient himself by means of questionnaires. It was not until the early 1990s that HRQOL questionnaires in the field of AR were introduced [Juniper and Guyatt, 1991]. Since then, assessment of HRQOL has come to stay in allergy research. Clinical studies have focused on the issues of impact of AR on sleep, work and school performance, social relationships, and family functioning. Depending on the purpose of the evaluation, two types of instruments can be used: generic or specific questionnaires.

Generic questionnaires

Generic questionnaires measure physical, mental, and psychosocial functions in all health conditions and, therefore, they allow a comparison of patients suffering from different diseases (medical conditions) as well as ill and healthy subjects. They can be used for any health condition and may evaluate an entire population's well-being. Because generic profiles must be broad and comprehensive, they may lack the detail to be responsive to small but significant changes in patients' HRQOL. As a result, generic instruments are generally thought to be of limited use in focused clinical trials and clinical practice. There are several validated generic questionnaires and the most commonly used are summarized in Table 1 [Majani *et al.* 2002; Sintonen, 2001; Ware and Sherbourne, 1992; Stewart *et al.* 1988; Bergner and Bobbitt, 1981; Hunt *et al.* 1980].

The Medical Outcome Study (MOS) was an observational study that assessed processes and outcomes of care for patients with a variety of medical conditions in a variety of medical settings. The first version of the MOS Short Form was a 20-item questionnaire (MOS SF-20) assessing six domains or subscales: physical functioning, role functioning, social functioning, mental health, health perceptions, and pain [Stewart *et al.* 1988]. The instrument was later expanded to a 36-item version (MOS SF-36) with additional subscales [Ware and Sherbourne, 1992]. The new subscales were developed by separating the original role functioning subscale of the MOS SF-20 into two scales reflecting physical and emotional role functioning. Authors of the MOS SF-36 also added a vitality subscale. These additions were designed with the goal of more comprehensively assessing the HRQOL construct. Each subscale is composed of a varying number of items. Patients provide subjective ratings for each item using a variety of Likert-like scales and yes/no response formats. The raw scores from these subscales are transformed into standardized scores ranging from 0 to 100 to allow for relatively easy and meaningful comparisons across different medical populations. The SF-36 has been used to characterize patients with perennial rhinitis [Pariente *et al.* 1997; Bousquet *et al.* 1994], seasonal [Nishiike *et al.* 2004; Ciprandi *et al.* 2002] and persistent AR [Canonica *et al.* 2006; Bachert *et al.* 2004]. Sickness Impact Profile (SIP) consists of 136 weighted items, grouped into 12

Table 1. Generic questionnaires.

	PRO Instrument	Items
Adult	Medical Outcome Study, Short Form 36 [Stewart <i>et al.</i> 1988]	36
	Medical Outcome Study, Short Form 20 [Ware and Sherbourne, 1992]	20
	Sickness Impact Profile [Bergner and Bobbitt, 1981]	136
	Nottingham Health Profile [Hunt <i>et al.</i> 1980]	45
Pediatric	15-Dimensional Health-related Quality of Life [Sintonen, 2001]	15
	Satisfaction Profile [Majani <i>et al.</i> 2002]	32
	Child Health Questionnaire (CHQ-PF50) [Raaijmakers <i>et al.</i> 2006]	50
	Child Health Questionnaire (CHQ-PF28) [Raaijmakers <i>et al.</i> 2006]	28
	Child Health Questionnaire (CHQ-CF87) for adolescents [Raaijmakers <i>et al.</i> 2006]	87
	Pediatric Quality of Life Inventory (PedsQL) [Raaijmakers <i>et al.</i> 2006]	23

categories: ambulation (A); body care and movement (BCM); mobility (M); emotional behavior (EB); social interaction (SI); alertness behavior (AB); communication (C); work (W); sleep and rest (SR); eating (E); home management (HM); and recreation and pastimes (RP) [Bergner and Bobbitt, 1981]. The scale scores are expressed as a percentage of maximum dysfunction to form a 0–100 scale. A score of 0 indicates no dysfunction, a score 0–10 indicates slight to moderate dysfunction and a score >10 marked dysfunction. The scores of the categories A, BCM and M form a physical dimension (Physical) and categories EB, SI, AB and C form a psychosocial dimension (Psychosocial). All 12 categories are included in an overall SIP score. Nottingham Health Profile (NHP) is a self evaluation, well-validated and reliable generic scale assesses general health across a number of dimensions, including physical, psychological, and social functions [Hunt *et al.* 1980]. It is a questionnaire which is completed by the patient and has 38 items covering six subscales: pain, emotional reactions, sleep, physical mobility, energy, and social isolation. Each is weighted to give a score out of 100, with greater ill health giving a higher score. The 15-Dimensional Health-related QOL (15D) includes the dimensions mobility, vision, hearing, breathing, sleeping, eating, speech, elimination, usual activities, mental function, discomfort and symptoms, depression, distress, vitality, and sexual activity [Sintonen, 2001] [Appendix 1]. Each dimension has five grades

of severity. The 15D can be used both to obtain a profile across the 15 dimensions and a single index score ranging from 0 (being dead) to 1 (full health). The Satisfaction Profile (SAT-P) is a self-administered questionnaire which provides a satisfaction profile in daily life [Majani *et al.* 2002]. Satisfaction can be defined as the cognitive product of the comparison between ideal life and reality, and can therefore be quantitatively measured. The subject is asked to evaluate their satisfaction about 32 life aspects with reference to the last month (on 32 10 cm horizontal visual analog scale [VAS]) independently of their objective health status. It provides 32 individual scores and five factor scores, all ranging from 0 (lowest level of satisfaction) to 100 (highest level of satisfaction); 32 items in SAT-P questionnaire were built from 10 psychological functioning (Mood, Self-confidence, Couple relationship), 9 physical functioning (Physical well-being, Quality of sexual intercourse, Resistance to stress), 5 work (Organization of work, Financial situation), 5 sleep/eating/leisure (Quality of sleep, Amount of spare time, Relationship with friends) and 3 social functioning (Relationship with friends) items. SAT-P was used in seasonal AR and was found to correlate with the SF-36 data [Majani *et al.* 2002]. The relevant dimensions and the item content of pediatric quality of life questionnaires differ from those of adult questionnaires, and vary with developmental age. In young children it is essential to use a proxy rater to complete the questionnaire; the proxy rater is

generally one of the parents. Parent and self-reports comparison at adolescent age can provide different outlooks on QOL. The Child Health Questionnaire (CHQ) covers physical and psychosocial aspects. Since 1998 from the first use of CHQ, 150 pediatric papers were published. The CHQ is available in different languages and countries since a cross-cultural validation project was carried out in 32 countries. The most frequently applied version is the 50-item parent form (CHQ-PF50) for children aged 5 years and older and consists of 11 multi-item and 2 single-item scales, of which four scales pertain to the impact of child's ill health on parents and the family. The CHQ permits the calculation of a physical summary measure and a psychosocial summary measure. A 28-item version with the same scales but fewer items is available (CHQ-PF28). Recently, a validation study of the 28-item CHQ-PF version showed that the summary measures of the CHQ-PF28 are highly reliable, as is the CHQ-PF50. The CHQ-CF87 is an 87-item self-report questionnaire for adolescents and children at least 10 years old and validation studies are in progress [Raat *et al.* 2006].

However, Kosciak and colleagues' study on the QOL of children with cystic fibrosis showed that generic quality of life questionnaire (CHQ) was not adequately sensitive to the consequences of this condition; the disease-specific cystic fibrosis questionnaire was more informative for evaluation of the effects of cystic fibrosis [Kosciak *et al.* 2005].

Specific questionnaires

Specific questionnaires are designed to evaluate a particular disease or to a specific function (e.g. sexuality) or problem (e.g. pain). These questionnaires are much more likely than generic questionnaires to describe more accurately the disease-associated problems of the patients. Moreover, they seem to be more responsive to changes in HRQOL than generic instruments. These tools do not allow comparison between different diseases, but are very useful to evaluate the same patients at different times (e.g. before and after treatment). Numerous instruments are currently available to evaluate the HRQOL in AR and most commonly used questionnaires are summarized in Table 2 [Baiardini *et al.* 2003; Juniper *et al.* 2003, 2000, 1999, 1996; Berdeaux *et al.* 1998; Juniper, 1998].

Specific health-profile questionnaires designed to evaluate the HRQOL in AR include the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ) and its age-specific adaptations: the Adolescent RQLQ (ARQLQ) for patients 12–17 years of age and the Pediatric RQLQ (PRQLQ) for patients 6–12 years of age [Juniper *et al.* 1999, 1994; Juniper, 1998]. The RQLQ is one of the most widely used rhinitis-specific questionnaires [Juniper *et al.* 1999]. It has 28 questions in seven domains (activity limitation, sleep problems, nose symptoms, eye symptoms, non-nose/eye symptoms, practical problems, and emotional function). There are three 'patient-specific' questions in the activity domain which allow patients to select three activities in which they are most limited by their rhinoconjunctivitis. Patients recall how bothered they have been by their rhinoconjunctivitis during the previous week and to respond to each question on a seven-point scale (0 = not impaired at all; 6 = severely impaired). The overall RQLQ score is the mean of all 28 responses and the individual domain scores are the means of the items in those domains. The RQLQ has been adapted to many different cultures and languages [Bunnag *et al.* 2005; Okuda *et al.* 2005; Nascimento Silva *et al.* 2001; Leong *et al.* 1999]. Also, the RQLQ has been tested in adult patients with seasonal, perennial as well as intermittent and persistent AR [Juniper and Guyatt, 1991]. Adaptations of the RQLQ for use with adolescents and children with AR have revealed that different aspects of HRQOL have varying levels of importance for adults, adolescents, and children. The Adolescent RQLQ has 25 questions in six domains (nose symptoms, eye symptoms, practical problems, activity limitation, nonhayfever symptoms, and emotional function) [Juniper *et al.* 1994]. The functional problems that are most troublesome to adolescents with rhinoconjunctivitis are very similar to those experienced by adults. They are bothered by the same nose, eye and systems symptoms, practical problems, and emotional impairments. The only differences are: (1) they are not quite so bothered by sleep problems as adults and, as a result, there is not a separate sleep domain in the ARQLQ, just a single sleep question in the practical problems domain, (2) they are unable to do their school work as well as usual (captured in the RQLQ by 'poor concentration' and 'reduced productivity'). The Pediatric RQLQ has 23 questions in five domains (nasal symptoms, ocular symptoms, other symptoms, practical problems, and

Table 2. Specific questionnaires.

PRO Instrument	Items
Rhinoconjunctivitis Quality of Life Questionnaire [Juniper <i>et al.</i> 1999]	28
Adolescent Rhinoconjunctivitis Quality of Life Questionnaire [Juniper <i>et al.</i> 1994]	25
Pediatric Rhinoconjunctivitis Quality of Life Questionnaire [Juniper, 1998]	23
Mini Rhinoconjunctivitis Quality of Life Questionnaire [Juniper <i>et al.</i> 2000]	14
The Parents of Children with ENT infections Quality of Life Questionnaire [Berdeaux <i>et al.</i> 1998]	17
Nocturnal Rhinoconjunctivitis Quality of Life Questionnaire [Juniper <i>et al.</i> 2003]	16
Rhinasthma Quality of Life Questionnaire [Baiardini <i>et al.</i> 2003]	30

activities) that children answer on the basis of the previous week [Juniper, 1998]. Validation of the instrument has shown that most children give reliable and accurate responses (although some younger children have difficulty understanding the concept of 'during the last week') and that the PRQLQ is appropriate for clinical trials, clinical practice, and surveys. According to the PRQLQ, children, adults, and adolescents are bothered by the physical symptoms of AR to a similar degree, but children are not as bothered by emotional problems or limitations of activities. The Mini Rhinoconjunctivitis Quality of Life Questionnaire (Mini-RQLQ) has been developed in response to a demand for a shorter, quicker version of the RQLQ(S) for large clinical trials and for managed care monitoring [Juniper *et al.* 2000]. This instrument has 14 questions in five domains (activity limitation, practical problems, nose symptoms, eye symptoms, and non-nose/eye symptoms) and has good reliability, cross-sectional validity, responsiveness, and longitudinal validity. However, as might be expected with a shorter questionnaire, none of these properties are quite so detailed as those of the original RQLQ. The Parents of Children with ENT infections Quality of Life Questionnaire (PAR-ENT-QOL) has been developed by Mapi Research Institute to measure the QOL of parents whose children have otolaryngologic disorders [Berdeaux *et al.* 1998]. This questionnaire primarily focuses on the consequences of otolaryngologic disorders on family life. Few standardized questionnaires exist that specifically examine work or school performance. Nonetheless, these issues are also important parameters for study because reduced performance may lead to a compromise of future opportunities. Nocturnal Rhinoconjunctivitis Quality of Life Questionnaire (NRQLQ) has been specially designed to measure the functional problems that are most troublesome to patients with nocturnal allergic rhinoconjunctivitis [Juniper *et al.*

2003] [Appendix 2]. In patients with nocturnal allergic rhinoconjunctivitis, the use of the NRQLQ in clinical practice and research enables us to measure the most troublesome functional impairments. An analysis of sleep quality reveals aspects of AR that cannot be established by analyzing daytime symptoms. The Rhinasthma Quality of Life Questionnaire consists of 30 items and for each of them patients have to indicate on a Likert scale (1 = not at all; 5 = very much) how much they were troubled by each problem [Baiardini *et al.* 2003]. This questionnaire takes into account the functional, physical, and emotional problems experienced by adult patients with respiratory allergy, and provides three separate scores for upper airways, lower airways, and respiratory allergy impact. Moreover, the Rhinasthma provides a composite score, namely the Global Summary, which computes the aggregate scores and indicates the overall impact of the disease. All four scores are from 0 to 100, where a higher score indicates worse QOL. The Rhinasthma questionnaire evaluates the HRQOL in the previous 2 weeks.

A methodological aspect is the choice between generic and specific instruments in clinical trials, as the two types of instruments measure different aspects [Kremer, 2004]. In the case of AR, specific instruments seem to have better discriminative and evaluative properties [Juniper *et al.* 2002b] than the generic assessments and generic questionnaires may not be able to detect the impact of mild disease [Passalacqua *et al.* 2006]. On the other hand, generic questionnaires allow comparing different populations, and also ill and healthy subjects. However, these generic instruments are not only less tailored to the problems of the patients compared with disease-specific questionnaires, but their performance in terms of responsiveness is also less. To date, the best solution would be using an instrument in association with a generic and a specific questionnaire.

In general, the effect on QOL runs parallel with the effect on conventional medical outcome measures. However, QOL and clinical/objective measurements are not fully interchangeable. There are studies documenting a clinical or functional improvement induced by medical treatment, not accompanied by detectable changes in the QOL [Van Cauwenberge and Juniper, 2000; Van der Molen *et al.* 1998]. In other studies, differences can be found indicating that patients perceive differences in efficacy, not captured by conventional symptom scores [Ciprandi *et al.* 2002; Juniper *et al.* 2002b]. Thus, QOL scales measure something different from the classical measures (symptom scores, pulmonary function, nasal airway resistance) and should integrate those measure in clinical studies.

Utilities in allergic rhinitis

Utilities are used to measure the value of health states, as determined by either the patient or society. They provide a single number denoting an individual's HRQOL. When first introduced, utility instruments were mostly generic, limiting their responsiveness to small but significant changes in patient status. Recent adaptations of some utility instruments improved their measurement properties as disease-specific instruments [Torrance, 1986]. A recent rhinitis-specific utility with 10 items, the Multiattribute Rhinitis Symptom Utility Index, has been developed for clinical trials and for cost-effectiveness studies comparing medical treatment for rhinitis [Revicki *et al.* 1998; Torrance *et al.* 1996].

Interpreting statistically significant patient-reported outcomes

Patient-reported outcomes (PROs) are generally incorporated in clinical trials comparing treatment modalities. These PROs measure HRQOL, symptoms, and treatment satisfaction rates. As the HRQOL scores are based on arbitrary scales and are not associated with any units, changes in HRQOL scores are often hard to interpret. There must be evidence documenting the PRO instrument's conceptual framework, validity, and psychometric qualities for these PRO endpoint data to be accepted as evidence of efficient treatment. For establishing a PRO instrument's construct validity responsiveness is a must, for responsiveness the PRO score's sensitivity to actual changes in health status should be documented. Minimal

important difference (MID) determination is also important for interpreting statistically significant PRO results [Revicki *et al.* 2008]. In the last 15 years responsiveness and interpretation of PRO scores have been discussed, recommendations about the best method for evaluating responsiveness and calculation of MIDs for PRO instruments are still unclear [Wyrwich *et al.* 2005].

Responsiveness is the PRO instrument's ability to detect changes while MID denotes the smallest change in score that would likely be significant from the patient's or clinician's perspective. This smallest significant change in the score, resulted from any positive or negative change in the QOL of the patient, leads to consideration of a change in the treatment modality [Jaeschke *et al.* 1989]. The MID varies with the population type, disease studied, grades of the diseases, and not an only one MID value can be valid for all study applications involving the same PRO instrument.

HRQOL change can be compared with change in clinical status, intervening health events, interventions of known or expected efficacy, and retrospective reports of change by patients or providers. Responsiveness to change is most frequently evaluated using the effect size (ES), standardized response mean, or the responsiveness statistic. For all of these indices, the numerator is the mean change and the denominators are the standard deviation (SD) at baseline (ES), the SD of change for the sample (standardized response mean) and the SD of change for people who are deemed to have not changed according to an external standard (responsiveness statistic).

Evaluating the MID is a special case of examining responsiveness to change that is limited to the subgroup of people who are deemed to have had minimal change. Hence, a fundamental aspect of estimating the MID is to define the subgroup of people who have changed by a minimal amount. This is done using external information or anchors. These anchors include clinical parameters, retrospective measures of change (self or physician reported), or knowledge about the course of health over time. For example, people who have changed by a minimal amount might be identified by asking study participants at follow up to report how much they changed

since the baseline of a study using a multiple categorical response scale, such as:

- got a lot better;
- got a little better;
- stayed the same;
- got a little worse;
- got a lot worse.

People who reported either getting a little better or a little worse would constitute the minimal change subgroup according to the anchor. The average change in HRQOL reported by this subgroup of people (the change in HRQOL for the group who said they had become a little worse would be multiplied by -1 to account for the directional difference) would typically be used to index the MID as perceived by the patient. This variant of estimating the MID has been referred to by some as the minimally detectable difference.

The same principles apply to whatever anchor is used to establish the subgroup of people upon which the MID calculation is based. For a clinical parameter it is necessary to establish the amount of change on the anchor that is a reasonable indicator of minimal. Hence, estimating the MID requires agreement on what constitutes a minimal change in the anchor.

The MID for a PRO instrument may vary across populations, context, and treatments but it is not an ignorable characteristic. There is an evolving consensus to determine MID and Responsiveness. Accumulating information across multiple studies will help clinicians and researchers gain confidence in interpreting statistically significant PROs.

Conclusions

HRQOL has gained great attention and relevance in the field of allergy, as well as in most fields of clinical medicine. The impact of AR on well-being has been clearly documented, as well as the effects of the different treatments. In this study we aimed getting more attention on HRQOL for the assessment of the effect of AR on the patients. With specific pretreatment and posttreatment questionnaires the clinical success determination can be standardized with upgrading and perfecting these specific questionnaires. Thus, it is universally agreed that HRQOL should be included as mandatory

supportive outcome in clinical trials. The next step could be that we not only simply use those instruments in clinical trials, but also find ways to implement them in the process of understanding and managing our patients in daily care.

There are several feasible, reliable, and validated QOL questionnaires that can be used in clinical trials. These include generic and disease-specific questionnaires. Appropriate selection of outcome measures will enhance the quality of studies and the ability to assess treatment outcomes in clinical trials.

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References

- Bachert, C., Bousquet, J., Canonica, G.W., Durham, S.R., Klimek, L., Mullol, J. *et al.* (2004) Levocetirizine improves quality of life and reduces costs in long-term management of persistent allergic rhinitis. *J Allergy Clin Immunol* 114: 838–844.
- Baiardini, I., Pasquali, M., Giardini, A., Specchia, C., Passalacqua, G., Venturi, S. *et al.* (2003) Rhinasthma: a new specific QoL questionnaire for patients with rhinitis and asthma. *Allergy* 58: 289–294.
- Berdeaux, G., Hervie, C., Smajda, C. and Marquis, P. (1998) Parental quality of life and recurrent ENT infections in their children: development of a questionnaire: Rhinitis Survey Group. *Qual Life Res* 7: 501–512.
- Bergner, M. and Bobbitt, R.A. (1981) The sickness impact profile: development and final revision of a health status measure. *Med Care* 19: 787–805.
- Blaiss, M.S. (2004) Allergic rhinitis and impairment issues in schoolchildren: a consensus report. *Curr Med Res Opin* 20: 1937–1952.
- Blanc, P.D., Trupin, L., Eisner, M., Earnest, G., Katz, P.P., Israel, L. *et al.* (2001) The work impact of asthma and rhinitis: findings from a population based survey. *J Clin Epidemiol* 54: 610–618.

- Bousquet, J., Bullinger, M., Fayol, C., Marquis, P., Valentin, B. and Burtin, B. (1994) Assessment of quality of life in patients with perennial allergic rhinitis with the French version of the SF-36 Health Status Questionnaire. *J Allergy Clin Immunol* 94: 182–188.
- Bousquet, J., Demarteau, N., Mullol, J., van den Akker-van Marle, M.E., Van Ganse, E. and Bachert, C. (2005) Costs associated with persistent allergic rhinitis are reduced by levocetirizine. *Allergy* 60: 788–794.
- Bousquet, J., Khaltayev, N., Cruz, A.A., Denburg, J., Fokkens, W.J., Togias, A. *et al.* (2008) Allergic Rhinitis and its Impact on Asthma (ARIA) 2008 update (in collaboration with the World Health Organization, GA(2)LEN and AllerGen). *Allergy* 63(Suppl. 86): 8–160.
- Bousquet, J., Neukirch, F., Bousquet, P.J., Gehano, P., Klossek, J.M., Le Gal, M. *et al.* (2006) Severity and impairment of allergic rhinitis in patients consulting in primary care. *J Allergy Clin Immunol* 117: 158–162.
- Bunnag, C., Leurmarukul, W., Jareoncharsri, P., Tunsuriyawong, P., Assanasen, P. and Pawankar, R. (2005) Quality of life assessment in Thai patients with allergic rhinoconjunctivitis using the SF-36 questionnaire (Thai version). *Rhinology* 43: 99–103.
- Canonica, G.W., Bousquet, J., Van Hamme, G., Bachert, C., Durham, S.R., Klimek, L. *et al.* (2006) Levocetirizine improves health-related quality of life and health status in persistent allergic rhinitis. *Respir Med* 100: 1706–1715.
- Casale, T.B., Blaiss, M.S., Gelfand, E., Gilmore, T., Harvey, P.D., Hindmarch, I. *et al.* (2003) First do no harm: managing antihistamine impairment in patients with allergic rhinitis. *J Allergy Clin Immunol* 111: S835–S842.
- Cingi, C., Topuz, B., Songu, M., Kara, C.O., Ural, A., Yaz, A. *et al.* (2010) Prevalence of allergic rhinitis among adult population in Turkey. *Acta Otolaryngol* 130: 600–606.
- Ciprandi, G., Canonica, W.G., Grosclaude, M., Ostinelli, J., Brazzola, G.G. and Bousquet, J. (2002) Effects of budesonide and fluticasone propionate in a placebo-controlled study on symptoms and quality of life in seasonal allergic rhinitis. *Allergy* 57: 586–591.
- Cockburn, I.M., Bailit, H.L., Berndt, E.R. and Finkelstein, S.N. (1999) Loss of work productivity due to illness and medical treatment. *J Occup Environ Med* 41: 948–953.
- Crystal-Peters, J., Crown, W.H., Goetzel, R.Z. and Schutt, D.C. (2000) The cost of productivity losses associated with allergic rhinitis. *Am J Manag Care* 6: 373–378.
- EMEA. (2007) Reflection paper on the regulatory guidance for the use of health related Quality of life (HRQOL) measures in the evaluation of medicinal products. Available at: <http://www.emea.europa.eu/pdfs/human/ewp/13939104en.pdf>.
- Fireman, P. (1997) Treatment of allergic rhinitis: effect on occupation productivity and work force costs. *Allergy Asthma Proc* 18: 63–67.
- Gupta, R., Sheikh, A., Strachan, D.P. and Anderson, H.R. (2004) Burden of allergic disease in the UK: secondary analyses of national databases. *Clin Exp Allergy* 34: 520–526.
- Hunt, S.M., McKenna, S.P., McEwen, J., Backett, E.M., Williams, J. and Papp, E. (1980) A quantitative approach to perceived health status: a validation study. *J Epidemiol Community Health* 34: 281–286.
- Jaeschke, R., Singer, J. and Guyatt, G.H. (1989) Measurement of health status: ascertaining the minimal clinically important difference. *Controlled Clin Trials* 10: 407–415.
- Juniper, E.F. (1998) Impact of upper respiratory allergic diseases on quality of life. *J Allergy Clin Immunol* 101: 386–391.
- Juniper, E.F. and Guyatt, G.H. (1991) Development and testing of a new measure of health status for clinical trials in rhinoconjunctivitis. *Clin Exp Allergy* 21: 77–83.
- Juniper, E.F., Guyatt, H. and Dolovich, J. (1994) Assessment of quality of life in adolescents with allergic rhinoconjunctivitis: development and testing of a questionnaire for clinical trials. *J Allergy Clin Immunol* 93: 413–423.
- Juniper, E.F., Rohrbach, T. and Meltzer, E.O. (2003) A questionnaire to measure quality of life in adults with nocturnal allergic rhinoconjunctivitis. *J Allergy Clin Immunol* 111: 484–490.
- Juniper, E.F., Thompson, A.K., Ferrie, P.J. and Roberts, J. (1999) Validation of the standardized version of the rhinoconjunctivitis quality of life questionnaire. *J Allergy Clin Immunol* 104: 364–369.
- Juniper, E.F., Thompson, A.K., Ferrie, P.J. and Roberts, J. (2000) Development and validation of the mini rhinoconjunctivitis quality of life questionnaire. *Clin Exp Allergy* 30: 132–140.
- Juniper, E.F., Thompson, A.K. and Roberts, J.N. (2002b) Can the standard gamble and rating scale be used to measure quality of life in rhinoconjunctivitis? Comparison with the RQLQ and SF-36. *Allergy* 57: 201–206.
- Kremer, B. (2004) Quality of life scales in allergic rhinitis. *Curr Opin Allergy Clin Immunol* 4: 171–177.
- Koscik, R.L., Douglas, J.A., Zaremba, K., Rock, M.J., Splaingard, M.L., Laxova, A. *et al.* (2005) Quality of life of children with cystic fibrosis. *J Pediatr* 147(3 Suppl): S64–S68.
- Lavie, P., Gertner, R., Zomer, J. and Podoshin, L. (1981) Breathing disorders in sleep associated with

- microarousals in patients with allergic rhinitis. *Acta Otolaryngol* 92: 529–533.
- Léger, D., Annesi-Maesano, I., Carat, F., Rugina, M., Chanal, I., Pribil, C. *et al.* (2006) Allergic rhinitis and its consequences on quality of sleep: an unexplored area. *Arch Intern Med* 166: 1744–1748.
- Leong, K.P., Chan, S.P., Tang, C.Y., Yeak, S.C., Saurajen, A.S., Mok, P.K. *et al.* (1999) Quality of life of patients with perennial allergic rhinitis: preliminary validation of the Rhinoconjunctivitis Quality of Life Questionnaire in Singapore. *Asian Pac J Allergy Immunol* 17: 163–167.
- Lierl, M.B. (1995) Allergy of the upper respiratory tract, In: Lawlor, G.M.Jr., Fischer, T.J. and Adelman, D.C. (eds). *Manual of Allergy and Immunology*, 3rd edn, Boston, MA: Little, Brown and Company.
- Majani, G., Biardini, I., Giardini, A., Senna, G.E., Minale, P., D’Ulisse, S. *et al.* (2002) Health-related quality of life assessment in young adults with seasonal allergic rhinitis. *Allergy* 56: 313–317.
- Marshall, P.S. and Colon, E.A. (1993) Effects of allergy season on mood and cognitive function. *Ann Allergy* 71: 251–258.
- McNicholas, W.T., Tarlo, S., Cole, P., Zamel, N., Rutherford, R., Grin, D. *et al.* (1982) Obstructive apneas during sleep in patients with seasonal allergic rhinitis. *Am Rev Respir Dis* 126: 625–628.
- Nascimento Silva, M., Naspitz, C. and Sole, D. (2001) Evaluation of quality of life in children and teenagers with allergic rhinitis: adaptation and validation of the Rhinoconjunctivitis Quality of Life Questionnaire (RQLQ). *Allergol Immunopathol (Madr)* 29: 111–118.
- Nishiike, S., Ogino, S., Irifune, M., Arimoto, H., Sakaguchi, Y., Takeda, M. *et al.* (2004) Measurement of quality of life during different clinical phases of Japanese cedar pollinosis. *Auris Nasus Larynx* 31: 135–139.
- Okuda, M. (1998) Cost implication of allergic rhinitis. *Allergy Immunol* 5: 86–91.
- Okuda, M., Ohkubo, K., Goto, M., Okamoto, H., Konno, A., Baba, K. *et al.* (2005) Comparative study of two Japanese rhinoconjunctivitis quality-of-life questionnaires. *Acta Otolaryngol* 125: 736–744.
- Pariente, P.D., LePen, C., Los, F. and Bousquet, J. (1997) Quality-of-life outcomes and the use of anti-histamines in a French national population-based sample of patients with perennial rhinitis. *Pharmacoeconomics* 12: 585–595.
- Passalacqua, G., Pasquali, M., Ariano, R., Lombardi, C., Giardini, A., Baiardini, I. *et al.* (2006) Randomized double blind controlled study with sublingual carbamylated allergoid immunotherapy in mild rhinitis due to mites. *Allergy* 61: 849–854.
- Raat, H., Mohangoo, A.D. and Grootenhuys, M.A. (2006) Pediatric health-related quality of life questionnaires in clinical trials. *Curr Opin Allergy Clin Immunol* 6: 180–185.
- Reed, S.D., Lee, T.A. and McCrory, D.C. (2004) The economic burden of allergic rhinitis: a critical evaluation of the literature. *Pharmacoeconomics* 22: 345–361.
- Revicki, D., Hays, R.D., Cella, D. and Sloan, J. (2008) Recommended methods for determining responsiveness and minimally important differences for patient-reported outcomes. *J Clin Epidemiol* 61: 102–109.
- Revicki, D.A., Leidy, N.K., Brennan-Diemer, F., Thompson, C. and Togias, A. (1998) Development and preliminary validation of the multiattribute Rhinitis Symptom Utility Index. *Qual Life Res* 7: 693–702.
- Santos, C.B., Pratt, E.L., Hanks, C., McCann, J. and Craig, T.J. (2006) Allergic rhinitis and its effect on sleep, fatigue, and daytime somnolence. *Ann Allergy Asthma Immunol* 97: 579–586.
- Schipper, H.C.J. and Powell, V. (1990) Definitions and conceptual issues, In: Spilker, B. (ed.). *Quality of Life Assessment in Clinical Trials*, New York: Raven Press.
- Schramm, B., Ehlken, B., Smala, A., Quednau, K., Berger, K. and Nowak, D. (2003) Cost of illness of atopic asthma and seasonal allergic rhinitis in Germany: 1-yr retrospective study. *Eur Respir J* 21: 116–122.
- Sears, M.R., Burrows, B., Herbison, G.P., Holdaway, M.D. and Flannery, E.M. (1993) Atopy in childhood: II. Relationship to airway responsiveness, hay fever and asthma. *Clin Exp Allergy* 23: 949–956.
- Shedden, A. (2005) Impact of nasal congestion on quality of life and work productivity in allergic rhinitis: findings from a large online survey. *Treat Respir Med* 4: 439–446.
- Sintonen, H. (2001) The 15D instrument of health-related quality of life: properties and applications. *Ann Med* 33: 328–336.
- Stewart, A.L., Hays, R.D. and Ware Jr., J.E. (1988) The MOS short-form general health survey. Reliability and validity in a patient population. *Med Care* 26: 724–735.
- Stuck, B.A., Czajkowski, J., Hagner, A.E., Klimek, L., Verse, T., Hormann, K. *et al.* (2004) Changes in daytime sleepiness, quality of life, and objective sleep patterns in seasonal allergic rhinitis: a controlled clinical trial. *J Allergy Clin Immunol* 113: 663–668.
- Sundberg, R., Toren, K., Hoglund, D., Aberg, N. and Brisman, J. (2007) Nasal symptoms are associated with school performance in adolescents. *J Adolesc Health* 40: 581–583.

Torrance, G.W. (1986) Measurement of health state utilities for economic appraisal. *J Health Econ* 5: 1–30.

Torrance, G.W., Feeny, D.H., Furlong, W.J., Barr, R.D., Zhang, Y. and Wang, Q. (1996) Multiattribute utility function for a comprehensive health status classification system: Health Utilities Index Mark 2. *Med Care* 34: 702–722.

Van Cauwenberge, P. and Juniper, E.F. (2000) Comparison of the efficacy, safety and quality of life provided by fexofenadine hydrochloride 120 mg, loratadine 10 mg and placebo administered once daily for the treatment of seasonal allergic rhinitis. *Clin Exp Allergy* 30: 891–899.

Van der Molen, T., Sears, M.R., de Graaff, C.S., Postma, D.S. and Meyboom-de Jong, B. (1998) Quality of life during formoterol treatment: comparison between asthma-specific and generic questionnaires. Canadian and the Dutch formoterol investigators. *Eur Respir J* 12: 30–34.

Vuurman, E.F., van-Veggel, L.M., Uiterwijk, M.M., Leutner, D. and O'Hanlon, J.F. (1993) Seasonal allergic rhinitis and antihistamine effects on children's learning. *Ann Allergy* 71: 121–126.

Walker, S., Khan-Wasti, S., Fletcher, M., Cullinan, P., Harris, J. and Sheikh, A. (2007) Seasonal allergic rhinitis is associated with a detrimental effect on examination performance in United Kingdom teenagers: case-control study. *J Allergy Clin Immunol* 120: 381–387.

Ware, J.E. and Sherbourne, C.D. (1992) The MOS 36-item short form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 30: 473–483.

Wyrwich, K.W., Bullinger, M., Aaronson, N., Hays, R.D., Patrick, D.L., Symonds, T. *et al.* (2005) Estimating clinically significant differences in quality of life outcomes. *Qual Life Res* 14: 285e95.

Appendix 1. Quality of Life Questionnaire (New 15D) [Sintonen, 2001].

Please read through all the alternative responses to each question before placing a cross (x) against the alternative which best describes your present status. Continue through all 15 questions in this manner, giving only one answer to each.

Question 1 Mobility

1. () I am able to walk normally (without difficulty) indoors, outdoors and on stairs.
2. () I am able to walk without difficulty indoors, but outdoors and/or on stairs I have slight difficulties.
3. () I am able to walk without help indoors (with or without an appliance), but outdoors and/or on stairs only with considerable difficulty or with help from others.
4. () I am able to walk indoors only with help from others.
5. () I am completely bed-ridden and unable to move about.

Question 2 Vision

1. () I see normally, ie I can read newspapers and TV text without difficulty (with or without glasses).
2. () I can read papers and/or TV text with slight difficulty (with or without glasses).
3. () I can read papers and/or TV text with considerable difficulty (with or without glasses).
4. () I cannot read papers or TV text either with glasses or without, but I can see enough to walk about without guidance.
5. () I cannot see enough to walk about without a guide, ie I am almost or completely blind.

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Question 3 Hearing

1. () I can hear normally, ie normal speech (with or without a hearing aid).
2. () I hear normal speech with a little difficulty.
3. () I hear normal speech with considerable difficulty; in conversation I need voices to be louder than normal.
4. () I hear even loud voices poorly; I am almost deaf.
5. () I am completely deaf.

Question 4 Breathing

1. () I am able to breathe normally, ie with no shortness of breath or other breathing difficulty.
2. () I have shortness of breath during heavy work or sports, or when walking briskly on flat ground or slightly uphill.
3. () I have shortness of breath when walking on flat ground at the same speed as others my age.
4. () I get shortness of breath even after light activity, eg washing or dressing myself.
5. () I have breathing difficulties almost all the time, even when resting.

Question 5 Sleeping

1. () I am able to sleep normally, ie I have no problems with sleeping.
2. () I have slight problems with sleeping, eg difficulty in falling asleep, or sometimes waking at night.
3. () I have moderate problems with sleeping, eg disturbed sleep, or feeling I have not slept enough.
4. () I have great problems with sleeping, eg having to use sleeping pills often or routinely, or usually waking at night and/or too early in the morning.
5. () I suffer severe sleeplessness, eg sleep is almost impossible even with full use of sleeping pills, or staying awake most of the night.

Question 6 Eating

1. () I am able to eat normally, ie with no help from others.
2. () I am able to eat by myself with minor difficulty (eg slowly, clumsily, shakily, or with special appliances).
3. () I need some help from another person in eating.
4. () I am unable to eat by myself at all, so I must be fed by another person.
5. () I am unable to eat at all, so I am fed either by tube or intravenously.

Question 7 Speech

1. () I am able to speak normally, ie clearly, audibly and fluently.
2. () I have slight speech difficulties, eg occasional fumbling for words, mumbling, or changes of pitch.
3. () I can make myself understood, but my speech is eg disjointed, faltering, stuttering or stammering.
4. () Most people have great difficulty understanding my speech.
5. () I can only make myself understood by gestures.

Question 8 Elimination

1. () My bladder and bowel work normally and without problems.
2. () I have slight problems with my bladder and/or bowel function, eg difficulties with urination, or loose or hard stools.
3. () I have marked problems with my bladder and/or bowel function, eg occasional 'accidents', or severe constipation or diarrhoea.
4. () I have serious problems with my bladder and/or bowel function, eg routine 'accidents', or need catheterization or enemas.
5. () I have no control over my bladder and/or bowel function.

Question 9 Usual activities

1. () I am able to perform my usual activities (eg employment, studying, housework, free-time activities) without difficulty.
2. () I am able to perform my usual activities slightly less effectively or with minor difficulty.
3. () I am able to perform my usual activities much less effectively, with considerable difficulty, or not completely.
4. () I can only manage a small proportion of my previously usual activities.
5. () I am unable to manage any of my previously usual activities.

Question 10 Mental function

1. () I am able to think clearly and logically, and my memory functions well
2. () I have slight difficulties in thinking clearly and logically, or my memory sometimes fails me.
3. () I have marked difficulties in thinking clearly and logically, or my memory is somewhat impaired.
4. () I have great difficulties in thinking clearly and logically, or my memory is seriously impaired.
5. () I am permanently confused and disoriented in place and time.

Question 11 Discomfort and symptoms

1. () I have no physical discomfort or symptoms, eg pain, ache, nausea, itching etc.
2. () I have mild physical discomfort or symptoms, eg pain, ache, nausea, itching etc.
3. () I have marked physical discomfort or symptoms, eg pain, ache, nausea, itching etc.
4. () I have severe physical discomfort or symptoms, eg pain, ache, nausea, itching etc.
5. () I have unbearable physical discomfort or symptoms, eg pain, ache, nausea, itching etc.

Question 12 Depression

1. () I do not feel at all sad, melancholic or depressed.
2. () I feel slightly sad, melancholic or depressed.
3. () I feel moderately sad, melancholic or depressed.
4. () I feel very sad, melancholic or depressed.
5. () I feel extremely sad, melancholic or depressed.

Question 13 Distress

1. () I do not feel at all anxious, stressed or nervous.
2. () I feel slightly anxious, stressed or nervous.
3. () I feel moderately anxious, stressed or nervous.
4. () I feel very anxious, stressed or nervous.
5. () I feel extremely anxious, stressed or nervous.

Question 14 Vitality

1. () I feel healthy and energetic.
2. () I feel slightly weary, tired or feeble.
3. () I feel moderately weary, tired or feeble.
4. () I feel very weary, tired or feeble, almost exhausted.
5. () I feel extremely weary, tired or feeble, totally exhausted.

Question 15 Sexual activity

1. () My state of health has no adverse effect on my sexual activity.
2. () My state of health has a slight effect on my sexual activity.
3. () My state of health has a considerable effect on my sexual activity.
4. () My state of health makes sexual activity almost impossible.
5. () My state of health makes sexual activity impossible.

Appendix 2. Nocturnal rhinoconjunctivitis quality of life questionnaire [Juniper *et al.* 2003].

NOCTURNAL RHINOCONJUNCTIVITIS

PATIENT ID:

QUALITY OF LIFE QUESTIONNAIRE

DATE:

SELF- ADMINISTERED

(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	Somewhat troubled	Moderately troubled	Quite abit 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

NOCTURNAL RHINOCONJUNCTIVITIS

PATIENT ID:

QUALITY OF LIFE QUESTIONNAIRE

DATE:

SELF- ADMINISTERED

(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	Somewhat troubled	Moderately troubled	Quite abit troubled	Very troubled	Extremely troubled
SYMPTOMS ON WAKING 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 night time 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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