

REVIEW ARTICLE

Measuring asthma-specific quality of life: structured review

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Abstract

Measuring quality of life (QoL) has become an increasingly important dimension of assessing patient well-being and drug efficacy. As there are now several asthma QoL questionnaires to choose from, it is important to appreciate their strengths and weaknesses. To assist in this choice, we have reviewed the existing questionnaires in a structured way. Information relating to the conceptual and measurement model, reliability, validity, interpretability, burden, administration format and translations was extracted from the published literature. The instruments differ in almost all criteria considered, and therefore it cannot be assumed that they measure the same thing. We recommend the selection of questionnaires that are designed only for asthma and that do not assess symptoms as part of QoL. Only two of the questionnaires reviewed fulfill these requirements: the Sydney Asthma QoL Questionnaire (AQLQ-S) and the Living with Asthma Questionnaire (LWAQ). However, for multinational studies, it may be convenient or practical to use questionnaires that have been linguistically validated in many languages (AQLQ-J, SGRQ). It remains unclear which of these questionnaires best reflects patient perceptions of QoL. Our review did not involve patients, so for the time being choosing from existing questionnaires requires a compromise based on the rigor of the development process and the target patient group.

Quality of life (QoL) measurement has gained popularity as a clinical outcome, reaching beyond measurement of physical health or functional status. The concept of health-related quality of life (HRQoL) refers to the part of QoL which is primarily influenced by health status (1), and there are measures to assess generic and specific HRQoL. Generic measures are broad-based instruments that can measure quality of life over different disease states and conditions, treatment interventions, and populations. In medical research, the generic instrument used most often is the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36) (2). Those measures that are disease-specific instruments include items that are more relevant to a particular condition and are thus more responsive than generic instruments. This review focuses exclusively on disease-specific instruments in asthma.

Asthma is a common condition affecting about 300 million people worldwide and characterized by variable airflow obstruction causing symptoms of wheezing, breathlessness, chest tightness, and coughing (3). In the 1990s, several

asthma-specific QoL instruments were published as well as two for patients with fixed or reversible airway obstruction (4–11). These instruments have later undergone refinement (12) including adaptation for different age groups (13, 14), standardization (15), reduction in length (16, 17), and one instrument has been developed specifically for patients with both asthma and rhinitis (18).

Given the variety of measures now available, and their widespread use in epidemiology, research, audit, and clinical practice, a review of existing instruments is overdue. Some skepticism and confusion has been expressed about the measurement of QoL (19). Eight years ago, a bibliographic study of the development and evaluation of QoL measures identified the need for a structured review to guide users (20). A standard review on subjective health outcome measures addressed validity, reliability, and responsiveness to change (21) with little attention given to the way in which each instrument had been developed. In contrast, the Scientific Advisory Committee of the Medical Outcomes Trust (MOT) considers the conceptual and measurement model as one of

eight principal foci for reviewing health status and QoL instruments (22). Similarly, the US Food and Drug Administration has emphasized the importance of identifying concepts and domains that are important to patients and of developing a conceptual framework for patient-reported outcome instruments (23).

The aim of this paper is to review published QoL measures designed for use in adults with asthma. We conducted a literature search in PubMed, Google, and the QoL Resource of the American Thoracic Society (<http://www.atsqol.org/sections/specific-diseases/adult-asthma.html>) to identify papers published before December 2009, the primary objective of which was to describe the development and/or validation of asthma QoL measures. The search terms used were 'asthma' and 'quality of life'. Articles relating to generic QoL measures used for asthma were excluded as were those developed for pediatric asthma. As in a recent quality assessment of disease-specific QoL questionnaires for rhinitis and rhinosinusitis (24), studies reporting measurement properties as secondary outcomes (for example within a trial) were excluded.

Six QoL measures were identified: the Asthma Quality of Life Questionnaire (AQLQ-J) (4, 5), the Asthma Quality of Life Questionnaire (AQLQ-S) (6, 7), the Living With Asthma Questionnaire (LWAQ) (8), the St George's Respiratory Questionnaire (SGRQ) (10, 11), the Quality of Life for Respiratory Illness Questionnaire (QOL-RIQ) (25), and the Rhinasthma questionnaire (18).

Our data extraction and critique were guided by the attributes and criteria suggested by the MOT for reviewing health status and QoL measures (22), but unlike the approach taken by the MOT, responsiveness was incorporated into validity (26). The seven aspects considered were as follows:

- Conceptual and measurement model (rationale for and description of the concept, target population, item generation, and reduction technique)
- Reliability (degree to which an instrument is free from random error) including internal consistency [the homogeneity of the scale's items at one point in time, often measured by Cronbach's alpha (27)] and test-retest reliability [stability of an instrument over time, often measured by an intraclass correlation coefficient (ICC)]
- Validity, including responsiveness (the degree to which an instrument measures what it purports to measure, and reflects change over time)
- Interpretability (degree to which easily understood meaning can be assigned to an instrument's quantitative scores)
- Burden of administration
- Administration format
- Cultural and language adaptations or translations

In addition, each questionnaire was rated using a quantitative quality assessment

AQLQ-J

The Asthma Quality of Life Questionnaire (4, 5) (AQLQ-J) was developed in Canada.

No formal statement is made about the conceptual model, but several assumptions are alluded to, including QoL should include physical and emotional health, subjective health status, and domains of functioning that are important to patients.

One hundred and fifty-two items were generated from a wide range of sources, e.g. previous work on a QoL questionnaire for clinical trials in chronic lung disease (28) and the researcher's experience working with patients (personal communication). Items were reduced to 32 using the 'importance method': patients rated the importance of each item, and items were then selected based on overall impact (i.e. frequency multiplied by importance). Four domains were identified: activity limitation, symptoms, emotional function, and exposure to environmental stimuli.

An unusual feature of the original AQLQ-J is that five of the eleven activity items represent an idiographic component, i.e. patients choose activities of importance to themselves, rather than being constrained by a fixed activity list (29). Patients can choose from a list of 26 activities the five most important to them. Later, the questionnaire was standardized with a fixed activity list (15) replacing the five individualized questions with five generic activities (strenuous, moderate, social, work-related, and sleeping).

Construct validity was evaluated by testing associations between the AQLQ-J scores and lung function as predicted by an asthma specialist, and generic QoL (5). Longitudinally, strong correlations were found between changes in AQLQ-J scores and changes in asthma control as well as medication usage. However, associations between changes in AQLQ-J and expiratory flow rates and airway hyperresponsiveness were weaker. Relationships with changes as measured by generic instruments [Rand General Health Survey (30), Sickness Impact Profile (SIP) (31)] were only found for some domains of these measures. Somewhat unexpectedly, the emotional domain of the AQLQ-J correlated more closely with the physical than with the emotional domain of the Rand Survey. There were strong correlations with ratings when change was assessed by asking patients whether they had experienced any asthma-related changes since their last clinic visit.

When comparisons were made cross-sectionally, strong relationships were found between asthma control, but not asthma severity and AQLQ-J domains. This was contrary to the weak correlations predicted. The AQLQ-J domains were also significantly correlated with generic QoL as measured by the SIP and the Rand.

The AQLQ-J was found to be responsive to within-subject change. The differences in total and domain scores between the group of patients with stable asthma and the group of patients in whom asthma changed were found to be highly significant.

The properties of the AQLQ-J were also assessed in 52 patients in an Emergency Department in Canada (32), using a modified version of the AQLQ-J with a three-day recall period. Correlations between the SIP and AQLQ-J measures were moderate. Correlations found between pulmonary function results and AQLQ-J domains were low, except for activity limitations. High correlations were found between

symptoms and the AQLQ-J. The same group reported the AQLQ-J to be acceptable to both patients and physicians (33).

The minimal important difference (MID) is the smallest difference in score which patients perceive as beneficial and would mandate, in the absence of unwanted side-effects and excessive cost, a change in patient management (34). The MID is derived by comparing QoL score changes to global ratings of change. For the AQLQ-J, the MID is around 0.5 (range 0.42–0.58) for overall QoL and for individual domains (35).

The AQLQ-J was initially developed for interviewer administration and pretested in 30 patients. After modification for self-administration, it was tested in five patients with 'limited education' in whom completion problems were anticipated, but no further modification was needed.

The AQLQ-J is currently available in 79 languages (personal communication). All have undergone linguistic validation by the MAPI Institute (<http://www.mapi-research.fr/>).

A French version of the AQLQ-J was used in a study comparing occupational with nonoccupational asthma which found that patients with occupational asthma experienced greater impairment of QoL than matched controls (36). A detailed description of the translation/back translation process into Spanish is available (37). A separate validation study of the Spanish version was carried out later in 116 patients (38). This study found the AQLQ to show high internal consistency (Cronbach's alphas: 0.78–0.96) and a high 2-week reproducibility (ICC: 0.82–0.92). Expected differences were observed with regard to disease severity [as measured by symptoms, medication, use of services and recruitment setting (hospital, outpatient, primary care)]. Correlations between the AQLQ and the SGRQ were strong, between the AQLQ and dyspnea moderate to strong and between AQLQ and FEV₁ weak to moderate. Changes in the AQLQ scores were significantly different in patients who either improved or deteriorated compared with those patients who remained stable ($P < 0.0001$ and $P < 0.01$, respectively, for overall AQLQ).

Psychometric performance was evaluated in a US English-speaking sample ($N = 161$) (39), with internal consistency ranging from 0.90 to 0.95 and reproducibility ranging from 0.81 to 0.93. AQLQ was significantly correlated with an asthma disease severity scale, but not with FEV₁% predicted. QoL was better in men and worse in those with high school education or less.

When validated in Serbo-Croat (40) disease severity, place of residence, weather conditions, age, and FEV₁% predicted were all significantly related to QoL. Cronbach's alpha ranged from 0.72 to 0.93.

AQLQ-S

The Asthma Quality of Life Questionnaire-Sydney (AQLQ-S) (6) was developed in Australia. The developers consider QoL to be a 'broad-based outcome measure' of greater relevance than disease severity when assessing the impact of environmental exposures or treatments on asthma. Disease severity and QoL are described as overlapping but distinct concepts.

Features listed as defining boundaries of QoL are risk of death, risk of future disability, impact on family and community outside the realm of an individual's QoL, social situation, psychological makeup, and expectations inside the realm of QoL.

The original item pool was sourced from patient focus groups, interviews with asthma nurse educators, and the clinical experience of the investigators. Eight patients took part in focus groups after considering in advance the impact of their asthma in four areas: usual functioning; moods, feelings, and relationships; restrictions on life, and overall sense of well-being. These aspects are considered the minimum standards for judging the content validity of health measures (41).

From these three sources, a 69 statement questionnaire, relating to the past 4 weeks, was constructed. The item pool was reduced in two steps. After a pilot study ($n = 18$), items with low prevalence were deleted or combined with others, and then statements were reworded to increase clarity. The modified questionnaire was then administered to a larger sample ($n = 283$). Items with highly skewed distributions or large amounts of missing data were removed, as were items with strong multicollinearity or low factor loadings after principal component analysis. The remaining 31 items gave six principal components (breathlessness, concerns, mood, social, cough, and control). Items loading on the latter two domains were then dropped because of low item-total correlations.

This item reduction procedure resulted in a 20-item questionnaire with four subscales: breathlessness, concerns, mood, and social. Item phrasing varies with domain.

Construct validity was assessed in a community sample by correlating AQLQ-S scores with medical markers of disease severity. Weak, nonsignificant correlations were found in the expected direction with FEV₁% predicted and the degree of bronchial hyperresponsiveness. The correlations with physiological measures were strongest for the domains of 'breathlessness' and 'concerns', followed by 'social', and weakest for 'mood'. Mean QoL scores were closely linked to the number of asthma medications ($P = 0.003$).

In a separate study, the AQLQ-S was evaluated as a measure of change. Responsiveness was assessed by comparing change over 4 months in AQLQ-S scores in a group of 19 patients with improving asthma and 20 with stable asthma. The AQLQ-S was able to detect differences between the two groups ($P = 0.007$). As predicted, a change in AQLQ-S score was correlated with changes in symptom score and in bronchial hyperresponsiveness. The correlations with changes in peak flow variability and changes in SIP scores were in the expected direction, but weaker than expected.

Formal validation studies have been carried out for American English (42), Spanish (43), and German versions of the AQLQ-S (44).

LWAQ

The Living with Asthma Questionnaire (LWAQ) was developed in the United Kingdom in 1993 for adults with asthma (8, 9).

The original paper emphasizes that 'quality of life' refers to the patient's own subjective interpretation of their life ('functional effect of an illness and its consequent therapy upon a patient, as perceived by the patient'), in contrast to the physician's assessment. The scale was developed to be consistent with this definition. The authors also emphasize that QoL is multidomain, 'in that a particular condition may affect life experiences in a variety of ways'. The method used to elicit patient responses in the item generation phase reveals the implicit conceptual model adopted, in which patients were asked about their 'everyday life experiences of living with asthma'.

Item selection was informed by focus groups as it was considered that one-to-one interviews might be intimidating. The first questionnaire included 101 items, grouped into eleven domains: social/leisure, sport, sleep, holidays, work and other activities, colds, mobility, effects on others, medication usage, doctors, and dysphoric states and attitudes. A two-item domain on sexual behavior was later added in recognition that the groups may have felt inhibited discussing sexual activity.

The first version of the questionnaire was completed by 101 primary care patients. Data were subjected to principal factor analysis. Items were deleted if >70% patients gave one response (indicating poor discrimination), factor loading on the first factor was <0.3, or if questions were reported as problematic. Seventy-seven items were retained, and these were then administered to patients ($n = 150$) recruited from General Practice. Further principal factor analysis indicated a single-factor solution. Some negative items with low factor loading were made positive, assuming that their negativity had led to problems in comprehension. The revised questionnaire consisted of 43 negative and 29 positive items that were piloted in 405 patients, and four further items were deleted following factor analysis.

A further factor analysis ($n = 282$) indicated a one-factor solution again, indicating unidimensionality of the construct, but the variance explained by the first factor (30%) was higher compared with the third version.

The final questionnaire includes 68 items in eleven domains: social/leisure (six items), sport (three items), holidays (three items), sleep (four items), work and other activities (six items), colds (five items), mobility (six items), effects on others (five items), medication usage (six items), sex (one item), and over one-third of items are grouped into the one domain 'dysphoric states and attitudes'. The questionnaire includes both negative and positive items, for instance 'I sleep badly because of my asthma' or 'I can run like other people'. In this way, it compensates for acquiescence bias, that is the tendency to respond 'yes' irrespective of item content.

Validity was established by comparing different subgroups of patients (age, sex, and route of recruitment) and by confirming expected differences. It was found that QoL decreased with age, was slightly lower in men, and was lower in participants recruited through the Asthma Society compared with those recruited through GPs. Further evidence of validity comes from positive correlations with the Sickness Impact Profile ($r = 0.66$) and negative correlations with peak

flow ($r = -0.44$) (9). In another study, QoL correlated with steroid prescribing ($r = 0.35$) (45).

Responsiveness of the LWAQ has not been reported in separate validation studies, only in the context of clinical trials (46).

The LWAQ has been validated in Norwegian (47). An unvalidated Bulgarian version is available from the Web site of the research group 'Psychology of Holistic Health' (<http://www.psychhealth.org.uk/questionnaires.html>).

SGRQ

The St George's Respiratory Questionnaire (SGRQ) was developed in 1991 for adults with chronic airflow obstruction/limitation aged >20 (10, 11).

The authors had previously noted 'considerable restrictions on the physical and social aspects of the lives of patients with this chronic disease' resulting in impaired QoL (48). The development of the SGRQ was inspired by an established measure of general health, the Sickness Impact Profile (SIP) (31), which was being used in patients with chronic airflow limitation (49) but was felt to be insufficiently sensitive for people with mild to moderate airway disease.

The two SGRQ validation papers state that the final version of the questionnaire consists of 76 items, but actually it has 50 items with 76 weighted responses (Jones, personal communication). The items are organized into three content areas: symptoms [originally frequency and severity of symptoms in the 'past 12 months', later validated for 'past month' and also satisfactorily used for 'past 3 months' (50)], activities (causing or limited by breathlessness), and impacts (social functioning impairment and psychological disturbances resulting from airways disease). It is stated that items relating to anxiety and depression were not included in the SGRQ because established measures existed for these constructs (11).

Each item in the SGRQ has an empirically derived weight (range 0–100) (48). The scores are calculated as the percentage of the summed weights of positive items relative to the summed weights of all items (for each component, and in total) (50), so the scores for the domains as well as the total score range from 0 to 100%. Demographic and disease characteristics had only minimal effects on the weights (48, 51).

Validity of the SGRQ was established by a comparison with other measures of disease activity and general health (11). Each domain of the questionnaire correlated with reference measurements relevant to the different sections of the questionnaire in a multivariable regression model. Cough and wheeze were the strongest correlates with SGRQ symptom score, while the SGRQ activity score correlated best with the 6-min walking distance test (6MWD) and the MRC dyspnea grade. The correlations with the SGRQ impacts section and the total score were more evenly distributed and included anxiety, walking distance, dyspnea, and wheeze. Significant correlations of the SGRQ with FEV₁, FVC, 6MWD, dyspnea, anxiety, and depression [measured by the Hospital Anxiety and Depression Scale (52)] were similar compared with the correlations with the SIP. However, the regression slopes

against the reference measures were greater when the SGRQ was used as outcome compared with the SIP (11). Hence, it was concluded that the SGRQ was more sensitive to differences in the health of patients with airflow limitation.

Furthermore, when re-administered after 1 year ($n > 120$), significant correlations were found between change in SGRQ total score and changes in FVC, anxiety, and dyspnea (10). It was concluded that the measure was able to quantify change over an extended period of time. It is also noteworthy that correlations between different measures of disease activity in cross-sectional comparisons were higher than correlations between changes in the same variables over 1 year.

When relating differences in questionnaire score to differences in disease activity, it was found that a four-point change in SGRQ score corresponded to a 6% change in 6MWD (11). This change was the mean change following therapy as calculated from a number of published studies, and hence a four-point change in SGRQ score is considered to indicate a clinically significant difference.

The SGRQ exists in 73 languages. Most of these versions were produced as collaborations between St George's University of London and the MAPI Institute of Health Research Associates (<http://www.hrainc.net>).

Spanish (53), Swedish (54), American English (55), Polish (56), and Chinese (57) versions of the SGRQ have been formally validated, but only the Polish and Chinese validation studies included patients with asthma.

QOL-RIQ

The Quality of Life for Respiratory Illness Questionnaire (QOL-RIQ) was developed in 1997 for use in chronic nonspecific lung disease (CNSLD), i.e. asthma and COPD (25, 58).

The authors state two guiding principles: first, that QoL questionnaires should at least include the areas of physical and functional status, psychological status, and social functioning (59). Second, that the development would encompass the stages described by Guyatt et al. (60).

Initially, 221 items were generated and grouped into 12 subscales: breathing problems; other physical problems related to CNSLD; situations and/or substances that can trigger or enhance breathing problems; other problems, such as financial, relating to the treatment of CNSLD; emotions relating to breathing problems; general activities; daily and domestic activities; sport, hobbies, and leisure pursuits; social activities; sexuality and relationships; occupation and work; and schooling/training.

Factor analysis was used to reduce the item pool to 55 items grouped into seven subscales: breathing problems; physical problems related to chest problems; emotions related to chest problems; problems with general activities; situations that might trigger or enhance breathing problems; daily and domestic activities; and social activities, relationships, and sexuality.

Construct validity was assessed by analyzing correlations between the total score and its seven subscales with illness severity indicators (degree of dyspnea, frequency of attacks, subjective severity, GP visits, absence from work). When all

subscales were combined, and all illness severity indicators were combined, the correlation was $r = 0.65$. A regression analysis was also performed, using the QoL score as the dependent variable. Most of the variance was explained by indicators of illness severity, particularly subjective severity of attacks that explained 25.3% of the variance. Less than 10% of the variance was explained by symptoms of chronic wheeze or chronic cough. The contribution of background characteristics (gender, diagnosis, age, smoking, illness duration) was not significant.

Further evidence for validity was obtained from the longitudinal study ($n = 108$) discussed previously (61). All QOL-RIQ scores were significantly correlated with self-rated change in health, in disease symptoms and with change in self-assessed health status. There were also significant correlations between QoL-RIQ change scores and change in experienced invalidity, emotional well-being, anxiety, depressive symptoms, and RAND-36 domains. This study also provides evidence for responsiveness in that domains and total QoL-RIQ score changed significantly over time.

A MID of 0.5 was calculated, using a retrospective global rating of change question. The authors concede that retrospective computation might be biased because of poor patient recall of their initial health status. It has been shown separately that retrospective assessment of change tends to be significantly higher than serial assessment of change (62).

The questionnaire is available in English and Dutch.

Rhinasthma

The Rhinasthma questionnaire was developed for adult patients suffering from rhinitis and/or asthma (18) to reflect the united airways disease hypothesis (63, 64).

Quality of life is considered to be the patient's subjective point of view and to offer a more comprehensive description of the impact of both disease and its therapy on everyday life, when compared to the physician-defined concept of health status. It is emphasized that the new instrument includes the functional, physical, and emotional problems experienced by adult patients with respiratory allergy.

A 42-item pool of symptoms, problems, and limitations arising from asthma and rhinoconjunctivitis was generated, and the items were administered to 148 outpatients. Patients were asked to rate items from 1 = 'not important' to 4 = 'very important' to enable an importance score to be calculated (frequency of item selection $\times$ mean importance). Based on this composite score, 12 items were deleted.

In the validation phase, 104 patients with respiratory allergy [rhinoconjunctivitis alone (42), asthma and rhinoconjunctivitis (62)] completed the Rhinasthma questionnaire and the SF-36. Criterion validity was assessed by comparing Rhinasthma scores of patients with rhinitis to scores of patients with both asthma and rhinitis. The average scores of 14 items differed significantly between the patients with rhinitis alone and those with both asthma and rhinitis.

Following principal component analysis, a three-factor solution explained 52% of the variance. In addition, concordance between SF-36 and Rhinasthma was evaluated to

verify the ability of the new instrument to differentiate between patients with rhinitis alone and patients with rhinoconjunctivitis and asthma. All SF-36 domains were significantly different between these two patient groups.

Responsiveness of the instrument was evaluated in 27 patients with respiratory allergy (persistent rhinitis and intermittent asthma) who were assessed at baseline and after 3 weeks treatment with cetirizine. Eighteen items of the Rhinasthma showed a significant difference after 3 weeks. One formal validation study of Rhinasthma has been conducted in German (65).

Summary

A full summary of the information relating to the review criteria is presented in Tables 1 and 2. In addition, the tables contain information on reliability assessment, burden of completion, scoring and administration format together with estimated coefficients and effect sizes relating to the validity assessment of the questionnaires.

The asthma QoL questionnaires reviewed here differ from each other in several aspects, including the underlying (often implicit) concepts operationalized, the sources used for item generation, the way in which the items are generated, the statistical approach used to reduce the initial item pool, the estimation of reliability, the degree to which patient feedback is used, how validity is assessed, how to interpret a change in score, how the burden imposed on patients is assessed, and the rigor with which cultural and language adaptations are conducted.

The questionnaires also differ regarding the fractional content of symptom-related items (ranging from 0% to 38%). This considerable variation between instruments means that they must never be assumed to be measuring the same construct. However, the questionnaires form a family, because they resemble each other beyond random occurrence of similarity and share certain characteristics, most obviously the inclusion of items relating to activity limitation or mood disturbance. Strengths and potential weaknesses of the measures are listed in Table 3.

Conceptual model and questionnaire content

The ideal stages in HRQoL questionnaire development are set out in Table 4 (23). Interestingly, none of the questionnaires reviewed has been developed with the recommended first step, the identification of an explicit conceptual model of QoL. Instead, the developers seem to have defined what is being measured by the content of their questionnaire. This lack of conceptual model and the wide variation in methodological development have also been observed in other disease areas, for example in health outcome measures for osteoarthritis (66). The lack of clear definitions of QoL and the fact that it is operationalized in a number of ways were first noted in a review of empirical studies published between 1980 and 1994 (67). Four of the questionnaires reviewed here preceded this publication, and the subsequent ones (QoL-RIQ, Rhinasthma) were inattentive.

The questionnaires contain symptoms or symptom lists to a varying degree (from 0% in the Rhinasthma and the AQLQ-S to 38% in the AQLQ-J). While symptom scores do have a place in the assessment of patients with asthma (68), their inclusion in a QoL measure is questionable. Health-related QoL is a multidimensional concept representing the patient's overall perception of the impact of the illness and its treatment (23). The perception and impact of symptoms should thus be included in measures of QoL, but not symptoms *per se*. The need for QoL measures to be distinct from symptom scores is illustrated in this hypothetical example: imagine a patient with mild, controlled allergic asthma who still experiences symptoms such as wheezing during the pollen season. Suppose further that this patient has experienced this since childhood, has adjusted well, and perceives little QoL impairment. Assessing QoL with a questionnaire that captures the frequency of symptoms would exaggerate the impairment of QoL.

Variation in methodological development

While developers generally seem to follow the steps involved in questionnaire development (in contrast to defining a theoretical framework), there is wide variation in the methods they have chosen to adopt. The methodologies used for item generation involve patients, experts, and published literature to varying degrees. For item reduction, either the importance rating method (AQLQ-J, Rhinasthma) or factor analysis/principal components analysis (AQLQ-S, LWAQ, ROQ-QOL) was used. These methods differ fundamentally. When both methods were compared to reduce 152 items that are potentially troublesome to patients with asthma, two appreciably different instruments resulted (69). The psychometric method discarded the highest impact emotional and environmental items and included mainly items related to fatigue instead. The choice of method is rarely justified in the publication, and one is left to speculate that these different approaches arise because of variations in expertise or differing constraints of money and time.

Choosing a questionnaire

There are several possible approaches for choosing between the questionnaires, given that they are all similar, but also distinct.

Formal review and scoring system

The formal review process generates a lot of data that are difficult to assimilate. We developed a scoring system, but such a scoring system may give inappropriate precision because it may neglect the impact of weak conceptual foundations. It has been argued that the validation of weak constructs makes only a small contribution toward good science (70) because strong validation studies cannot compensate for a lack of conceptual modeling at the start of a questionnaire development procedure. Elements from the validation studies are thus overrepresented in a scoring system.

Table 1 Key characteristics of six asthma-specific Quality of Life Questionnaires (Country of origin, target group, conceptual model, item generation, item content areas, response format and scoring, reliability, interpretability, burden of administration, administration format, and cultural/linguistic adaptations or translations)

Characteristic	AQLO-J	AQLO-S	LWAQ	SGRQ	QOL-RIQ	Rhinasthma
Country of Origin	Canada	Australia	United Kingdom	United Kingdom	Netherlands	Italy
Target group	Adults with asthma	Adults with asthma	Adults with asthma	Adults (>20) with chronic airflow obstruction/limitation	Adults with mild to moderate chronic nonspecific lung disease	Adults with rhinitis and/or asthma
Conceptual model	Not explicitly stated	Not explicitly stated	Not explicitly stated	Not explicitly stated	Not explicitly stated	Not explicitly stated
Item generation	152 items sources: Literature; generic QoL measures; expert discussion; patient interviews ($n = 6$)	69 items sources: prestructured focus groups ($n = 8$); clinical experience of investigators; interviews with asthma nurse educators	101 items sources: six focus groups ($n = 3-10$)	Not reported	221 items sources: literature; contents of generic QoL questionnaires; consultation with medical care providers for patients with CNSLD; consultation with QoL experts; semi-structured interviews (11 patients)	42 items sources: published literature on HrQoL questionnaires & symptom scores; expert discussions (allergists, pulmonologists); unstructured interviews with outpatients ($n > 200$)
Item reduction	Impact analysis, based on importance scores (152 → 32 items)	Principal components analysis (69 → 20 items)	Factor analysis (101 items → 77 items → 72 items → 68 items → 68 items)	Not reported	Items included for analysis if applicable to > 70% of respondents; items combined if inter-item correlation ≥ 0.8 ; factor analysis (221 items → 55 items)	Impact analysis, based on importance scores (42 → 30 items)

Table 1 (Continued)

Characteristic	AQLQ-J	AQLQ-S	LWAQ	SGRQ	QOL-RIQ	Rhinasthma
Item content areas (domains)	32 items in 4 domains: • Activity limitation • Symptoms • Emotional functioning • Exposure to environmental stimuli	20 items in 4 domains: • Breathlessness • Concerns • Mood • Social	68 items in 11 domains: • Social/leisure • Sport • Holidays • Sleep • Work & other activities • Colds • Mobility • Effects on others • Medication usage • Sex • Dysphoric states & attitudes	50 items in 3 domains: • Symptoms (frequency & severity) • Activities (causing or limited by breathlessness) • Impacts (social functioning impairment & psychological disturbances resulting from airways disease)	55 items in 7 domains: • Breathing problems • Physical problems related to chest problems • Emotions related to chest problems • Problems with general activities • Situations that might trigger or enhance breathing problems • Daily & domestic activities • Social activities, relationships & sexuality [recall period: 12 months]	30 items, grouped into three factors which are not labeled
Response format & scoring	7-point Likert scale [recall period: 2 weeks]	5-point Likert scale [recall period: 4 weeks]	3-point Likert scale with 'not applicable' option [recall period: current time point of assessment]	Mostly binary (true/false), some items have three, four or five response options Each item in questionnaire has empirically derived weight, scores are calculated as % of summed weights of positive items relative to summed weights of all items (for each component & in total); total score range 0–100%; (where 100% = worst possible health status)	7-point Likert scale with 'not applicable' option [recall period: 2 weeks]	5 point Likert scale Responses to each of the 32 items are added and divided by 32 (same applies for domains); higher scores indicate worse QoL

Table 1 (Continued)

Characteristic	AQLQ-J	AQLQ-S	LWAQ	SGRQ	QOL-RIO	Rhinasthma
Reliability	Juniper 1993 Am Rev Respir Dis Test-retest reliability (intraclass correlation coefficient, ICC): Total 0.92 activities: 0.93, symptoms: 0.89 emotions: 0.91 environment: 0.94	Marks 1992 J Clin Epidemiol Test-retest reliability (ICC) Breathlessness 0.61 (0.44, 0.74) Mood 0.78 (0.67, 0.86) Social 0.78 (0.67, 0.86) Concerns 0.80 (0.69, 0.87) Total 0.80 (0.70, 0.88)	Hyland 1991 J Psychosom Research Test-retest reliability (correlation coefficient <i>r</i>) 0.95	Jones 1992 Am Rev Respir Dis Test-retest reliability in patients with asthma (<i>n</i> = 40) or COPD (<i>n</i> = 20) Coefficient of variation 19% for total score (same for asthma and COPD); intraclass correlation <i>r</i> = 0.91 for asthma, <i>r</i> = 0.92 for COPD; intraclass correlation according to domains: Symptoms: <i>r</i> = 0.91 Activity: <i>r</i> = 0.87 Impact: <i>r</i> = 0.88 (combined data for asthma & COPD)	Maille 1997 Resp Med Split-half reliability total score: 0.92 Breathing problems: 0.85 Physical problems: 0.85 Emotions: 0.84 General activities: 0.75 Situations triggering or enhancing breathing problems: 0.68 Daily & domestic activities: 0.86 Social activities, relationships and sexuality: 0.89	Baiardini 2003 Allergy Test-retest reliability [Pearson correlation coefficient <i>r</i>] <i>N</i> = 31 stable patients, 1 week apart <i>r</i> = 0.70–0.92 for 25 items, <i>r</i> = 0.61–0.69 for remaining 5 items
	Internal consistency: not reported	Internal consistency [Cronbach's alpha] Outpatient sample (<i>n</i> = 77) Breathlessness: 0.89 Mood: 0.82 Social: 0.88 Concerns: 0.84 Total: 0.92 (Item-total correlations ranged from 0.41 to 0.72) Community sample (<i>n</i> = 87) Total: 0.92 Subscales: 0.87–0.94 (Item-total correlations ranged from 0.44 to 0.78)	Internal consistency: not reported	Internal consistency: not reported	Internal consistency [Cronbach's alpha] (for domain subscales without not applicable option) Breathing problems: 0.85 Physical problems: 0.84 Emotions: 0.88 Van Stel 2003 Qual Life Res (108 patients with moderate to severe asthma or COPD) Intraclass correlation of change for total score: 0.90	Internal consistency [Cronbach's alpha]: $\alpha > 0.70$ for all 30 items

Table 1 (Continued)

Characteristic	AQLQ-J	AQLQ-S	LWAQ	SGRQ	QOL-RIO	Rhinasthma
Interpretability	Minimal important difference approximately 0.5 (0.42–0.58)	Not reported	Not reported	Four-point change in SGRQ score corresponded to a 6% change in 6MWD and considered to indicate a clinically significant difference	Minimal important difference approximately 0.5	Not reported
Burden of administration	10–15 min	5 min	15–20 min	10 min	Not reported	Not reported*
Administration format	Self-administered, interviewer-administered	Self-administration	Self-administered, interviewer-administered	Supervised self-administration	Self-administration	Self-administered
Cultural & language adaptations or translations	79 languages Validation studies French: Malo 1993 Spanish: Sanjuas 1995 Sanjuas 2001 US English: Leidy 1998 Serbian: Tomic 2004	Validation studies American English: Gupchup 1997 Spanish: Perpina 1998 German: Miedinger 2006	Validation study Norwegian: Haave 2004; unvalidated Bulgarian version	73 languages Validation studies Spanish: Ferrer 1996 Swedish: Engstrom 1998 Polish: Kuzniar 1999 American English: Barr 2000 Chinese: Wang 2001	Dutch and English	Validation study German: Mosges 2007
Website	http://www.qoltech.co.uk	–	http://www.psychhealth.org.uk/	–	–	–

*Completion time of 5–10 minutes reported in the German validation study (65).

Table 2 Validity of the six asthma-specific QoL measures**(A) AQLQ-J***Juniper 1993 Am Rev Respir Dis**(39 patients with symptomatic asthma)***Cross-sectional correlations**• *Asthma QoL and clinical asthma*FEV1% predicted [activities: $r = 0.06$ (ns), symptoms: $r = 0.11$ (ns), emotions: $r = 0.18$ (ns), environment: $r = 0.08$ (ns)]Airway hyperresponsiveness to methacholine [PC20, mg/ml] [activities: $r = 0.07$ (ns), symptoms: $r = 0.00$ (ns), emotions: $r = 0.11$ (ns), environment: $r = 0.14$ (ns)]Asthma control [activities: $r = 0.31$ (ns), symptoms: $r = 0.69$ ($P < 0.001$), emotions: $r = 0.36$ ($P < 0.05$), environment: $r = 0.45$ ($P < 0.05$)]Peak expiratory flow rate [l/min] [activities: $r = 0.09$ (ns), symptoms: $r = 0.13$ (ns), emotions: $r = 0.04$ (ns), environment: $r = 0.16$ (ns)]• *Asthma QoL and generic QoL*

Sickness impact profile

- Physical domain [activities: $r = 0.52$ ($P < 0.001$), symptoms: $r = 0.38$ ($P < 0.05$), emotions: $r = 0.28$ (ns), environment: $r = 0.43$ ($P < 0.05$)]- Psychosocial function [activities: $r = 0.37$ ($P < 0.05$), symptoms: $r = 0.30$ (ns), emotions: $r = 0.39$ ($P < 0.05$), environment: $r = 0.40$ ($P < 0.05$)]

Rand general health survey

- Physical [activities: $r = 0.81$ ($P < 0.001$), symptoms: $r = 0.60$ ($P < 0.001$), emotions: $r = 0.53$ ($P < 0.001$), environment: $r = 0.69$ ($P < 0.001$)]- Emotional [activities: $r = 0.09$ (ns), symptoms: $r = 0.38$ ($P < 0.05$), emotions: $r = 0.49$ ($P < 0.05$), environment: $r = 0.32$ (ns)]**Longitudinal correlations**• *Change in asthma QoL and change in clinical asthma:*Asthma control [activities: $r = 0.57$ ($P < 0.001$), symptoms: $r = 0.67$ ($P < 0.001$), emotions: $r = 0.63$ ($P < 0.001$), environment: $r = 0.40$ ($P < 0.001$)]Medication requirements [activities: $r = 0.45$ ($P < 0.001$), symptoms: $r = 0.50$ ($P < 0.001$), emotions: $r = 0.30$ ($P < 0.05$), environment: $r = 0.34$ ($P < 0.05$)]FEV1, % predicted [activities: $r = 0.28$ ($P < 0.05$), symptoms: $r = 0.27$ ($P < 0.05$), emotions: $r = 0.43$ ($P < 0.001$), environment: $r = 0.29$ ($P < 0.05$)]Airway hyperresponsiveness to methacholine [PC 20, mg/ml] [activities: $r = 0.26$ ($P < 0.05$), symptoms: $r = 0.26$ ($P < 0.05$), emotions: $r = 0.30$ ($P < 0.05$), environment: $r = 0.30$ ($P < 0.05$)]Peak expiratory flow rate [l/min] [activities: $r = 0.41$ ($P < 0.001$), symptoms: $r = 0.42$ ($P < 0.001$), emotions: $r = 0.38$ ($P < 0.001$), environment: $r = 0.33$ ($P < 0.05$)]• *Change in asthma QoL and generic QoL*

Sickness impact profile (SIP)

- Physical domain [activities: $r = 0.24$ ($P < 0.05$), symptoms: $r = 0.20$ (ns), emotions: $r = 0.23$ (ns), environment: $r = 0.17$ (ns)]- Psychosocial function domain [activities: 0.07 (ns), symptoms: 0.19 (ns), emotions: 0.27 ($P < 0.05$), environment: 0.00 (ns)]

Rand general health survey

- Physical domain [activities: $r = 0.51$ ($P < 0.001$), symptoms: $r = 0.46$ ($P < 0.001$), emotions: $r = 0.49$ ($P < 0.001$), environment: $r = 0.36$ ($P < 0.05$)]- Emotional domain [activities: $r = 0.34$ ($P < 0.05$), symptoms: $r = 0.31$ ($P < 0.05$), emotions: $r = 0.30$ ($P < 0.05$), environment: $r = 0.37$ ($P < 0.001$)]• *Change in asthma QoL with asthma global ratings of change:*Activities [activities: 0.79 ($P < 0.001$), symptoms: 0.76 ($P < 0.001$), emotions: $r = 0.75$ ($P < 0.001$), environment: $r = 0.64$ ($P < 0.001$)]Symptoms [activities: $r = 0.78$ ($P < 0.001$), symptoms: $r = 0.82$ ($P < 0.001$), emotions: $r = 0.70$ ($P < 0.001$), environment: $r = 0.66$ ($P < 0.001$)]Emotions [activities: $r = 0.43$ ($P < 0.001$), symptoms: $r = 0.49$ ($P < 0.001$), emotions: $r = 0.52$ ($P < 0.001$), environment: $r = 0.38$ ($P < 0.001$)]**Responsiveness**

Questionnaire sensitive to within-subject change in 26 patients in whom asthma had changed (mean score change 1.06 ± 0.78 for overall QoL, $P < 0.001$; 0.84 ± 0.66 for activities, $P < 0.001$; 1.30 ± 1.08 for symptoms, $P < 0.001$; 1.18 ± 1.01 for emotions, $P < 0.001$; 0.66 ± 0.72 , $P = 0.007$ for environment); all changes significantly different compared with changes in 13 patients with stable asthma ($P < 0.001$ for overall QoL, activities, symptoms, emotions; $P = 0.007$ for environment)

(B) AQLQ-S*Marks 1992 J Clin Epidemiol***Cross-sectional correlations [Spearman's correlation coefficient and 95% CI]**• *Asthma QoL and clinical asthma*FEV1, % predicted ($n = 82$): breathlessness: $r = -0.20$ (-0.40 – 0.02); mood: $r = -0.10$ (-0.31 – 0.12); social: $r = -0.15$ (-0.36 – 0.07); concerns: $r = -0.18$ (-0.38 – 0.04); total: $r = -0.20$ (-0.40 – 0.01)

Table 2 (Continued)

Provocative dose histamine required to cause 20% fall in FEV₁ [PD₂₀FEV₁] ($n = 81$): breathlessness: $r = -0.19$ (-0.40 – 0.03); mood: $r = -0.01$ (-0.22 – 0.21); social: $r = -0.18$ (-0.38 – 0.04); concerns: $r = -0.20$ (-0.40 – 0.02); total: $r = -0.16$ (-0.36 – 0.06)

Number of drugs ($n = 85$): breathlessness: $r = 0.42$ (0.23 – 0.58); mood: $r = 0.15$ (-0.07 – 0.35); social: $r = 0.37$ (0.17 – 0.54); concerns: $r = 0.43$ (0.23 – 0.59); total: $r = 0.38$ (0.18 – 0.55)

Marks 1993 *J Clin Epidemiol*

Longitudinal correlations [Pearson's correlation coefficient]

• Change in asthma QoL and change in clinical asthma:

Symptoms: breathlessness: $r = 0.13$ (-0.27 – 0.48); mood: $r = -0.06$ (-0.43 – 0.33); social: $r = 0.52$ (0.18 – 0.75); concerns: $r = 0.37$ (-0.01 – 0.66); total: $r = 0.37$ (-0.04 – 0.64)

Peak flow variability: breathlessness: $r = -0.15$ (-0.49 – 0.24); mood: $r = -0.06$ (-0.43 – 0.22); social: $r = 0.51$ (0.17 – 0.74); concerns: $r = 0.02$ (-0.36 – 0.39); total: $r = 0.12$ (-0.26 – 0.47)

Log₁₀DRR (ratio of final %FEV₁ fall from baseline to final cumulative dose of histamine administered): breathlessness: $r = 0.21$ (-0.14 – 0.50); mood: $r = 0.14$ (-0.20 – 0.46); social: $r = 0.47$ (0.16 – 0.70); concerns: $r = 0.32$ (-0.01 – 0.56); total: $r = 0.38$ (0.06 – 0.64)

• Change in asthma QoL and generic QoL

SIP Total; breathlessness: $r = 0.03$ (-0.27 – 0.32); mood: $r = 0.19$ (-0.12 – 0.46); social: $r = 0.20$ (-0.13 – 0.44); concerns: $r = 0.23$ (-0.07 – 0.50); total: $r = 0.18$ (-0.12 – 0.45)

SIP Psychosocial; breathlessness: $r = -0.18$ (-0.45 – 0.12); mood: $r = 0.10$ (-0.20 – 0.39); social: $r = 0.04$ (-0.26 – 0.33); concerns: $r = 0.09$ (-0.21 – 0.38); total: $r = -0.01$ (-0.31 – 0.29)

Responsiveness* [responsiveness index, 95% CI]

Breathlessness: $r = 1.49$ (0.52 – 2.58); Mood: $r = 0.82$ (0.23 – 1.47); Social: $r = 1.24$ (0.47 – 2.11); Concerns: $r = 0.91$ (0.41 – 1.49); Total: $r = 1.31$ (0.62 – 2.09)

(C) LWAO

Hyland 1991 *J Psychosom Res*

Confirmation of expected group differences ($N = 228$):

Decrease of QoL with increasing and poorer QoL in males compared to females (no formal test carried out)

Hyland 1991 *Resp Med*

Cross-sectional correlation

SIP: $r = 0.66$ ($n = 76$)

Hyland 1993 *British Journal of Clinical Psychology*

Cross-sectional correlation (Pearson correlation coefficient), $n = 42$

Steroid prescribing: $r = 0.35$ ($P < 0.05$)

FVC: $r = -0.39$ ($P < 0.01$)

FEV₁: $r = 0.40$ ($P < 0.01$)

PEF: $r = -0.44$ ($P < 0.01$)

ASC[†], Panic-fear: $r = 0.41$ ($P < 0.01$); Airways obstruction: $r = 0.52$ ($P < 0.01$); Hyperventilation: $r = 0.47$ ($P < 0.01$); Fatigue: $r = 0.65$ ($P < 0.01$); Irritability: $r = 0.41$ ($P < 0.01$)

(D) SGRQ

Jones 1992 *Am Rev Respir Dis*

Comparison of SGRQ scores and reference measures of disease activity ($N = 141$):

• SGRQ symptom score significantly higher in patients with cough (70.4 ± 11.1 vs 51.9 ± 23.7 , $P < 0.0001$), sputum production (69.5 ± 12.0 vs 54.1 ± 15.2 , $P < 0.0001$) and frequent/daily wheeze (daily wheeze: 69.4 ± 23.3 , <daily wheeze: 53.2 ± 13.2 , no wheeze: 46.4 ± 12.5 ; $P < 0.0001$)

• Correlations (r^2) of SGRQ symptom score with FEV₁ % pred (-0.01 , $P > 0.01$), FVC % pred (-0.06 , $P < 0.01$), Sa_{o2}, rest[‡] (-0.02 , $P > 0.01$), 6-MWD[§] (-0.07 , $P < 0.01$), MRC dyspnea grade (0.13 , $P < 0.0001$), anxiety (0.12 , $P < 0.001$), depression (0.08 , $P < 0.001$), SIP physical (0.12 , $P < 0.0001$), SIP psychosocial (0.07 , $P < 0.01$), SIP total (0.11 , $P < 0.0001$)

• SGRQ activity score higher in patients with frequent wheeze (daily wheeze: 61.7 ± 23.3 , <daily wheeze: 48.8 ± 22.2 , no wheeze: 36.3 ± 19.3 ; $P < 0.0001$)

• Correlations of SGRQ activity score with

FEV₁ % pred (-0.08 , $P < 0.001$), FVC % pred (-0.10 , $P < 0.0001$), Sa_{o2}, rest[‡] (-0.04 , $P = 0.02$), 6-MWD[§] (-0.35 , $P < 0.0001$), MRC dyspnea grade (0.50 , $P < 0.0001$), anxiety (0.20 , $P < 0.001$), depression (0.23 , $P < 0.0001$), SIP physical (0.38 , $P < 0.0001$), SIP psychosocial (0.28 , $P < 0.0001$), SIP total (0.39 , $P < 0.0001$)

Table 2 (Continued)

- *SGRQ impact score* significantly higher in patients with cough (43.5 ± 23.3 vs 27.2 ± 18.8 , $P < 0.0001$), sputum (42.8 ± 22.9 vs 30.9 ± 19.9 , $P = 0.002$) and frequent wheeze (daily: 46.2 ± 22.5 , <daily: 25.8 ± 13.4 , none: 15.9 ± 13.0 ; $P < 0.0001$)
- *SGRQ impact score* significantly higher in patients with cough (43.5 ± 23.3 vs 27.2 ± 18.8 , $P < 0.0001$), sputum (42.8 ± 22.9 vs 30.9 ± 19.9 , $P = 0.002$) and frequent wheeze (daily: 46.2 ± 22.5 , <daily: 25.8 ± 13.4 , none: 15.9 ± 13.0 ; $P < 0.0001$)
- *Correlations (r^2)* of SGRQ impact score with FEV₁ % pred (-0.07 , $P < 0.01$), FVC % pred (-0.20 , $P < 0.0001$), SaO₂, rest[‡] (-0.01 , $P > 0.01$), 6-MWD[§] (-0.35 , $P < 0.0001$), MRC dyspnea grade (0.44 , $P < 0.0001$), anxiety (0.38 , $P < 0.001$), depression (0.39 , $P < 0.0001$), SIP physical (0.48 , $P < 0.0001$), SIP psychosocial (0.42 , $P < 0.0001$), SIP total (0.54 , $P < 0.0001$)
- *SGRQ total score* significantly higher in patients with cough (43.5 ± 19.7 vs 29.2 ± 17.0 , $p < 0.0001$), sputum (52.1 ± 19.5 vs 42.0 ± 18.5 , $P < 0.002$) and wheeze (daily wheeze: 55.2 ± 18.9 , <daily wheeze: 37.9 ± 13.4 , no wheeze: 27.2 ± 13.2 ; $P < 0.0001$)
- *Slopes of linear regressions* between total SGRQ score (dependent variable) and FVC [%pred] = -0.43 ; 6-MWD [Meters] = -0.11 ; Dyspnea [Grade] = 10.1 ; Anxiety [Units] = 2.52 ; Depression [Units] = 3.27 ; SIP total [Units] = 1.67 [correlation significant in each case, $P < 0.0001$]
- *ANOVA model with SGRQ symptom score as dependent variable [SS = sum of squares]:*
Cough: SS = 4799 ($P = 0.0001$); Wheeze: SS = 3443 ($P = 0.0001$); Dyspnea: SS = 919 ($P = 0.16$); 6-MWD[§]: SS = 434 ($P = 0.53$); Anxiety: SS = 652 ($P = 0.02$) [adjusted r^2 for model: 0.53]
- *ANOVA model with SGRQ activity score as dependent variable [SS=sum of squares]:*
Cough: SS = 0.8 ($P = 0.95$); Wheeze: SS = 1257 ($P = 0.09$); Dyspnea: SS = 12020 ($P = 0.0001$); 6-MWD[§]: SS = 2050 ($P = 0.005$); Anxiety: SS = 1559 ($P = 0.01$) [adjusted r^2 for model: 0.56]
- *ANOVA model with SGRQ impact score as dependent variable [SS = sum of squares]:*
Cough: SS = 367 ($P = 0.12$); Wheeze: SS = 3433 ($P = 0.0001$); Dyspnea: SS = 5180 ($P = 0.0001$); 6-MWD[§]: SS = 1483 ($P = 0.002$); Anxiety: SS = 7187 ($P = 0.0001$) [adjusted r^2 for model: 0.70]
- *ANOVA model with SGRQ total score as dependent variable [SS = sum of squares]:*
Cough: SS = 385 ($P = 0.03$); Wheeze: SS = 2569 ($P = 0.0001$); Dyspnea: SS = 5485 ($P = 0.0001$); 6-MWD[§]: SS = 1077 ($P = 0.02$); Anxiety: SS = 3625 ($P = 0.0001$) [adjusted r^2 for model: 0.72]

Responsiveness ($n = 133$)

Linear regressions between changes in SGRQ total score and changes in reference measures of disease activity 1 year apart (slopes)

FEV₁, % pred: -0.21 ($r^2 = 0.05$, $P = 0.01$)

FVC, % pred: -0.23 ($r^2 = 0.07$, $P = 0.002$)

6-MWD: -0.05 ($r^2 = 0.13$, $P = 0.0001$)

Exercise SaO₂, %: correlation not significant

Anxiety: 0.81 ($r^2 = 0.03$, $P = 0.03$)

Depression: 1.61 ($r^2 = 0.12$, $P = 0.0001$)

MRC dyspnea: 4.44 ($r^2 = 0.22$, $P = 0.0001$)

Sickness impact profile

- Physical: correlation not significant

- Psychosocial: 0.40 ($r^2 = 0.09$, $P = 0.0005$)

- Total: 0.51 ($r^2 = 0.51$, $P = 0.0002$)

ANOVA with change in total SGRQ score over 1 year as dependent variable and changes in reference measures of disease activity as factors (sum of squares)

Change in wheeze: 2261 ($P = 0.0001$)

Change in MRC dyspnea grade: 3455 ($P = 0.0001$)

Change in anxiety score: 1043 ($P = 0.002$)

Change in FVC, % pred: 411 ($P = 0.05$)

(E) QOL-RIQ

Maille 1997 Resp Med (146 patients)

Correlation with illness severity indicators [Spearman rank correlation coefficients]• *Degree of dyspnea (MRCQ)*

Total score ($r = 0.49$); breathing problems ($r = 0.34$); physical problems ($r = 0.41$); emotions ($r = 0.33$); general activities ($r = 0.40$); situations triggering or enhancing breathing problems ($r = 0.41$); daily and domestic activities ($r = 0.40$); social activities, relationships and sexuality ($r = 0.30$)

• *Frequency of attacks*

Total score ($r = 0.45$); breathing problems ($r = 0.32$); physical problems ($r = 0.39$); emotions ($r = 0.30$); general activities ($r = 0.31$); situations triggering or enhancing breathing problems ($r = 0.33$); daily and domestic activities ($r = 0.35$); social activities, relationships and sexuality ($r = 0.23$)

• *Subjective severity*

Total score ($r = 0.49$); breathing problems ($r = 0.34$); physical problems ($r = 0.41$); emotions ($r = 0.33$); general activities ($r = 0.40$); situations triggering or enhancing breathing problems ($r = 0.41$); daily and domestic activities ($r = 0.40$); social activities, relationships and sexuality ($r = 0.30$)

Table 2 (Continued)

- *Visits to GPs*

Total score ($r = 0.47$); breathing problems ($r = 0.48$); physical problems ($r = 0.40$); emotions ($r = 0.34$); general activities ($r = 0.26$); situations triggering or enhancing breathing problems ($r = 0.27$); daily and domestic activities ($r = 0.48$); social activities, relationships and sexuality ($r = 0.43$)

- *Absence from work*

Total score ($r = 0.46$); breathing problems ($r = 0.40$); physical problems ($r = 0.41$); emotions ($r = 0.40$); general activities ($r = 0.31$); situations triggering or enhancing breathing problems ($r = 0.32$); daily and domestic activities ($r = 0.29$); social activities, relationships and sexuality ($r = 0.31$)

(all correlations significant, $P \leq 0.01$)

Regression analysis with QoL-RIQ total score as dependent variable [explained variance]

Illness severity

Subjective severity of attacks: 25.3% ($P = 0.000$)

Grade of dyspnea (MRCQ score): 17.5% ($P = 0.000$)

Absence from work: 16.5% ($P = 0.000$)

Frequency of attacks: 12.8% ($P = 0.000$)

Visits to GP: 10.3% ($P = 0.000$)

Background characteristics

Gender: 1.7 (ns); diagnosis (asthma vs COPD): 1.3 (ns); age: 0.9 (ns); ever smoked: 0.9 (ns); duration of illness: 0.5 (ns)

Symptoms

Chronic wheeze: 9.8 ($P = 0.000$); chronic cough: 7.9 ($P = 0.001$)

Van Stel 2003 Quality of Life Research (108 patients)

Correlations of QoL-RIQ change scores with change in health status and psychological functioning [Spearman rank correlation coefficients]

- *Self-assessed health status*

Total score: 0.61 ($P < 0.001$); breathing problems: 0.39 ($P < 0.001$); physical problems: 0.45 ($P < 0.001$); emotions: 0.49 ($P < 0.001$); general activities: 0.54 ($P < 0.001$); triggers (weather): 0.37 ($P < 0.001$); daily/domestic activities: 0.48 ($P < 0.001$); social activities: 0.42 ($P < 0.001$)

- *Self-rated change in disease symptoms*

Total score: 0.48 ($P < 0.001$); breathing problems: 0.32 ($P < 0.01$); physical problems: 0.34 ($P < 0.001$); emotions: 0.37 ($P < 0.001$); general activities: 0.51 ($P < 0.001$); triggers (weather): 0.20 ($P < 0.001$); daily/domestic activities: 0.48 ($P < 0.001$); social activities: 0.42 ($P < 0.001$)

- *Emotional well-being*

Total score: 0.27 ($P < 0.05$); breathing problems: 0.18 (ns); physical problems: 0.34 ($P < 0.01$); emotions: 0.40 ($P < 0.001$); general activities: 0.25 ($P < 0.05$); triggers (weather): 0.12 (ns); daily/domestic activities: 0.15 (ns); social activities: 0.17 (ns)

- *Experienced invalidity*

Total score: 0.41 ($P < 0.001$); breathing problems: 0.31 ($P < 0.01$); physical problems: 0.37 ($P < 0.001$); emotions: 0.42 ($P < 0.001$); general activities: 0.25 ($P < 0.05$); triggers (weather): 0.17 (ns); daily/domestic activities: 0.34 ($P < 0.01$); social activities: 0.39 ($P < 0.01$)

- *Anxiety*

Total score: 0.20 ($P < 0.05$); breathing problems: 0.09 (ns); physical problems: 0.19 (ns); emotions: 0.40 ($P < 0.001$); general activities: 0.11 (ns); triggers (weather): 0.11 (ns); daily/domestic activities: 0.10 (ns); social activities: 0.16 (ns)

- *Depressive symptoms*

Total score: 0.30 ($P < 0.01$); breathing problems: 0.11 (ns); physical problems: 0.37 ($P < 0.001$); emotions: 0.47 ($P < 0.001$); general activities: 0.30 ($P < 0.01$); triggers (weather): 0.13 (ns); daily/domestic activities: 0.13 (ns); social activities: 0.31 ($P < 0.05$)

Correlations of QoL-RIQ change scores with Rand-36 change scores [Spearman rank correlation coefficients]

- *Health change*

Total score: 0.54 ($P < 0.01$); breathing problems: 0.49 ($P < 0.01$); physical problems: 0.35 ($P < 0.05$); emotions: 0.41 ($P < 0.05$); general activities: 0.45 ($P < 0.05$); triggers (weather): 0.41 ($P < 0.05$); daily/domestic activities: 0.54 ($P < 0.01$); social activities: 0.38 (ns)

- *Physical functioning*

Total score: 0.52 ($P < 0.01$); breathing problems: 0.28 (ns); physical problems: 0.25 (ns); emotions: 0.22 (ns); general activities: 0.66 ($P < 0.001$); triggers (weather): 0.29 (ns); daily/domestic activities: 0.51 ($P < 0.01$); social activities: 0.68 ($P < 0.01$)

- *Social functioning*

Total score: 0.56 ($P < 0.01$); breathing problems: 0.35 (ns); physical problems: 0.05 (ns); emotions: 0.47 ($P < 0.01$); general activities: 0.46 ($P < 0.05$); triggers (weather): 0.29 (ns)

Daily/domestic activities: 0.43 ($P < 0.05$); social activities: 0.45 (ns)

- *Role-physical*

Total score: 0.57 ($P < 0.001$); breathing problems: 0.47 ($P < 0.01$); physical problems: 0.19 (ns); emotions: 0.61 ($P < 0.001$); general activities: 0.57 ($P < 0.01$); triggers (weather): 0.19 (ns); daily/domestic activities: 0.46 ($P < 0.05$); social activities: 0.34 (ns)

Table 2 (Continued)

- *Role-mental*

Total score: 0.25 (ns); breathing problems: 0.25 (ns); physical problems: 0.23 (ns); emotions: 0.12 (ns); general activities: 0.29 (ns); triggers (weather): 0.13 (ns); daily/domestic activities: 0.11 (ns); social activities: 0.21 (ns)

- *Mental health*

Total score: 0.55 ($P < 0.01$); breathing problems: 0.31 (ns); physical problems: 0.19 (ns); emotions: 0.54 ($P < 0.01$); general activities: 0.56 ($P < 0.01$); triggers (weather): 0.41 ($P < 0.05$); daily/domestic activities: 0.42 ($P < 0.05$); social activities: 0.46 (ns)

- *Vitality*

Total score: 0.52 ($P < 0.01$); breathing problems: 0.31 (ns); physical problems: 0.18 (ns); emotions: 0.32 (ns); general activities: 0.46 ($P < 0.01$); triggers (weather): 0.62 ($P < 0.001$); daily/domestic activities: 0.38 (ns); social activities: 0.36 (ns)

- *Bodily pain*

Total score: 0.16 (ns); breathing problems: 0.08 (ns); physical problems: 0.09 (ns); emotions: 0.09 (ns); general activities: 0.23 (ns); triggers (weather): 0.06 (ns); daily/domestic activities: 0.30 (ns); social activities: 0.18 (ns)

- *General health*

Total score: 0.22 (ns); breathing problems: 0.29 (ns); physical problems: 0.14 (ns); emotions: 0.19 (ns); general activities: 0.13 (ns); triggers (weather): 0.14 (ns); daily/domestic activities: 0.33 (ns); social activities: 0.22 (ns)

(F) Rhinasthma

Baiardini 2003 Allergy

Comparison of QoL scores between patients with rhinoconjunctivitis and patients with rhinoconjunctivitis and asthma (n = 104 patients with respiratory allergy)

- *14 Rhinasthma items showed significantly different scores between patients with rhinoconjunctivitis and patients with rhinoconjunctivitis and asthma*

Cough: $P = 0.0001$; wheezing: $P = 0.0001$; to clear one's throat: $P = 0.001$; shortness of breath: $P = 0.0001$; dyspnea: $P = 0.0001$; chest tightness: $P = 0.0001$; sport activities impairment: $P = 0.007$; having to avoid certain environments: $P = 0.002$; wake up in the night: $P = 0.0001$; leisure time activities limitations: $P = 0.001$; having to spend money: $P = 0.004$; having to take drugs: $P = 0.0001$; not being able to do whatever desired: $P = 0.0001$; limitations in everyday's activities: $P = 0.001$

- *All SF-36 domains showed significantly better scores in patients with rhinoconjunctivitis compared to patients with rhinoconjunctivitis and asthma*

Physical functioning: 94.51 ± 9.06 vs 86.23 ± 16.52 , $P = 0.0001$; role physical: 85.48 ± 23.96 vs 68.51 ± 36.14 , $P = 0.001$; bodily pain: 94.81 ± 13.73 vs 81.84 ± 26.60 , $P = 0.0001$; general health: 68.71 ± 20.48 vs 59.00 ± 20.38 , $P = 0.0001$; vitality: 64.03 ± 20.26 vs 49.67 ± 22.69 , $P = 0.005$; social functioning: 82.26 ± 17.61 vs 63.58 ± 22.95 , $P = 0.0001$; role emotional: 87.09 ± 22.24 vs 57.25 ± 36.29 , $P = 0.0001$; mental health: 70.06 ± 15.96 vs 60.52 ± 18.83 , $P = 0.033$

Responsiveness

[Twenty-seven patients with respiratory allergy (persistent rhinitis and intermittent asthma) assessed at baseline and 3 weeks after treatment with cetirizine] Eighteen items showed significant difference after 3 weeks: difficulty in concentrating on problems: $P = 0.034$; sport activities impairment: $P = 0.003$; itchy nose: $P = 0.0001$; stuffy nose: $P = 0.001$; cough: $P = 0.004$; having to avoid certain environments: $P = 0.004$; watery eyes: $P = 0.001$; sore eyes: $P = 0.002$; eyes redness: $P = 0.0001$; drugs' side-effects: $P = 0.034$; itchy eyes: $P = 0.0001$; wheezing: 0.014; worried of not having drugs: $P = 0.046$; runny nose: $P = 0.0001$; sneezing: $P = 0.0001$; limitations in everyday's activities: $P = 0.034$; to clear one's throat: $P = 0.025$; always having to carry tissues: $P = 0.021$

*Calculated according to (75); magnitude of responsiveness index signifies the relative utility in distinguishing improved from stable subjects.

†Asthma Symptom Checklist (76, 77).

‡Arterial oxygen saturation.

§6-min walking distance.

Head-to-head comparisons

A limited number of attempts have been made to compare some of the asthma-specific questionnaires with each other. A Spanish group compared the performance of the AQLQ-J and the SGRQ (reliability, validity, responsiveness) and concluded that neither performed better than the other (71), while a Japanese research group reported differences in their comparison of the responsiveness of the AQLQ-J, the LWAQ, and a shortened version of the SGRQ (AQ20) (72). The AQLQ-J proved to be the most responsive measure during asthma

treatment, followed by the AQ20. The correlation between change in the questionnaire and the change in airflow limitation (as measured by FEV_1) was weaker with the LWAQ (Spearman correlation coefficient $r = -0.23$) compared with the AQLQ-J ($r = 0.38$) and the AQ20 ($r = -0.40$). The changes in AQLQ-J, LWAQ, and AQ20 were only moderately correlated with each other (AQLQ-J and LWAQ: $r = -0.54$, AQLQ-J and AQ20: $r = -0.62$, LWAQ and AQ20: $r = 0.60$). It remains speculative to what extent these observed differences represent true differences in validity or relate to the diverse constructs measured by each questionnaire.

Table 3 Strengths and potential weaknesses of the six asthma-specific QoL measures

Questionnaire	Strengths	Potential weaknesses
AQLQ-J	Specifically designed for asthma Linguistically validated in many languages Validation studies in a number of languages Potentially fine discrimination (7 response options) Idiographic component of the original version Widely used	Contains a symptom list
AQLQ-S	Specifically designed for asthma Quick to complete (20 items) Response format (5 options) compromise between ease of completion and accuracy	Few linguistic validations
LWAQ	Specifically designed for asthma Has 'not applicable' option Compensates for acquiescence bias	Lengthy questionnaire (68 items) Few linguistic validations
SGRQ	Combines questions on current problems with questions on problems in recall period (4 weeks, 3 months, 12 months) Linguistically validated in many languages Weights are applied to obtain domain and summary scores Widely used (but mainly in COPD)	Rather long questionnaire (50 items) Contains a symptom list Designed for asthma and COPD Complex calculation of scores (weights need to be applied)
QOL-RIQ	Has 'not applicable' option	Rather long questionnaire (55 items) Designed for chronic nonspecific lung disease Role of symptom items unclear Few linguistic validations
Rhinasthma	Good for patients who suffer from both asthma and rhinitis	Limited evidence for validity (in use for only a few years) Potentially decreased sensitivity in patients who suffer from either rhinitis or asthma Few linguistic validations

In another study using data from a trial comparing inhaled salmeterol with inhaled salbutamol (73), the AQLQ-J was again found to be more responsive compared with the LWAQ (effect size AQLQ-J: 0.820, effect size LWAQ: 0.694; effect size = mean score in salmeterol group/within-subject standard deviation in salmeterol plus salbutamol group). The correlation of change in lung function (FEV1, % pred) and change in QoL was low for the LWAQ (Spearman rank correlation coefficient: -0.05 , n.s.), but not for the AQLQ ($r = 0.32$, $P \leq 0.001$). However, a Dutch-Canadian group studied QoL during formoterol treatment and found the LWAQ to be responsive, but not the AQLQ-J [effect size of change (Cohen's d) in QoL during treatment with formoterol compared with placebo: LWAQ: 0.394 (-0.003 – 0.796); AQLQ: 0.128 (-0.267 – 0.532)] (74). Only the symptom domain of the AQLQ-J was responsive to change (effect size of change (Cohen's d): 0.316 (-0.083 – 0.724)). These inconsistent and diametrically opposed findings require further exploration and at the current time make it difficult to comment on the relative strengths of asthma-specific questionnaires.

Horses for courses

Beyond empirical grounds, the choice of instrument mostly depends on the target population. The SGRQ and the QOL-RIQ were developed for both chronic and reversible

airway obstruction. The SGRQ is now mainly used for COPD (Jones, personal communication). The Rhinasthma questionnaire is used for the concomitant assessment of both the impact of rhinitis and asthma.

Among the six questionnaires reviewed, three were designed solely for asthma (AQLQ-J, AQLQ-S, and LWAQ). Of these asthma-specific questionnaires, the LWAQ is the most comprehensive one. It also compensates for acquiescence bias and has a 'not applicable' response option. This questionnaire should be recommended where a comprehensive assessment is the goal, for instance where small groups of patients are assessed. Despite these strengths, the LWAQ's three response options may render it less sensitive to detect differences or change, compared to the seven response options offered in the AQLQ-J. The AQLQ-J therefore offers the finest discrimination and has, in its original version, the unique feature of leaving five items for the choice of those affected. This feature has the potential to increase responsiveness in clinical trials.

Where brevity is an issue, we would recommend the AQLQ-S as it is the shortest of the asthma-specific questionnaires, does not include symptom-based items, and has a flexible response format (five response options). It would thus be the most suitable instrument to be used in population-based cross-sectional studies where large numbers of participants are included. The AQLQ-J appears not suitable for this

Table 4 Ideal process for QoL questionnaire development (23)

1. Identify concepts and develop conceptual framework
 - a. Identify concepts and domains that are important to patients
 - b. Determine intended population and research application
 - c. Hypothesize expected relationships among concepts
2. Create instrument
 - a. Generate items
 - b. Choose administration method, recall period, and response scales
 - c. Draft instructions
 - d. Format instrument
 - e. Draft procedures for scoring and administration
 - f. Pilot test draft instrument
 - g. Refine instrument and procedures
3. Assess measurement properties
 - a. Assess score reliability, validity and ability to detect change
 - b. Evaluate administrative and respondent burden
 - c. Add, delete, or revise items
 - d. Identify meaningful differences in scores
 - e. Finalize instrument formats, scoring, procedures, and training materials
4. Modify instrument
 - a. Concepts measured
 - b. Populations studied
 - c. Research application
 - d. Instrumentation
 - e. Method of administration

purpose, because it has an idiographic component and hence would not yield comparable results. The standardized version of the AQLQ-J, however, is suitable for large cross-sectional studies.

In the quantitative quality assessment we conducted (Table 5), the AQLQ-S obtained the highest score. However, for use in multinational studies, it might be most convenient to choose those questionnaires that have been linguistically validated in many languages (AQLQ-J, SGRQ). It is very important that questionnaires are culturally and linguistically adapted, recognizing individuals are likely to interpret scale items of a QoL measure in light of culturally available subjective constructs of QoL (29). As it is specific for asthma, the AQLQ-J would be preferable compared with the SGRQ in multinational studies.

Strengths and limitations

The strength of this review is that it attempts to be comprehensive in the attributes considered as review criteria. We have not provided a recommendation based on a distinction between evaluation/discrimination/prediction because we believe that if a measure is valid, then it will be good for discriminative purposes as well as for evaluative or predictive purposes. This is also reflected in including responsiveness as an aspect of validity, rather than a separate measurement property. We have, however, developed a more flexible 'horses for courses' approach.

Table 5 Result from quantitative quality assessment*

Measure	Points Scored/ Maximum	Percentage Score (%)
AQLQ-S	25.5/26.5	96.2
AQLQ-J	22.5/26.5	84.9
LWAQ	18.5/26.5	69.8
QoLRIQ	18/26.5	67.9
Rhinasthma	16/25.5	62.7
SGRQ	15/25.5	58.8

*Points are assigned according to the following criteria, yielding a total score of 25.5 or 26.5: target population stated (1 point), Purpose of the questionnaire development stated (1 point), concept to be measured stated (1 point), conceptual model provided (1 point), patients' experiences elicited for item generation (1 point), literature review performed for item generation (0.5 point), clinical experience used for item generation (0.5 points), qualitative research on patients' experiences described or cited, sufficient for replication (1 point), statistical analysis used for item reduction described or cited (1 point), items and domains described (1 point), patient feedback used during item reduction (1 point), items and domains described (1 point), response format described fully for all items (1 point), scoring described (1 point), recall period specified (1 point), questionnaire pretested in different patients (1 point), questionnaire pretested for comprehensibility/wording (1 point), scale published in the public domain (1 point), test-retest reliability (reproducibility) assessed (1 point), internal consistency assessed, either for total number of items or for domains (0.5 point), evidence for content validity (1 point), evidence for construct validity (1 point), evidence for responsiveness (1 point), guidance on interpretation of scores provided (1 point), patient burden assessed (time) (1 point), patient burden assessed (effort) (1 point), information on administration format provided (1 point), separate validation studies for different administration formats, if applicable (1 point), further information on application of questionnaire provided (1 point).

A limitation of this review is that it is restricted to published literature and to studies that reported measurement properties as primary outcomes; however, this approach is similar to that taken in other rigorous reviews (24). We also acknowledge that other groups might develop different criteria for the review of questionnaires.

Conclusion

It cannot be assumed that all questionnaires that are used to measure QoL in asthma measure the same thing. We recommend to choose a QoL measure that is specifically designed for asthma and that does not include a symptom list. However, these requirements need to be offset against the need for linguistically equivalent questionnaires in multinational studies. Also, in reality few patients may suffer from asthma alone, but most either suffer from asthma and rhinitis or have a form of airways obstruction in which the line between asthma and COPD cannot be firmly established.

For all the aforementioned questionnaire development procedures, user involvement decreases as development progresses and psychometric analysis becomes central. We are

not aware of any study where patients have been asked about their preference regarding the questionnaires. It is patients who should ultimately decide about ease of completion and the ability of the existing questionnaires to reflect their experi-

ences. It is now time to seize the opportunity and involve those whose quality of life is affected by asthma to decide which of the existing questionnaires is most suitable. This might involve de novo development of a new questionnaire.

References

- Juniper EF, Norman GR, Cox FM, Roberts JN. Comparison of the standard gamble, rating scale, AQLQ and SF-36 for measuring quality of life in asthma. *Eur Respir J* 2001;**18**:38–44.
- Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care* 1992;**30**:473–483.
- Masoli M, Fabian D, Holt S, Beasley R. Global Burden of Asthma; 2004.
- Juniper EF, Guyatt GH, Epstein RS, Ferrie PJ, Jaeschke R, Hiller TK. Evaluation of impairment of health related quality of life in asthma: development of a questionnaire for use in clinical trials. *Thorax* 1992;**47**:76–83.
- Juniper EF, Guyatt GH, Ferrie PJ, Griffith LE. Measuring quality of life in asthma. *Am Rev Respir Dis* 1993;**147**:832–838.
- Marks GB, Dunn SM, Woolcock AJ. A scale for the measurement of quality of life in adults with asthma. *J Clin Epidemiol* 1992;**45**:461–472.
- 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**:1103–1111.
- Hyland ME, Finnis S, Irvine SH. A scale for assessing quality of life in adult asthma sufferers. *J Psychosom Res* 1991;**35**:99–110.
- Hyland ME. The Living with Asthma Questionnaire. *Respir Med* 1991;**85**(Suppl B):13–16. discussion 33–17.
- Jones PW, Quirk FH, Baveystock CM. The St George's Respiratory Questionnaire. *Respir Med* 1991;**85**(Suppl. B):25–31. discussion 33–27.
- 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**:1321–1327.
- van Wijk RG. Quality of life, should we bother? *Allergy* 2003;**58**:284–286.
- Juniper EF, Guyatt GH, Feeny DH, Ferrie PJ, Griffith LE, Townsend M. Measuring quality of life in children with asthma. *Qual Life Res* 1996;**5**:35–46.
- Juniper EF, Svensson K, Mork AC, Stahl E. Modification of the asthma quality of life questionnaire (standardised) for patients 12 years and older. *Health Qual Life Outcomes* 2005;**3**:58.
- Juniper EF, Buist AS, Cox FM, Ferrie PJ, King DR. Validation of a standardized version of the Asthma Quality of Life Questionnaire. *Chest* 1999;**115**:1265–1270.
- Ried LD, Nau DP, Grainger-Rousseau TJ. Evaluation of patient's Health-Related Quality of Life using a modified and shortened version of the Living With Asthma Questionnaire (ms-LWAQ) and the medical outcomes study, Short-Form 36 (SF-36). *Qual Life Res* 1999;**8**:491–499.
- Juniper EF, Guyatt GH, Cox FM, Ferrie PJ, King DR. Development and validation of the Mini Asthma Quality of Life Questionnaire. *Eur Respir J* 1999;**14**:32–38.
- Baiardini I, Pasquali M, Giardini A, Specchia C, Passalacqua G, Venturi S et al. Rhinasthma: a new specific QoL questionnaire for patients with rhinitis and asthma. *Allergy* 2003;**58**:289–294.
- Muldoon MF, Barger SD, Flory JD, Manuck SB. What are quality of life measurements measuring? *BMJ* 1998;**316**:542–545.
- Garratt A, Schmidt L, Mackintosh A, Fitzpatrick R. Quality of life measurement: bibliographic study of patient assessed health outcome measures. *BMJ* 2002;**324**:1417.
- Garratt AM, Schmidt L, Fitzpatrick R. Patient-assessed health outcome measures for diabetes: a structured review. *Diabet Med* 2002;**19**:1–11.
- Scientific Advisory Committee of the Medical Outcomes Trust. Assessing health status and quality-of-life instruments: attributes and review criteria. *Qual Life Res* 2002;**11**:193–205.
- US Department of Health and Human Services FDA Center for Drug Evaluation and Research, US Department of Health and Human Services FDA Center for Biologics Evaluation and Research, US Department of Health and Human Services FDA Center for Devices and Radiological Health. Guidance for industry: patient-reported outcome measures: use in medical product development to support labeling claims: draft guidance. *Health Qual Life Outcomes* 2006;**4**:79.
- van Oene CM, van Reij EJ, Sprangers MA, Fokkens WJ. Quality-assessment of disease-specific quality of life questionnaires for rhinitis and rhinosinusitis: a systematic review. *Allergy* 2007;**62**:1359–1371.
- Maille AR, Koning CJ, Zwiderman AH, Willems LN, Dijkman JH, Kaptein AA. The development of the 'Quality-of-life for Respiratory Illness Questionnaire (QOL-RIQ)': a disease-specific quality-of-life questionnaire for patients with mild to moderate chronic non-specific lung disease. *Respir Med* 1997;**91**:297–309.
- Hays RD, Hadorn D. Responsiveness to change: an aspect of validity, not a separate dimension. *Qual Life Res* 1992;**1**:73–75.
- Cronbach LJ. Coefficient Alpha and the Internal Structure of Tests. *Psychometrika* 1951;**16**:297–334.
- Guyatt GH, Berman LB, Townsend M, Pugsley SO, Chambers LW. A measure of quality of life for clinical trials in chronic lung disease. *Thorax* 1987;**42**:773–778.
- Stenner PH, Cooper D, Skevington SM. Putting the Q into quality of life; the identification of subjective constructions of health-related quality of life using Q methodology. *Soc Sci Med* 2003;**57**:2161–2172.
- Stewart AL, Hays RD, Ware JE Jr. The MOS short-form general health survey. Reliability and validity in a patient population. *Med Care* 1988;**26**:724–735.
- 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.
- Rowe BH, Oxman AD. Performance of an asthma quality of life questionnaire in an outpatient setting. *Am Rev Respir Dis* 1993;**148**:675–681.
- Rowe BH, Oxman AD. An assessment of the sensibility of a quality-of-life instrument. *Am J Emerg Med* 1993;**11**:374–380.
- Jaeschke R, Singer J, Guyatt GH. Measurement of health status. Ascertaining the minimal clinically important difference. *Control Clin Trials* 1989;**10**:407–415.
- 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.
- 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**:1121–1127.
- Sanjuas C, Alonso J, Sanchis J, Casan P, Broquetas JM, Ferrie PJ et al. [The quality-of-life questionnaire with asthma patients: the Spanish version of the Asthma Quality of Life Questionnaire]. *Arch Bronconeumol* 1995;**31**:219–226.
- Sanjuas C, Alonso J, Ferrer M, Curull V, Broquetas JM, Anto JM. Adaptation of the Asthma Quality of Life Questionnaire to a

- second language preserves its critical properties: the Spanish version. *J Clin Epidemiol* 2001;**54**:182–189.
39. Leidy NK, Coughlin C. Psychometric performance of the Asthma Quality of Life Questionnaire in a US sample. *Qual Life Res* 1998;**7**:127–134.
 40. Tomic Spiric V, Bogic M, Jankovic S, Maksimovic N, Matovic Miljanovic S, Peric Popadic A et al. Assessment of the Asthma Quality of Life Questionnaire (AQLQ): Serbian translation. *Croat Med J* 2004;**45**:188–194.
 41. Ware JE Jr. Standards for validating health measures: definition and content. *J Chronic Dis* 1987;**40**:473–480.
 42. Gupchup GV, Wolfgang AP, Thomas J III. Reliability and validity of the Asthma Quality of Life Questionnaire—marks in a sample of adult asthmatic patients in the United States. *Clin Ther* 1997;**19**:1116–1125.
 43. Perpina M, Belloch A, Marks GB, Martinez-Moragon E, Pascual LM, Compte L. Assessment of the reliability, validity, and responsiveness of a Spanish Asthma Quality of Life questionnaire. *J Asthma* 1998;**35**:513–521.
 44. Miedinger D, Chhajed PN, Stolz D, Leimenstoll B, Tamm M, Fiechter R et al. Reliability and validity of a German asthma quality of life questionnaire. *Swiss Med Wkly* 2006;**136**:89–95.
 45. Hyland ME, Kenyon CA, Taylor M, Morice AH. Steroid prescribing for asthmatics: relationship with Asthma Symptom Checklist and Living with Asthma Questionnaire. *Br J Clin Psychol* 1993;**32**(Pt 4):505–511.
 46. Hyland ME, Crocker GR. Validation of an asthma quality of life diary in a clinical trial. *Thorax* 1995;**50**:724–730.
 47. Haave E, Hyland ME. Norwegian versions of the Living with Asthma Questionnaire (LWAAQ) and Asthma Bother Profile (ABP), validation and comparison of two asthma groups. *Scand J Psychol* 2004;**45**:163–167.
 48. Quirk FH, Jones PW. Patients' perception of distress due to symptoms and effects of asthma on daily living and an investigation of possible influential factors. *Clin Sci (Lond)* 1990;**79**:17–21.
 49. Jones PW, Baveystock CM, Littlejohns P. Relationships between general health measured with the sickness impact profile and respiratory symptoms, physiological measures, and mood in patients with chronic airflow limitation. *Am Rev Respir Dis* 1989;**140**:1538–1543.
 50. Jones PW, Spencer S, Adie S. The St George's Respiratory Questionnaire Manual. Version 2.1. 2003.
 51. Quirk FH, Baveystock CM, Wilson R, Jones PW. Influence of demographic and disease related factors on the degree of distress associated with symptoms and restrictions on daily living due to asthma in six countries. *Eur Respir J* 1991;**4**:167–171.
 52. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983;**67**:361–370.
 53. Ferrer M, Alonso J, Prieto L, Plaza V, Monso E, Marrades R et al. Validity and reliability of the St George's Respiratory Questionnaire after adaptation to a different language and culture: the Spanish example. *Eur Respir J* 1996;**9**:1160–1166.
 54. Engstrom CP, Persson LO, Larsson S, Sullivan M. Reliability and validity of a Swedish version of the St George's Respiratory Questionnaire. *Eur Respir J* 1998;**11**:61–66.
 55. Barr JT, Schumacher GE, Freeman S, LeMoine M, Bakst AW, Jones PW. American translation, modification, and validation of the St. George's Respiratory Questionnaire. *Clin Ther* 2000;**22**:1121–1145.
 56. Kuzniar T, Patkowski J, Liebhart J, Wytrychowski K, Dobek R, Slusarz R et al. Validation of the Polish version of St. George's respiratory questionnaire in patients with bronchial asthma. *Pneumonol Alergol Pol* 1999;**67**:497–503.
 57. Wang KY, Chiang CH, Maa SH, Shau WY, Tarn YH. Psychometric assessment of the Chinese language version of the St. George's Respiratory Questionnaire in Taiwanese patients with bronchial asthma. *J Formos Med Assoc* 2001;**100**:455–460.
 58. Maille AR, Kaptein AA, Koning CJ, Zwinderman AH. Developing a quality-of-life questionnaire for patients with respiratory illness. *Monaldi Arch Chest Dis* 1994;**49**:76–78.
 59. Spilker B. Introduction. In: Spilker B, editor. *Quality of Life Assessments in Clinical Trials*. New York: Raven Press 1990:3–10.
 60. Guyatt GH, Bombardier C, Tugwell PX. Measuring disease-specific quality of life in clinical trials. *CMAJ* 1986;**134**:889–895.
 61. van Stel HF, Maille AR, Colland VT, Everaerd W. Interpretation of change and longitudinal validity of the quality of life for respiratory illness questionnaire (QoLRIQ) in inpatient pulmonary rehabilitation. *Qual Life Res* 2003;**12**:133–145.
 62. Fischer D, Stewart AL, Bloch DA, Lorig K, Laurent D, Holman H. Capturing the patient's view of change as a clinical outcome measure. *JAMA* 1999;**282**:1157–1162.
 63. Passalacqua G, Ciprandi G, Canonica GW. United airways disease: therapeutic aspects. *Thorax* 2000;**55**(Suppl. 2):S26–S27.
 64. Passalacqua G, Ciprandi G, Canonica GW. The nose-lung interaction in allergic rhinitis and asthma: united airways disease. *Curr Opin Allergy Clin Immunol* 2001;**1**:7–13.
 65. Mosges R, Schmalz P, Koberlein J, Kaciran M, Baiardini I. The Rhinasthma-Quality of Life Scale German Adapted Version: validation of a new disease specific quality of life scale for patients suffering from allergic rhinitis and bronchial hyperreactivity. *HNO* 2007;**55**:357–364.
 66. Pollard B, Johnston M, Dixon D. Theoretical framework and methodological development of common subjective health outcome measures in osteoarthritis: a critical review. *Health Qual Life Outcomes* 2007;**5**:14.
 67. Maille AR, Kaptein AA, de Haes JC, Everaerd WT. Assessing quality of life in chronic non-specific lung disease—a review of empirical studies published between 1980 and 1994. *Qual Life Res* 1996;**5**:287–301.
 68. Steen N, Hutchinson A, McColl E, Eccles MP, Hewison J, Meadows KA et al. Development of a symptom based outcome measure for asthma. *BMJ* 1994;**309**:1065–1068.
 69. Juniper EF, Guyatt GH, Streiner DL, King DR. Clinical impact versus factor analysis for quality of life questionnaire construction. *J Clin Epidemiol* 1997;**50**:233–238.
 70. Hyland ME. Quality-of-life assessment in respiratory disease: an examination of the content and validity of four questionnaires. *Pharmacoeconomics* 1992;**2**:43–53.
 71. Sanjuas C, Alonso J, Prieto L, Ferrer M, Broquetas JM, Anto JM. Health-related quality of life in asthma: a comparison between the St George's Respiratory Questionnaire and the Asthma Quality of Life Questionnaire. *Qual Life Res* 2002;**11**:729–738.
 72. Oga T, Nishimura K, Tsukino M, Sato S, Hajiro T, Mishima M. Comparison of the responsiveness of different disease-specific health status measures in patients with asthma. *Chest* 2002;**122**:1228–1233.
 73. Rutten-van Molken MP, Custers F, van Doorslaer EK, Jansen CC, Heurman L, Maesen FP et al. Comparison of performance of four instruments in evaluating the effects of salmeterol on asthma quality of life. *Eur Respir J* 1995;**8**:888–898.
 74. van der Molen T, Sears MR, de Graaff CS, Postma DS, Meyboom-de Jong B. Quality of life during formoterol treatment: comparison between asthma-specific and generic questionnaires. Canadian and the Dutch Formoterol Investigators. *Eur Respir J* 1998;**12**:30–34.
 75. Tuley MR, Mulrow CD, McMahan CA. Estimating and testing an index of responsiveness and the relationship of the index to power. *J Clin Epidemiol* 1991;**44**:417–421.
 76. Kinsman RA, Luparello T, O'Banion K, Spector S. Multidimensional analysis of the subjective symptomatology of asthma. *Psychosom Med* 1973;**35**:250–267.
 77. Brooks CM, Richards JM Jr, Bailey WC, Martin B, Windsor RA, Soong SJ. Subjective symptomatology of asthma in an outpatient population. *Psychosom Med* 1989;**51**:102–108.