

Impact of upper respiratory allergic diseases on quality of life

Elizabeth F. Juniper, MCSP, MSc *Hamilton, Ontario, Canada*

Over the past 10 years, there has been increasing awareness of the importance of including health-related quality of life (HRQL) in clinical assessments. For many clinicians, HRQL is a new term but certainly not a new concept. Quality-of-life questionnaires ask patients the questions that clinicians have been asking for many generations: How are you feeling? Are you limited in your daily activities? Does this bother you? Did the new medication help? The questionnaires provide a standardized, quantified, and recorded summary of the problems patients themselves consider important, quickly identify any specific impairments that are troublesome, and record—more accurately than recall—changes over time. This allows the clinician more time to focus on specific problems and the clinical management of the patient.

WHAT IS HRQL?

“Quality of life” is a rather nebulous expression often meaning different things to different people, and this has made defining it very difficult. However, most agree that many factors—such as finances, spirituality, and health—contribute to quality of life, and also affect each other. Taken very simply, HRQL is the component of overall quality of life that is determined primarily by a person’s health and which can be influenced by clinical interventions. For simplicity and focus, I like the definition of HRQL by Schipper and colleagues: “The functional effects of an illness and its consequent therapy upon a patient, as perceived by the patient.”¹ The final phrase is important because it emphasizes that these are the impairments that patients themselves consider important.

WHY IS HRQL IMPORTANT IN ASTHMA AND RHINITIS?

It has been proposed that there are three reasons for treating patients: to prevent mortality, to reduce the probability of future morbidity, and to improve patient well-being.² Most conventional clinical measures of the severity of asthma and rhinitis assess the status of the airways, with the aim of addressing the first two objectives. In the past, it was frequently

assumed that these measures also provided insight into the patient’s well-being. Certainly, patients with very impaired airways tend to have a worse HRQL than do patients with milder disease, but there is a growing body of evidence, in both asthma and rhinitis, that correlations between clinical measures and how patients feel and how they are able to function in daily activities are only weak to moderate.³⁻⁶ Therefore, if one is going to obtain a complete picture of a patient’s health status, HRQL must be measured along with the conventional clinical indices.

Why should the relationship between clinical measures and HRQL be so weak? Let us take as an example two hypothetical patients with identical clinical rhinitis. The first patient is really bothered by the symptoms themselves. In addition, she is a light sleeper and finds that her rhinitis prevents her from getting a good night’s sleep, so she feels tired during the day. She is a model, is susceptible to headaches, and her appearance prevents her from working. She also is a very tense person, and her rhinitis tends to make her feel very irritable. The second patient ignores her symptoms and is a very sound sleeper. She rarely gets a headache and cares little about how she looks. All in all, she is a very relaxed person. Although these two patients have identical clinical rhinitis, HRQL in the former patient is likely to be much more impaired than in the latter. If we take this one step further and treat both patients with an identical medication that produces an identical improvement in clinical rhinitis, the improvement in HRQL is likely to be much greater in the former patient than in the latter, because the first patient’s symptoms are far less troublesome; she can sleep well and function normally at work. Similar scenarios can easily be imagined for patients with asthma.

WHAT PROBLEMS ARE MOST TROUBLESOME TO PATIENTS WITH ASTHMA?

Extensive HRQL research in asthma has highlighted the functional impairments that are most troublesome to patients.⁷⁻¹¹ Adults with asthma are bothered by the symptoms themselves. The most troublesome are usually shortness of breath, chest tightness, wheeze, and cough. Many patients have problems with physical activities such as sports, hurrying, going up stairs, and shopping. Allergens may cause difficulties with daily activities, such as vacuuming and other household chores, gardening, and hobbies, and like other environmental stimuli, such as cigarette smoke, strong smells, and troublesome weather conditions, may limit family activities and visits to friends. Asthma patients are bothered by inability to

From the Department of Clinical Epidemiology and Biostatistics, McMaster University Medical Centre, Hamilton, Ontario.

Reprint requests: Elizabeth F. Juniper, MCSP, MSc, Department of Clinical Epidemiology and Biostatistics, McMaster University Medical Centre, 1200 Main St. West, Hamilton, Ontario, Canada L8N3Z5.

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TABLE I. HRQL Questionnaires* for adult asthmat

Instrument	Type	Patients	No. questions
Asthma Quality of Life Questionnaire ⁷	Disease-specific	Asthma	32
Asthma Quality of Life Questionnaire ⁸	Disease-specific	Asthma	20
Living With Asthma Questionnaire ⁹	Disease-specific	Asthma	68
St. George's Respiratory Questionnaire ¹⁰	Disease-specific	COPD and asthma	76
Respiratory Illness Quality of Life Questionnaire ⁴¹	Disease-specific	COPD and asthma	55
Life Activities Questionnaire for Asthma ¹¹	Disease-specific	Asthma	71
Asthma Bother Profile ⁴²	Disease-specific	Asthma	22
Sickness Impact Profile ^{4, 22}	Generic		137
MOS Short Form 36 ^{23, 27}	Generic		36

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†HRQL questionnaires for which there are published validation studies in adults with asthma.

COPD, chronic obstructive pulmonary disease; MOS, Medical Outcomes Survey.

get a good night's sleep, and often feel tired. In addition, they experience fears and concerns about having asthma, and become frustrated by the disease. Occupational asthma causes its own special problems, with HRQL being poorer in these patients than in clinically matched patients whose asthma is not of occupational origin.¹²

The burden of illness and functional impairments for children with asthma is similar to that experienced by adults. In addition, children are troubled because they cannot integrate fully with their peers; they feel isolated and left out, and this often causes them to feel frustrated, sad, and angry.¹³⁻¹⁷ There is growing evidence that parents of a child with asthma often have a poor perception of the problems and emotions that are troubling their child, making it essential to obtain this information directly from the child.¹⁸

WHAT PROBLEMS ARE MOST TROUBLESOME TO PATIENTS WITH RHINITIS?

Adults with rhinitis and rhinoconjunctivitis are certainly bothered by the symptoms themselves, particularly a stuffy/blocked or runny nose and sneezing. They are bothered by the inability to sleep well at night, and often feel tired and worn out during the day. They experience nonnasal symptoms that are troublesome, such as thirst, poor concentration, and headache. They find practical problems annoying (e.g., having to carry tissues, always having to blow their noses), are limited in their daily activities, and feel frustrated and irritable.^{6, 19, 20}

Adolescents (12 to 17 years of age) with rhinoconjunctivitis experience very similar problems to those of adults, except that insomnia is not so troublesome, but they have more problems with concentration, particularly with schoolwork.²¹

Younger children (6 to 12 years of age) appear to present a different picture.^{21a} They are certainly bothered by their symptoms and the practical problems of carrying tissues and taking medications, but they tend to experience less interference in their normal daily activities, and do not express the emotional dysfunction experienced by adults and adolescents. We observed that parents seemed to be much more bothered by their child's rhinitis than was the child.

SELECTING A QUALITY OF LIFE INSTRUMENT

We now have a range of valid instruments for measuring HRQL in patients with asthma and rhinitis (though not yet with the two conditions together). There is no best instrument; each has been developed for a different purpose and has different measurement properties. The purpose of the following section is to help those who wish to select the most appropriate instrument for the task at hand.

Generic versus specific questionnaires

There are two types of HRQL questionnaire: generic and specific. Generic instruments are designed to be applicable to patients in all health states. The most commonly used and best validated are the Sickness Impact Profile,²² the Medical Outcomes Survey Short Form 36,²³ the Nottingham Health Profile,²⁴ and the McMaster Health Index Questionnaire.²⁵ Although each profile attempts to measure all important aspects of health-related function, each achieves this in different ways. For instance, the Medical Outcomes Survey Short Form 36 contains 9 domains that can be combined into two primary functions, mental and physical. In contrast, the Sickness Impact Profile has 2 major domains, physical and psychosocial, that combine to give one overall score.

The great advantage of generic instruments is that burden of illness can be compared across different medical conditions; for example, one can compare the burden of illness experienced by patients with rhinitis and asthma.^{26, 27} However, because generic instruments are required to be broad in their comprehensiveness, they have very little depth and, as a result, may not include impairments that are important to patients with a specific condition. Consequently, in many conditions, including rhinitis and asthma, generic instruments may be unresponsive to small, but what to patients are important, changes in their HRQL (Juniper, Guyatt, Griffith, Ferrie, Unpublished data, 1998).^{4, 28} Therefore, the use of generic instruments in clinical trials and clinical practice—in which one wants to examine the effect of treatment within individuals or groups of patients—is limited.

TABLE II. HRQL Questionnaires* for pediatric asthma†

Instrument	Type	Patients	No. questions
Paediatric Asthma Quality of Life Questionnaire ¹⁷	Disease-specific	7-17 years	23
Life Activities Questionnaire for Childhood Asthma ⁴³	Disease-specific	5-17 years	71
Childhood Asthma Questionnaires (CAQ) ¹⁴	Disease-specific		
CAQA		4-7 years	18
CAQB		8-11 years	34
CAQC		12-16 years	?
Paediatric Asthma Caregivers' Quality of Life Questionnaire ⁴⁴	Disease-specific	Parents of children with asthma	36

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†HRQL questionnaires for which there are published validation studies in children with asthma.

This lack of depth of focus of generic instruments has led to the development of specific instruments. These may be specific for a group of patients (e.g., the elderly), a particular function (e.g., pain, sexual function), or a disease. Disease-specific instruments are developed by asking patients themselves about the impairments that are most important to them, and these instruments therefore really focus on problems that are targets for interventions. As a result, disease-specific instruments are much more likely to detect clinically important changes in the patient's problems.

Utilities

Utilities measure the value that either the patient or society places on various health states. They are very popular with health economists, not only because they provide a single number representing HRQL (from 0 = death to 1 = perfect health), but also because the majority of utility instruments meet the assumptions for utility theory. For measuring the value that patients themselves place on their own health state, the most common instruments are the Standard Gamble,²⁹ the Time Trade-Off,²⁹ and the Feeling Thermometer.²⁹ For measuring the value that society places on various health states, there is the Quality of Well-Being Scale,³⁰ the Multiattribute Health Utilities Index,³¹ and the Euro-Qol.³² For a long time, these utility instruments were used only in generic form (i.e., they were applicable in all medical conditions), and in this form they have the same weakness as the generic health profiles: they are unresponsive to small but important changes.⁴ Recently, the Standard Gamble and the Feeling Thermometer have been modified for use as disease-specific instruments in children with asthma, and appear to have much-improved measurement properties.²⁸ As yet, there have been no evaluations of these instruments in rhinitis.

Measurement properties

After the decision about whether to use a generic or a specific instrument is made, the clinician's next step is to determine which instrument has the best measurement properties for the task.

Face and content validity. When selecting an instrument, one needs first to ensure that it has face and

content validity, that is to say, on reading over the items, the instrument appears to measure what it purports to measure (face validity), and the items on the questionnaire have been selected by using recognized procedures that ensure the capture of all areas of function that are considered important by patients (content validity). Feinstein has called these properties "sensitivity."³³ Questionnaires in which items have been selected by clinicians rarely meet this criterion because some impairments that patients themselves consider important may have been omitted.

Evaluation versus discrimination

Instruments used in cross-sectional studies (e.g., screening, surveys) are known as *discriminative instruments* because they are required to discriminate between patients with different levels of impairment. Instruments used in longitudinal studies (e.g., clinical trials, clinical practice) are called *evaluative instruments* because they are required to evaluate change in impairment over time. The two types of instrument require quite different measurement properties, although some well-constructed instruments will be capable of both functions.

Discriminative properties. An instrument that is to be used to distinguish between individuals or groups of patients at a single point in time, such as between individuals who do or do not have impaired HRQL or, within asthma/rhinitis patients, between those who have mild, moderate, or severe impairment, requires reliability and cross-sectional construct validity.³⁴

Reliability is the ability of an instrument to measure differences between patients at a single point in time. If one considers this in terms of a signal-to-noise ratio, the signal is the between-subject variance and the noise is the within-subject variance. The test statistic usually used to express reliability is the intraclass correlation coefficient, which relates the between-subject variance to the total variance. Cronbach's alpha, which measures internal consistency, does not give an indication of this property.

When there is no "gold standard" against which to demonstrate that an instrument is actually measuring what it purports to measure, the developer puts forward hypotheses or constructs, which if they are met, provide

TABLE III. HRQL questionnaires* for rhinitis†

Instrument	Type	Patient	No. questions
MOS SF-36 ^{23, 26}	Generic	Adults	36
Rhinoconjunctivitis Quality of Life Questionnaire ⁶	Disease-specific	Adults	28
Rhinitis Quality of Life Questionnaire ²¹	Disease-specific	Adults	24
Adolescent Rhinoconjunctivitis Quality of Life Questionnaire ⁴⁵	Disease-specific	12-17 years	25
Paediatric Rhinoconjunctivitis Quality of Life Questionnaire	Disease-specific	6-12 years	23

*All these questionnaires are copyrighted and should not be altered or translated without the author's permission. (The manuscript for the Paediatric Rhinoconjunctivitis Quality of Life Questionnaire is in preparation.^{21a})

†HRQL questionnaires for which there are published validation studies in patients with rhinitis.

evidence that the instrument is valid (construct validity). The approach frequently used with a new HRQL instrument is to demonstrate that its various domains correlate in a predicted manner with other indices of disease severity and with other HRQL instruments.

Evaluative properties. An instrument that is used to measure longitudinal change within an individual or group of patients must have good responsiveness and longitudinal validity.³⁵ Responsiveness is the ability of the instrument to respond to small but clinically important changes that occur either spontaneously or as the result of an intervention. The signal is the true within-subject change over time, and the noise is the within-subject variance unrelated to the true within-subject change; the relationship between the two is known as the responsiveness index.³⁵ If a formal estimate of the responsiveness index is not available, an instrument that has already performed well in a clinical trial will probably have acceptable responsiveness.

Evaluative instruments also require longitudinal validity. When there is a change in score, this must reflect a true change in HRQL. Longitudinal validity is usually demonstrated by showing that changes in the various domains of the new HRQL instrument correlate in a predicted manner with changes in other outcome measures, such as disease severity and generic HRQL.

Most developers of instruments for assessing HRQL publish reliability and cross-sectional validity data, but as good as these may be, they are no guarantee that an instrument will be capable of performing well in a clinical trial. There are now a number of studies of asthma and rhinitis in which patients experienced clinically important changes in HRQL that generic instruments with good reliability and cross-sectional validity failed to detect (Juniper, Guyatt, Griffith, Ferrie. Unpublished data, 1997).^{4, 28}

INTERPRETING QUALITY OF LIFE DATA

Repeated experience with a wide variety of physiologic measures allows clinicians to interpret HRQL data meaningfully. For instance, the experienced clinician will have little difficulty in interpreting a 0.5-L increase in FEV₁. In contrast, the meaning of a change in score of 0.5 on an HRQL instrument is less intuitively obvious, not only because there are no units, but also because

health professionals are only just beginning to use HRQL measures in clinical practice, and each instrument has its own scoring system.

Two approaches have been suggested for the interpretation of HRQL data.³⁶ The first, or "distribution based" approach, is founded entirely on the statistical distribution of the results, the most commonly used statistic being the effect size, which is derived from the magnitude of change and the variability in stable subjects. The problem with this approach is that it offers no indication of whether the effect is important to the patient. The second approach, which is the one we use and which has been used for the St. George's Respiratory Questionnaire, is referred to as "anchor based," and involves comparing, or "anchoring," the changes in HRQL measures to other clinically meaningful outcomes. For our instruments, we have calculated the minimal important difference (defined as the smallest difference in score in the domain of interest that 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), using patients' global rating-of-change questionnaires.^{37, 38} Other instrument developers have determined the minimal important difference from patient-perceived benefits during clinical trials³⁹ and patients' perceptions of their own illness relative to that of other patients.⁴⁰

THE PLACE OF HRQL ASSESSMENTS IN CLINICAL TRIALS AND CLINICAL PRACTICE

Recognition of the importance of HRQL, the poor correlation between conventional clinical indices and HRQL, and the advent of instruments for assessing HRQL that have strong measurement properties have already ensured that most clinical trials involving patients with asthma and rhinitis include an assessment of HRQL as one of the primary end points. Most instruments are short, easily understood, and self-administered, making their completion of little burden either to the investigator or to the patient. In fact, we have found that patients enjoy completing HRQL questionnaires because they can relate to the questions and know that the problems that are important to them are being taken into consideration. In addition, it is likely that national pharmaceutical regula-

tory agencies will soon ask for evidence of patient benefit for new-product submissions.

The use of HRQL instruments in clinical practice is growing. Tables I through III provide information on HRQL questionnaires used for adult and pediatric asthma and in rhinitis. Disease-specific quality of life questionnaires constitute a formalized, quantified method for taking a simple patient history. The advantages are that: (1) the patient can complete the questionnaire while sitting in the waiting room; (2) a quick scan of the responses will save consultation time; (3) the interviewer does not have to remember all the important questions; (4) the questionnaire will reveal problems not spontaneously identified by the patient; (5) the clinician can quickly focus on areas of particular importance to the patient; and (6) responses at each clinic visit can be compared to determine whether interventions have been beneficial. Therefore, from a practical viewpoint, including HRQL assessments in clinical practice appears to be beneficial. In addition, as more clinicians start using HRQL data in innovative ways, such as for the improvement of treatment compliance, further uses of HRQL assessments are likely to emerge.

REFERENCES

- Schipper H, Clinch J, Powell V. Definitions and conceptual issues. In: Spilker B, editor. *Quality of life assessment in clinical trials*. New York: Raven Press, 1990. p. 11-24.
- Guyatt GH, Naylor D, Juniper EF, Heyland D, Cook D, and the Evidence-Based Medicine Working Group. Users' guides to the medical literature. XII. How to use articles about health-related quality of life. *JAMA* 1997;277:1232-7.
- Juniper EF, Johnston PR, Borkhoff CM, Guyatt GH, Boulet LP, Haukioja A. Quality of life in asthma clinical trials: comparison of salmeterol and salbutamol. *Am J Respir Crit Care Med* 1995;151:66-70.
- Rutten-van Molken MPMH, Clusters F, Van Doorslaer EKA, Jansen CCM, Heurman L, Maesen FPV, et al. Comparison of performance of four instruments in evaluating the effects of salmeterol on asthma quality of life. *Eur Respir J* 1995;8:888-98.
- de Graaf-in't Veld T, Koenders S, Garrelds IM, Gerth van Wijk R. Relationship between nasal hyperreactivity, quality of life and nasal symptoms in perennial rhinitis. *J Allergy Clin Immunol* 1996;98:508-13.
- 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.
- Juniper EF, Guyatt GH, Ferrie PJ, Griffith LE. Measuring quality of life in asthma. *Am Rev Respir Dis* 1993;147:832-8.
- Marks GB, Dunn SM, Woolcock AJ. An evaluation of an asthma quality of life questionnaire as a measure of change in adults with asthma. *J Clin Epidemiol* 1993;46:1103-11.
- Hyland ME, Finniss S, Irvine SH. A scale for assessing quality of life in adult asthma sufferers. *J Psychom Res* 1991;35:99-110.
- Jones PW, Quirk FH, Baveystock CM, Littlejohns P. A self-complete measure of health status for chronic airflow limitation: the St. George's Respiratory Questionnaire. *Am Rev Respir Dis* 1992;145:1321-7.
- Creer TL, Wigal JK, Kotses H, McConaughy K, Winder JA. A life activities questionnaire for adult asthma. *J Asthma* 1992;29:393-9.
- Malo JL, Boulet LP, Dewitte JD, Cartier A, L'Archeveque J, Cote J, et al. Quality of life of subjects with occupational asthma. *J Allergy Clin Immunol* 1993;91:1121-7.
- Townsend M, Feeny DH, Guyatt GH, Seip AE, Dolovich J. Evaluation of the burden of illness for pediatric asthmatic patients and their parents. *Ann Allergy* 1991;67:403-8.
- Christie MJ, French D, Sowden A, West A. Development of child-centered disease-specific questionnaires for living with asthma. *Psychosom Med* 1993;55:541-8.
- Nocon A. Social and emotional impact of childhood asthma. *Arch Dis Child* 1991;66:458-60.
- Usherwood TP, Scrimgeour A, Barber JH. Questionnaire to measure perceived symptoms and disability in asthma. *Arch Dis Child* 1990;65:779-81.
- Juniper EF, Guyatt GH, Feeny DH, Ferrie PJ, Griffith LE, Townsend M. Measuring quality of life in children with asthma. *Quality Life Res* 1996;5:35-46.
- Guyatt GH, Juniper EF, Feeny DH, Griffith LE. Children and adult perceptions of childhood asthma. *Pediatrics*. In press.
- Marshall PS, Colon EA. Effects of allergy season on mood and cognitive function. *Ann Allergy* 1993;71:251-8.
- Gauci M, King MG, Saxarra H, Tulloch BJ, Husband AJ. A Minnesota Multiphasic Personality Inventory Profile of a woman with allergic rhinitis. *Psychosom Med* 1993;55:533-40.
- Juniper EF, Guyatt GH, Dolovich J. Assessment of quality of life in adolescents with allergic rhinoconjunctivitis: development and testing of a questionnaire for clinical trials. *J Allergy Clin Immunol* 1994;93:413-23.
- Juniper EF, Howland WC, Roberts NB, Thompson AK, King DR. Measuring quality of life in children with rhinoconjunctivitis. *J Allergy Clin Immunol* 1998;101:163-70.
- Bergner M, Bobbitt RA, Carter WB, Gilson BS. The Sickness Impact Profile: development and final revision of a health status measure. *Med Care* 1981;19:787-805.
- Stewart AL, Hays R, Ware JE. The MOS short-form general health survey. Reliability and validity in a patient population. *Med Care* 1988;26:724-32.
- Hunt SM, McKenna SP, McEwen J, Backett EM, Williams J, Papp E. A quantitative approach to perceived health status: a validation study. *J Epidemiol Community Health* 1980;34:281-6.
- Sackett DL, Chambers LW, MacPherson AS, Goldsmith CH, McAuley RG. The development and application of indices of health: general methods and summary of results. *Am J Public Health* 1977;67:423-8.
- Bousquet J, Bullinger M, Fayol C, Marquis P, Valentine B, Burtin B. Assessment of quality of life in patients with perennial rhinitis with the French version of the SF-36 health status questionnaire. *J Allergy Clin Immunol* 1994;94:182-8.
- Bousquet J, Knani J, Dhivert H, Richard A, Chicoye A, Ware JE, et al. Quality of life in asthma. 1. Internal consistency and validity of the SF-36 questionnaire. *Am J Respir Crit Care Med* 1994;149:371-5.
- Juniper EF, Guyatt GH, Feeny DH, Griffith LE, Ferrie PJ. Minimum skills required by children to complete health-related quality of life instruments: comparison of instruments for measuring asthma-specific quality of life. *Eur Respir J* 1997;10:2285-94.
- Torrance GW. Measurement of health state utilities for economic appraisal. *J Health Econ* 1986;5:1-30.
- Kaplan RM, Anderson JP, Wu AW, Matthews WC, Kozin F, Orenstein D. The Quality of Well-Being Scale: application in AIDS, cystic fibrosis and arthritis. *Med Care* 1989;27:S27-43.
- Feeny D, Furlong W, Barr RD, Torrance GW, Rosenbaum P, Weitzman S. A comprehensive multi-attribute system for classifying the health status of survivors of childhood cancer. *J Clin Oncol* 1992;10:923-8.
- The EuroQol Group. A new facility for the measurement of health-related quality of life. *Health Policy* 1990;16:199-208.
- Feinstein A. The theory and evaluation of sensibility. In: Feinstein A, editor. *Clinimetrics*. Hartford, CT: Yale University Press, 1987. p. 141-66.
- Guyatt GH, Kirshner B, Jaeschke R. Measuring health status: what are the necessary measurement properties? *J Clin Epidemiol* 1992;45:1341-5.
- Guyatt GH, Walter S, Norman G. Measuring change over time: assessing the usefulness of evaluative instruments. *J Chronic Dis* 1987;40:171-8.

36. Lydick E, Epstein RS. Interpretation of quality of life changes. *Quality Life Res* 1993;2:221-6.
37. Juniper EF, Guyatt GH, Wallan A, Griffith LE. Determining a minimal important change in a disease-specific quality of life questionnaire. *J Clin Epidemiol* 1994;47:81-7.
38. Juniper EF, Guyatt GH, Griffith LE, Ferrie PJ. Interpretation of rhinoconjunctivitis quality of life questionnaire data. *J Allergy Clin Immunol* 1996;98:843-5.
39. Jones PW, Lasserson D. Relationship between change in St. George's Respiratory Questionnaire score and patients' perception of treatment efficacy after one year of therapy with nedocromil sodium. *Am J Respir Crit Care Med* 1994;149:A211.
40. Wells GA, Tugwell P, Kraag GR, Baker PRA, Groh J, Redelmeier DA. Minimum important difference between patients with rheumatoid arthritis: the patient's perspective. *J Rheumatol* 1993;20:557-60.
41. Maille AR, Kaptein AA, Koning CJM, Zwinderman AH. Developing a quality of life questionnaire for patients with respiratory illness. *Monaldi Arch Chest Dis* 1994;49:76-8.
42. Hyland ME, Ley A, Fisher DW, Woodward V. Measurement of psychological distress in asthma and asthma management programs. *Br J Clin Psychol* 1995;34(Pt 4):601-11.
43. Creer TL, Wigal JK, Kotses H, Hatala JC, McConnaughty K, Winder JA. A life activities questionnaire for childhood asthma. *J Asthma* 1993;30:467-73.
44. Juniper EF, Guyatt GH, Feeny DH, Ferrie PJ, Griffith LE, Townsend M. Measuring quality of life in the parents of children with asthma. *Quality Life Res* 1996;5:27-34.
45. Juniper EF, Guyatt GH, Anderson B, Ferrie PJ. Comparison of powder and aerosolized budesonide in perennial rhinitis: validation of rhinitis quality of life questionnaire. *Ann Allergy* 1993;70:225-30.