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**The applicability of patient-reported outcomes
in primary care:**

*Monitoring of patients with asthma or
chronic obstructive pulmonary disease*

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Stockholm 2009

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ISBN 978-91-7409-563-0

Till Malgorzata, Martin och Michelle

Abstract

Aims of the thesis: The general objective of this project was to identify and to some extent remove obstacles in the incorporation of disease-specific quality of life and/or health-status assessments in the management of asthma and COPD patients in primary care. The measurement properties, the design and the administrative complexity of the instruments at hand have been scrutinized with the intent to make it possible for primary care to integrate a patient perspective in the treatment and monitoring of asthma and COPD.

Methods: Psychometric analysis of the measurement properties and performance of the questionnaires ACQ and MiniAQLQ in primary care (paper I). Psychometric analysis of the measurement properties and the performance of the CCQ in primary care (paper II). A cluster randomised study of the influence of information and monitoring on asthma control. Analysis were made of group differences on the ACQ and the MiniAQLQ and estimates of responsiveness of both questionnaires were calculated (paper III) . Semi-structured interviews with patients with COPD with an extended version of the SEIQoL-DW (paper IV).

Results: The Mini-AQLQ and ACQ correlated well with the criterion measure AQLQ(S). Reliability coefficients were good. Both questionnaires detected improvement or deterioration of patients at the group level (paper I).

Overall correlations between the criterion measure SGRQ and CCQ were strong for all patients with clinical COPD (0.84). These correlations between CCQ and SGRQ were moderate to good, regardless of COPD severity. Reliability was good but not sufficient for individual level assessment (paper II).

ACQ score changes differed between the study groups ($p < 0.05$). In the intervention group, these changes in asthma control were close to clinical significance (MID 0.5). Both groups improved in disease-specific quality of life scores. For the intervention group, which changed the most ($p < 0.05$), the change exceeded the threshold for the MID. (paper III).

The cue areas rated as most important with the generic part was the subjects' own health and relation to partner and family. The cue areas rated most important with the disease-specific part was; worries about own health, and independence. When comparing the results of the SEIQoL with standardised questionnaires content it seems as several areas of importance as nominated by the COPD patients are not addressed in standardised questionnaires, especially the areas of social life and mental health (paper IV).

Conclusions: The asthma-specific instruments ACQ and MiniAQLQ exhibited measurement properties that allow use on an individual level in primary care. The CCQ did not meet the measurement requirements set for use on an individual level. Further, development is proposed in order to enhance performance of the instrument.

Keywords: Asthma, COPD, Primary care, Health related quality of life

Populärvetenskaplig sammanfattning

Astmapatienter kan idag med rätt behandling i de flesta fall uppnå ett tillstånd som kan betecknas som nästan besvärsfritt. Trots det har flera internationella studier visat att astmapatienter skulle kunna må bättre. Många astmapatienter skulle kanske kunna må bättre än vad de själva ens tror är möjligt. Astmatiker har själva ofta en uppfattning om att de har god sjukdomskontroll, samtidigt som de beskriver sina symtom på ett sådant sätt att det talar för motsatsen. Vid KOL är utsikten för behandlingen inte lika positiv, men rätt behandling kan ändå ge symtomlindring och minska försämringstakten. Precis som astma-patienter har KOL-patienter avsevärt försämrad livskvalitet, även i jämförelse med andra patientgrupper. En möjlig lösning som föreslagits för att förbättra behandlingsutfallet är att med hjälp av livskvalitets-/hälsostatusinstrument införa ett patient perspektiv i behandlingen.

Det övergripande syftet med denna avhandling är att identifiera och i någon mån undanröja hinder för införandet av utvärdering av hälsorelaterad livskvalitet i behandlingen av astma-och KOL-patienter i primärvården. Mätgenskaper, utformning och administrativ börda hos befintliga livskvalitetsinstrument har granskats, i syfte att möjliggöra för primärvården att integrera ett patientperspektiv i behandlingen och utvärderingen av astma och KOL.

I delstudie ett granskades astma-specifika livskvalitetsinstrument. Vi prövade instrumentens förmåga att producera giltiga och tillförlitliga resultat när de användes i primärvården på primärvårdens patienter. I delstudie två gjorde vi samma sak på befintliga KOL-specifika livskvalitetsinstrument. Resultaten för astma-specifika instrument var lovande. Instrumenten hade tillräckliga mätgenskaper för att kunna användas på individnivå. KOL instrumenten hade dock inte tillräcklig tillförlitlighet för att användas på individnivå.

I delstudie tre undersökte vi de astma-specifika livskvalitetsinstrumentens känslighet för förändring i samband med behandlingsförändring. Resultatet var positivt, då instrumenten var känsliga nog att upptäcka behandlingseffekter som kan betecknas som relativt små.

I delstudie fyra ville vi undersöka vilka områden i deras livskvalitet som patienter med KOL upplever att sjukdomen har påverkat och vilken betydelse de tillskriver dessa områden. Vi ville också jämföra hur de resultaten stämmer överens med vad som mäts med befintliga instrument. Resultatet visade att det patienter med KOL själva upplever som viktigt och påverkat av sjukdomen inte helt sammanfaller med det som mäts med befintliga instrument. Patienterna själva betonade områden som oro för den egna hälsan, isolering, självständighet och trötthet.

Utifrån de studier som presenteras i avhandlingen kan man dra slutsatsen att integration av patientperspektivet i vården av astma och KOL är en möjlighet men att en hel del arbete kvarstår. De befintliga astma-specifika instrumenten kan med lite arbete börja integreras, men de KOL instrument som finns behöver finslipas innan de lämpar sig för detta ändamål.

List of publications

The thesis is based on the following papers, referred to in the text by their Roman numerals.

- I. Ehlers PO, Nokela M, Stallberg B, Hjemdahl P, Wikström Jonsson E. Brief questionnaires for patient-reported outcomes in asthma: validation and usefulness in a primary care setting. *Chest*. 2006 Apr;129(4):925-32.
- II. Stallberg B, Nokela M, Ehlers PO, Hjemdahl P, Jonsson EW: Validation of the clinical COPD Questionnaire (CCQ) in primary care. *Health Qual Life Outcomes* 2009, 7:26.
- III. Nokela M, Ehlers PO, Arnlin M, Krakau I, Forslund L, Wikström Jonsson E. The influence of patient education on treatment outcome in primary care treated asthma: a cluster randomised study. *Respiration* 2009.
- IV. Nokela M, Langius-Eklöf A, Wikström Jonsson E. Constitutive elements of Individual QoL in COPD. Manuscript.

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List of abbreviations

ACQ	Asthma Control Questionnaire
AQLQ(S)	Asthma Quality of Life Questionnaire with standardized activities
CCQ	Clinical COPD Questionnaire
CMID	Clinically Minimal Important Difference
COPD	Chronic Obstructive Pulmonary Disease
CTT	Classical Test Theory
FEV1	Forced Expiratory Volume in one second
GINA	The Global Initiative for Asthma
GP	General Practitioner
GOLD	The Global Initiative for Chronic Obstructive Lung Disease
HRQoL	Health Related Quality of Life
ICC	Intra-class correlation coefficient
ICS	Inhaled Corticosteroids
IRT	Item Response Theory
LWAQ	Living with Asthma Questionnaire
MID	Minimal Important Difference
QoL	Quality of Life
SEIQoL	Schedule for the Evaluation of the Individual Quality of Life
SEIQoL-DW	Schedule for the Evaluation of the Individual Quality of Life Direct Weighting
SF-36	Short-form-36 Health Survey
SRM	Standardized Response Mean
SGRQ	The St. George's Respiratory Questionnaire
WHO	The World Health Organization

The applicability of patient-reported outcomes in primary care:

Monitoring of patients with asthma or COPD

By

Mika Nokela

Introduction

Asthma and COPD are both known as obstructive pulmonary diseases. In the case of asthma, the obstruction is usually variable and reversible and there is effective therapy. However, patients with long disease histories may have poor reversibility[1]. Use of inhaled anti-inflammatory agents yields well-controlled asthma for a large proportion of the patients[2]. In COPD the obstruction is chronic and available therapy has not been as successful. To date there is no treatment that can ensure long-term positive outcomes. Nevertheless, there is treatment that can alleviate the symptoms[3].

Patient-reported outcomes (PRO)

The effectiveness of treatment can be assessed with results from many different sources; lab tests, clinical assessment and patient reports. Patient-Reported Outcomes (PRO) is a concept commonly used to refer to measures of self-report. This includes questionnaires of health-related quality of life.

Chronic Obstructive Pulmonary Disease (COPD)

Chronic Obstructive Pulmonary Disease (COPD) is, as the name implies, a chronic, slowly progressive lung disease characterized by an airflow limitation that is not fully reversible[4]. The airflow limitation is functionally manifested

in a lowered FEV1/VC quotient that can be confirmed with spirometry. COPD is diagnosed on the basis of this lowered quotient[5].

The chronic airflow limitation characteristic of COPD is caused by a mixture of inflammation-mediated structural changes in small airways (obstructive bronchiolitis) and parenchymal destruction (emphysema)[4]. The relative contribution of obstructive bronchiolitis and parenchymal destruction may vary between individuals. The terms emphysema and chronic bronchitis are no longer used in the definition of COPD adopted by the Global Initiative for COPD[4].

The characteristic symptoms of COPD are cough, sputum production, and breathlessness upon exertion[4]. Smoking and exposure to irritants such as dust and fumes are the major causes of COPD[4]. Other risk factors are heredity for lung diseases and low socioeconomic status. Since the disease is progressive by nature its severity will increase with increasing age.

Globally COPD is a leading cause of morbidity and mortality[4]. In 2001, COPD was the fifth leading cause of death in high-income countries, and it was the sixth leading cause of death in nations of low and middle income[6]. It is expected that the burden of COPD will continue to increase as the world's population ages[7].

To aid in the assessment of the severity of disease, the Global Initiative for Chronic Obstructive Lung Disease group (GOLD) has developed a staging system, based mainly on lung function. The stages are as follows:

GOLD 1 (mild) $FEV1 \geq 80\%$ of predicted

GOLD 2 (moderate) $80\% > FEV1 \geq 50\%$ of predicted

GOLD 3 (severe) $50\% > FEV1 \geq 30\%$ of predicted

GOLD 4 (very severe) FEV1 < 30% of predicted or FEV1 < 50% of predicted plus chronic respiratory failure[4].

The management of COPD involves the avoidance of risk factors, to prevent disease progression, and pharmacotherapy as needed to control symptoms[4]. There is also a large need for patient education and health advice. Patients with COPD should always receive specific counselling about smoking cessation[8]. In addition patients may need instructions on physical exercise, nutritional advice, and continued nursing support. The potential benefit of each approach should be assessed at each stage of the illness[8].

Asthma

The guidelines from the Global Initiative for Asthma (GINA) give the following operational description of asthma: “Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is associated with airway hyperresponsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness, and coughing, particularly at night or in the early morning. These episodes are usually associated with widespread, but variable, airflow obstruction within the lung that is often reversible either spontaneously or with treatment.”[2].

Patients with asthma are a heterogeneous group, presenting a wide range of eliciting factors, airway hyperresponsiveness, airway inflammation, and relations between physiological and inflammatory components[9]. This has led to a discussion of several different asthma phenotypes[10], and is currently an expanding research field.

Asthma is a common chronic disease worldwide, with an estimated 300 million affected individuals. The prevalence, especially in children, is increasing in many countries[11] A recent report stated that, in Sweden, approximately 10% of the adult population has asthma[12]. In the US, asthma affects approximately 15 million persons, which means 6 to 7% of the population, and its prevalence has been described to be about the same in the rest of the western world[13-15].

The management of asthma patients is aimed at achieving and maintaining clinical control[2]. Disease control can be reached in a majority of patients with a proper pharmacologic treatment[16]. To guide the pharmacologic treatment of asthma a stepwise approach has been proposed by both GINA[2] and the Swedish Medical Products Agency[17]. The Swedish approach consists of five steps with treatment adjustments at every step. The recommendation is that patients on step 1-3 be treated in primary care and patients on step 4-5 by specialists either in primary care or at a chest clinic[17].

Distinguishing asthma from COPD

Asthma and COPD can coexist in a single patient; however, the inflammation characteristic of COPD is distinct from that of asthma[4]. Asthmatic inflammation is mainly eosinophilic and in COPD the inflammation – at least in the larger airways – is mainly neutrophilic[18]. Apart from the cellular differences, asthma and COPD share features such as airflow obstruction and persistent inflammatory processes[18], which can make them difficult to distinguish from each other. Clinically, the best way to distinguish asthma from COPD is to perform a procedure known as a post bronchodilator test alongside a spirometry test. The bronchodilator test is performed to assess reversibility of airway constriction. Large reversibility of airways constriction ($\geq 12\%$) is a common feature in asthma but not in COPD[1, 2].

Health Related Quality of Life

Quality of life (QoL) has become an important outcome in clinical trials, partly due to demands from regulatory agencies. However, despite the growing popularity of QoL as an outcome measure, research continues to be troubled by the lack of a clear and concise definition of the concept[19]. In general terms, QoL refers to how good an individual's life is, and – in relation to health – to the goodness of those aspects of life affected by health[19].

Over 50 years ago, the World Health Organization (WHO)[20] defined health as “a state of complete physical, mental and social well-being, not merely the absence of disease or infirmity.” In concordance with this definition of health, definitions of health-related QoL (HRQoL) have been proposed. It has been defined as: “the value assigned to duration of life as modified by impairments, functional states, perceptions, and social opportunities that are influenced by disease, injury, treatment, or policy”[21] and “the functional effect of an illness and its consequent therapy upon a patient, as perceived by a patient”[22].

From these definitions of HRQoL we can conclude that it is a multidimensional construct with a core consisting of the dimensions physical functioning, symptoms, psychological functioning and social functioning. Further it is patient-centered and reflects the individual's subjective evaluation of his/her own functioning and well-being.

Even though a subject's HRQoL is the result of his/her evaluation of functioning and well-being, there is still a multitude of factors that will affect many subjects' HRQoL. Age, sex, socioeconomic status and social support have all been shown to play a part[23].

There is a consensus in the scientific community that improving not only the health of subjects, but also the HRQoL is an important goal of therapeutic interventions for both COPD and asthma[2, 4].

The burden of disease has been confirmed in both COPD and asthma. A recent Swedish study of hand eczema, which included a comparison of the QoL of populations with different diseases, showed that patients with COPD were worst off[24]. Many asthmatic persons, worldwide, still suffer from symptoms and limitations in their everyday life[25].

Test Theory

Psychometric test theory provides a basis for much of the measurement of self-reported health indicators, including HRQoL[26]. The psychometric approach offers two theoretical frameworks for test development: the Classical Test Theory (CTT) approach and the Item Response Theory (IRT) approach. The CTT has dominated the field during the last decade and is probably the most common approach of the two[26]. The IRT approach was originally developed in order to overcome problems associated with CTT. Most of the theoretical work was done in the 1960's[27] but the development of IRT continues and has now become a major theoretical framework used in the scientific field[28]. Even though the IRT approach offers a number of potential advantages over CTT in assessing self-reported health outcomes, the work in this thesis is based on CTT.

The CTT approach to measurement is founded on the true score model[29], which is based on the assumption that there is an observed score and a true score. The observed score is composed of the estimated true score plus measurement error[26].

Score meaning in CTT is often derived from comparison to a norm or standard[30]. In the field HRQoL measurement, the use of a criterion from which meaning is derived is common. The criterion is a threshold value referred to as the minimal important difference (MID) or sometimes the clinically minimal important difference (CMID). Changes larger than the (C)MID are considered meaningful and smaller changes are considered unimportant[31].

Validity

The quality of a test is assessed by evaluating its validity and reliability[26]. Validity and reliability relate to the interpretation of scores from psychometric instruments used in clinical practice and research[32]. Validity has traditionally been separated into several distinct types[33]. However, recent voices on the subject suggest that these distinctions are arbitrary[34] and that all validity concepts should be gathered under one and the same framework, that of “construct validity”. In this approach, the different types of validity (figure 1) are understood as sources of evidence about validity rather than as independent entities.

Construct validity has been defined as the degree to which an instrument measures the construct it is intended to measure[35]. In layman terms, validity describes how much one may trust the results of a test as interpreted for a specific purpose. Interpreting the meaning of results from assessments of, for example, HRQoL questionnaires, is not straightforward. A HRQoL scale does not have any inherent meaning; it was designed to measure an underlying construct, an “intangible collection of abstract concepts and principles”[36].

The results of any psychometric test or assessment have meaning only in the context of the construct they claim to assess[32]. Because the validity of an

instrument's scores depends on the construct, a clear definition of the intended construct is the first step in any validity evaluation. Further, validity is not a property of the instrument, but of the instrument's scores and their interpretations[33]. Thus, it is context-dependent. This has the important practical consequence that validity must be established for each intended interpretation. For example, a symptom-scale whose scores provided valid inferences when used under research conditions or in highly selected patients may need further evaluation before use in a typical clinical practice.

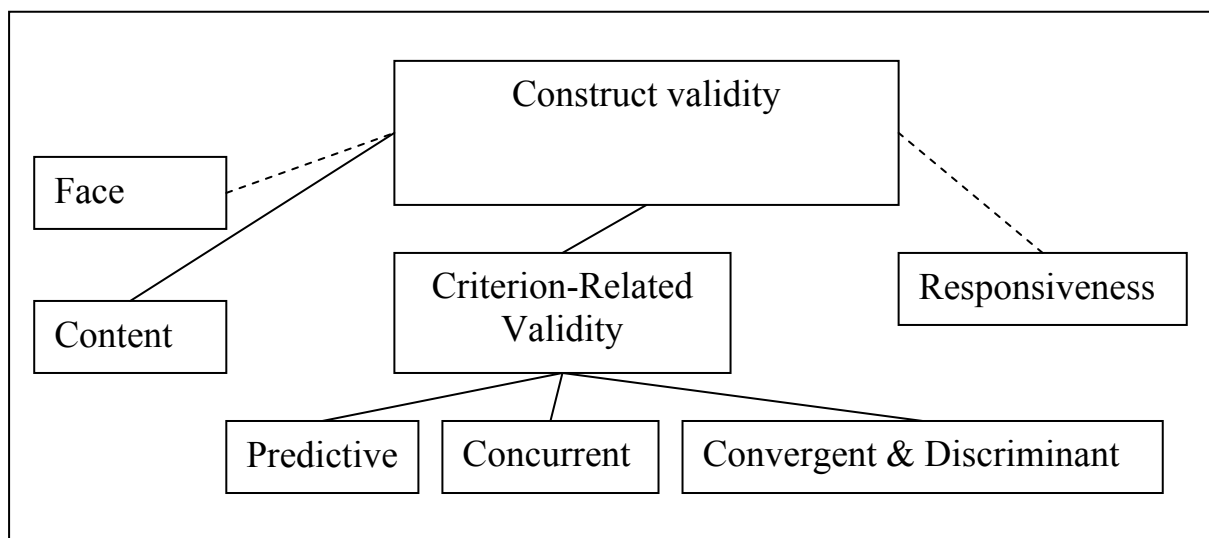


Figure 1. A model of Validity

Construct validity as conceptualized in figure 1 consists of several sub-concepts. Face validity refers to whether a test or instrument appears to be able to measure the construct of interest. Face validity is the weakest form of support for claims of construct validity and I claim that it should not really be considered as evidence. Content validity concerns evaluating the “relationship between a test’s content and the construct it is intended to measure.”[33]. The content of a test should represent the whole construct. Thus, we look at the construct definition, the instrument’s intended purpose, the process for developing and selecting

items¹ and the wording of individual items[37]. Content evidence is often presented as a description of steps taken to ensure that the items represent the construct[37].

Criterion-related validity, also referred to as instrumental validity, is used to demonstrate the validity of a measure or test by comparing it with another measure or test which has been demonstrated to be valid. However, this type of validity evidence runs the risk of criterion contamination, that is error in measurement of the criterion[38]. Criterion contamination leads to an exaggerated correlation between instrument and criterion variables, and thus to a faulty criterion-related validity estimate. Criterion-related validity has further been narrowed down to subtypes (figure 1).

Predictive validity refers to the ability to predict something which should theoretically be possible to predict. For instance, we might theorize that a measure of patient satisfaction should, reasonably well, predict the results of measured compliance. A high correlation between the results would provide evidence for predictive validity[38].

Concurrent validity is confirmed when scores measured on a scale are correlated to those measured on a criterion scale at the same point in time. This criterion score may be a measure of the same or a closely related construct. Preferably this criterion measure should previously have been validated. Note that in contrast to predictive validity, in concurrent validity, the two measurements are made at the same point in time[38].

Convergent and discriminant (sometimes referred to as divergent) validity are related concepts and fundamental aspects of construct validity. Convergent

¹ “Items” are the individual questions on the instrument.

validity refers to the extent to which different ways of measuring the same trait intercorrelate. Discriminant validity requires demonstrating that a measure does not correlate too strongly with measures that are intended to measure other constructs[38].

A final indicator of validity which is especially important in the context of HRQoL research is responsiveness[39]. Responsiveness refers to the ability of a measure to reflect change[40]. Changes in HRQoL measures can be compared to change in clinical status, health events, interventions of known or expected efficacy, and direct reports of change by patients or providers[40, 41]. There is some confusion about responsiveness in general and about what constitutes an adequate approach for evaluating responsiveness[42]. Irrespective of this confusion, any measure of change – and especially responsiveness – is threatened by what are known as floor and ceiling effects[43]. This occurs when baseline scores tend to “pile up” at the end of the measurement scales. The consequence of the floor and ceiling effect is that change can be measured in only one direction[43].

Reliability

Reliability refers to the reproducibility or consistency of scores from one assessment to another[33]. Reliability is a necessary, but not sufficient, component of validity[36]. An instrument that does not yield reliable scores does not permit valid interpretations. There are numerous ways to categorize and measure reliability[36] and not all will be presented here. The relative importance of each measure will vary according to the instrument type[36].

Test reliability can be thought of as the degree to which an instrument is not troubled by random error. Such a definition of reliability implies homogeneity of content on multi-item tests and internal consistency (i.e., high correlations)

among test items. A second definition of reliability is reproducibility or stability of an instrument over time (test-retest).

Reliability of an instrument or test in terms of internal consistency is usually estimated by using the Cronbach's alpha coefficient[44, 45]. The closer Cronbach's alpha coefficient is to 1.0 the greater the internal consistency of the items in the scale. Based upon the formula $\alpha = rk / [1 + (k - 1)r]$ where k is the number of items considered and r is the mean of the inter-item correlations the size of alpha is determined by both the number of items in the scale and the mean inter-item correlations. If all items are perfectly reliable and measure the same thing (true score), the coefficient alpha is 1[45].

Test-retest reliability is the degree to which an instrument yields stable scores over time among respondents who are assumed not to have changed on the domains being assessed. Intra-individual variability is used to estimate random error in test-retest assessments[46]. Often the Pearson product-moment correlation coefficient is computed to estimate test-retest reliability. If there are more than two assessment points, the test-retest reliability is preferably assessed with the intra-class correlation coefficient (ICC)[47]. The simplest form of ICC is the ratio of the between-subjects variance and total variance [48].

Health-related quality of life instruments

Many instruments to assess HRQoL are available for researchers. They can be classified into three main types: generic, disease-specific and domain-specific instruments[19].

The generic instruments are useful when one wishes to make comparisons between different diseases and conditions. These instruments aim to be broad

measures of HRQoL[19]. The disease-specific instruments are designed to enable one to better discriminate between patients' levels of severity of condition, and to be more sensitive to change[19]. A domain-specific instrument is usually used when a special aspect of a disease or condition is studied[19]. Domain-specific instruments are primarily used in research[19].

The vast majority of instruments for assessment of HRQoL are standardized questionnaires, where the respondents reply to a specific set of questions. The responses to questionnaires are then analyzed quantitatively, with individual experiences and perceptions added up and expressed as a group mean for comparison with other groups. There are options available that claim to measure individual QoL though[49]. These approaches allow assessment of the importance of issues that individuals themselves find relevant[50].

The development of new instruments is time-consuming and hard work. The work process can be summarized as presented in figure 2.[51]. Before any work on the actual development of an instrument can begin, the work with identifying and defining the construct that is to be measured needs to be completed. Needless to say, the more precise the definition the better. If insufficient effort is made with this there is considerable risk that the scale will have poor reliability and doubtful validity[51].

Second, the instrument is to be designed. This involves deciding on the format of the instrument, should it be self-administered or interviewer administered, selection of response choices and writing of items and instructions[51]. The general idea is to write an initial item pool, that will be subject to changes as the work progresses.

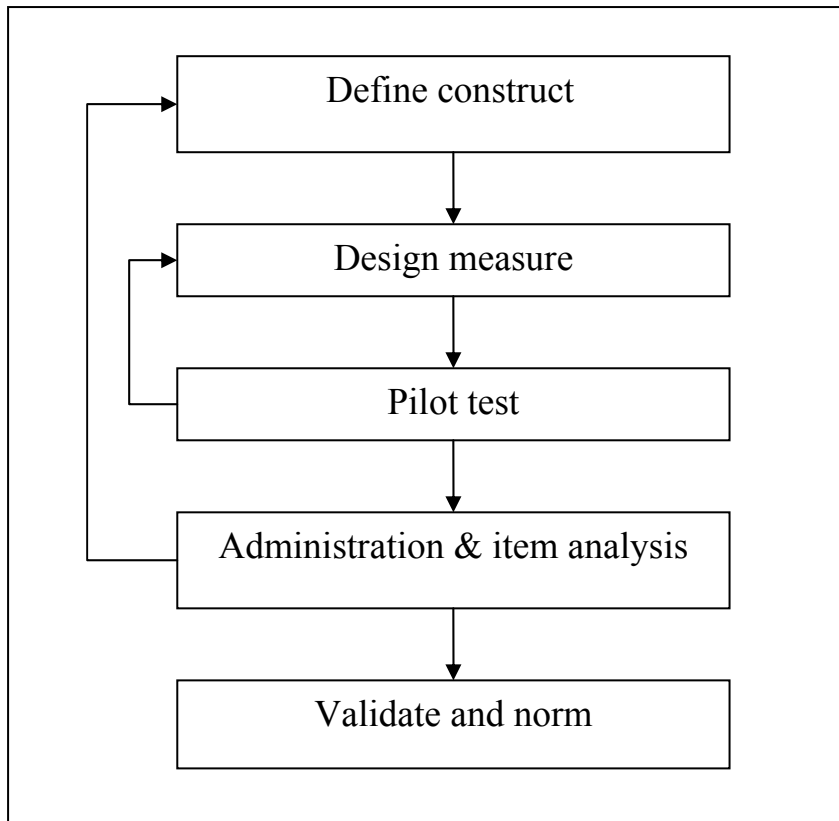


Figure 2. Major steps to developing a Summated Rating Scale*

Adapted from: Spector PE: *Summated rating scale construction: an introduction*. Newbury Park: Sage; 1992.

Before any work on the actual development of an instrument can begin, the work of identifying and defining the construct that is to be measured needs to be completed. Needless to say, the more precise the definition, the better. If insufficient effort is made with the definition, there is considerable risk that the scale will have poor reliability and doubtful validity[51].

Second, the instrument has to be designed. This involves deciding on the format of the instrument, and whether it should be self-administered or interviewer administered, selecting response alternatives, and writing items and instructions[51]. The general idea is to write an initial item pool, that will be subject to changes as the work progresses.

Third, the first version should be pilot tested on respondents who are instructed to critique the instrument in terms of layout, wording, response choices, etc. The feedback on the pilot will then form the foundation for a revision of the initial version of the instrument.

Fourth, the first full version of the instrument is ready for administration. The administration should include a sample of at least 100 respondents to complete the instrument. The data obtained can then be analyzed statistically according to psychometric test theory principles.

Fifth, the work on validation and norming then continues as the instrument is used [51].

Health-related quality of life in COPD

An American Lung Association survey revealed that 51% of all patients with COPD say their condition limits their ability to work. It also limits them in normal physical exertion (70%), household chores (56%), social activities (53%), sleeping (50%) and family activities (46%)[43].

To date no drug treatment has been consistently proven to stop the deterioration of lung function or decrease mortality in COPD[4]. The goal of pharmacological treatment for COPD is to relieve symptoms, prevent complications and slow progression of the disease [4].

Central to the management of symptoms of COPD are bronchodilator medications. They are given according to a prescribed schedule or on an as-needed basis to prevent or reduce symptoms. The principal bronchodilator treatments are β 2-agonists, anticholinergics, and theophylline used alone or in

combination. Additional treatments include inhaled corticosteroids (ICS) and oxygen therapy[4]. Vaccines against pneumococci and influenza are recommended.

There are many disease-specific and domain-specific instruments intended for use on COPD populations[52]. Unfortunately, very few of them are available in Swedish[53]. Until recently only two questionnaires were available in Swedish: the St. George's Respiratory Questionnaire (SGRQ) [54] and the Clinical COPD Questionnaire (CCQ) [55]. The Chronic Respiratory Questionnaire Self-Administered Standardized (CRQ-SAS)[56] has been translated to Swedish by the MAPI Research Institute[57]; however, it is still uncertain whether it has gone through full linguistic validation.

The SGRQ has 50 (76 weighted) items in 3 domains measuring Symptoms, Activity and Impacts, and 1 overall score. Each score ranges from 0 to 100% (0 = no impairment). The measurement properties of the SGRQ have been found to be satisfactory in a Swedish population[58]. The minimal important difference, MID, is a score change of ≥ 4 points between occasions[59].

The CCQ has 10 items, one overall score and 3 domains: Symptoms, Functional state and Mental state. All scores range from 0 to 6 (0 = no impairment). The first validation revealed some weaknesses, such as skewed distributions in functional and mental state domains[55]. The MID for CCQ is 0.41[60].

The original CRQ measure of health-related quality of life in patients with chronic airflow limitation consists of 20 items scored on a 7-point scale in four domains: dyspnea, fatigue, emotional function and mastery. The CRQ-SAS refers to the CRQ-Self administered format including Standardized Activities. It

is based on the original CRQ; however, it is self-administered and contains standardized questions on dyspnea. The MID for the original CRQ is ≈ 0.5 [61]

Health-related quality of life in asthma

Investigations and reality surveys around the world[25] revealed that the percentages of adults who lost workdays due to asthma were as follows: 25% in the United States; 17% in Western Europe; 27% in Asia-Pacific; 30% in Japan; and 23% in Central and Eastern Europe. Chronic symptoms were experienced by 61% in the US; 56% in Western Europe; 51% in the Asia-Pacific; 51% in Japan; 74% in Central and Eastern Europe. Restrictions in normal physical activity caused by asthma were experienced by 36% in the US; 32% in Western Europe; 45% in Asia-Pacific; 17% in Japan and 68% in Central and Eastern Europe. The survey concluded that there is direct evidence for suboptimal asthma control in many patients worldwide, despite the availability of effective therapies, with long-term management falling far short of the goals set in the GINA guidelines[25].

As with COPD there are a number of instruments designed for measurement of HRQoL or closely related constructs in patients with asthma[62], although very few of them are available in Swedish[53]. Four of the few that are available in Swedish are the Asthma Quality of Life Questionnaire (AQLQ)[63], the Asthma Quality of Life Questionnaire Standardized version (AQLQ(S))[64], the Mini Asthma Quality of Life Questionnaire (MiniAQLQ)[65] and the Living With Asthma Questionnaire (LWAQ) [66]. A frequently used domain-specific instrument, the Asthma Control Questionnaire (ACQ)[67], is also available in Swedish.

The AQLQ[63] has 32 items in four domains: symptoms, emotions, activities and environment. The activities domain in AQLQ differs from the others in that the five items on activities are selected by the patients themselves. The AQLQ(s) was developed from the AQLQ, with the difference that the activities domain is based on standardized activities.

In both questionnaires respondents are asked to recall their experiences during the last two weeks and to score each item on a 7-point scale, where 7 is excellent and 1 is the worst. A score change of ≥ 0.5 points on the 7-point scale is considered to be clinically important, and is termed the Minimal Important Difference (MID)[68].

A short version of AQLQ, the MiniAQLQ, was developed by reducing the original 32-item AQLQ to 15 items[65]. The MiniAQLQ contains five items on symptoms, four on activity limitations, three on emotional function and three concerning environmental stimuli.

The LWAQ is a 68-item questionnaire[66]. Originally the LWAQ only produced one single overall score, but has later on been revised and now identifies eleven domains and four constructs. The items are on a three-point scale with 0 indicating very high quality of life and 2 indicating very poor quality of life[69].

The ACQ is a questionnaire with seven items, five of which concern symptoms and activity limitations; one concerns the FEV1 in % of predicted, and one the use of β 2-agonists during the preceding week[67]. Later the authors of the ACQ have shown that FEV1-item and the β 2-agonist-item can be omitted[70]. All questions are scored on a 7-point scale (0 = good control; 6 = poor control) and overall control is the mean of the seven responses. A score change of ≥ 0.5 on the 7-point scale is considered clinically important[70].

Health-related quality of life in Clinical Practice

HRQoL questionnaires can be used for various purposes in clinical practice as well as in research[71, 72]. In research the HRQoL instruments can be used to evaluate, predict or discriminate, all depending on the research question at hand[71]. In clinical practice the potential use of HRQoL instruments has been identified as: screening for psychological and functional problems; monitoring disease symptoms or therapeutic response; facilitating physician–patient communication and assessing quality of care[73].

In clinical practice, many of the potential uses have not been realized[72]. There are many barriers against using HRQoL in clinical practice. Velikova and Wright (2005) identified them as practical barriers, methodological and conceptual barriers, relative lack of research data and finally an attitude barrier[72].

The practical barriers surround the data collection and scoring of responses. These tasks are time-consuming if done the traditional way without aid of computers, and time is a scarce resource in busy clinical practices. The practical barriers are not overwhelming though. An electronic version of the English AQLQ is available, and has been compared with a paper version. The measurement properties are not affected by mode of administration[74]. The AQLQ, AQLQ(S), ACQ and LWAQ are not yet available in Swedish in computerized form.

The key methodological concern that has been raised against the use of HRQoL instruments in clinical practice is the fact that most of them are designed to compare groups of patients and not individual patients[72]. The reliability coefficients of the instrument and its subscales are recommended to be >0.70 (ideally >0.80) for group comparisons and >0.90 (>0.95 ideally) for individual

comparisons[45, 75]. Some researchers have argued that more liberal reliability criteria might be acceptable[47]. However, the need for high reliability in individual comparisons becomes evident when calculating confidence intervals around individual scores. The lower the reliability coefficient the wider the interval.

The barrier involving research data concerns the relative lack of evidence supporting the idea that the patient's well-being and/or the quality of care actually benefit from implementation of HRQoL measurement in clinical practice. There is some evidence supporting that it is beneficial for the process of care, but there is hitherto no evidence showing that it affects the outcome of care[76].

The attitude barrier refers to the notion that there is a widespread scepticism among physicians and researchers about the validity and the importance of HRQoL[72]. However, patients' and general practitioners' (GPs') opinions about quality of life monitoring were positive in a study of the management of patients with asthma and COPD[77].

Aim of the thesis project

The general objective of this project was to identify and to some extent remove obstacles in the incorporation of disease-specific quality of life and/or health-status assessments in the management of asthma and COPD patients in primary care. The measurement properties, the design and the administrative complexity of the instruments at hand have been scrutinized with the intent to make it possible for primary care to integrate a patient perspective in the treatment and monitoring of asthma and COPD.

Aims of the present studies

The studies presented here aimed to address the following:

I: What are the measurement properties of asthma-specific quality of life questionnaires when used in primary care? How do brief asthma-specific quality of life questionnaires compare to a “gold standard”?

II: What are the measurement properties of COPD-specific quality of life questionnaires when used in primary care? How does a brief COPD-specific quality of life questionnaire compare to a “gold standard”?

III: Could patient education, resembling information in clinical trials, and monitoring by diary enhance the treatment outcome when given to asthmatic patients in routine primary care? How large is the responsiveness of asthma-specific patient-reported outcomes.

IV: What domains of quality of life do patients with COPD perceive as being affected by their disease and what relative importance do they attribute to these different domains? Do the patients’ perceptions of what domains of QoL are affected and the patient-perceived importance of these domains differ from those reported in the literature?

Methods

This thesis consists of four studies in patients with asthma or COPD. In two of the four studies the focus is purely methodological and concerns the measurement properties of instruments used in asthma and/or COPD. The third study is a cluster-randomized trial of the effect of information and monitoring on asthma control. The fourth is a study of individual QoL in COPD.

Paper I – Asthma validation study

This was a prospective, multicenter study that was performed in 24 primary health-care centers in the Stockholm region. One hundred seventeen patients aged 18 to 86 were included.

All participants were required to have GP-diagnosed asthma. All eligible patients that sought medical care for any reason were consecutively invited to participate in the study. Exclusion criteria were: age < 18 years, COPD (referred to COPD study, see below), malignant disease, severe psychiatric disease, and dementia. Participants were required to understand written Swedish, in order to be able to complete the questionnaires and to give written informed consent.

We used five questionnaires in this study, one of them generic, the Short Form-36 (SF-36). The result from SF-36 was used to characterize the patients. The other questionnaires used were the ACQ, AQLQ(S), MiniAQLQ and a two-item global rating of symptoms and disease severity.

The participants made two visits 2 to 3 months apart. If needed, the participants were advised and allowed to change their medication after the first visit.

The questionnaires were completed in the same order at both visits: the SF-36, AQLQ(S), the ACQ, the global rating of symptoms and disease severity, and the MiniAQLQ. The participants were allowed a maximum of 60 min to complete all questionnaires.

Paper II – COPD Validation study

This study was conducted parallel with the asthma validation study; the approach and design of the studies are in principle the same. It was again a prospective, multicenter study that was performed in 24 primary health-care centers in the Stockholm region.

The final study sample consisted of 111 participants. Eighty-five of these were diagnosed as having COPD only, whereas 26 patients were considered to have both COPD and asthma by their treating physician. Exclusion criteria were the same as in the parallel asthma study except for the COPD criterion. The diagnostic criteria for COPD were not always met, in the diagnosis of COPD by the GPs. Nonetheless, we chose to include all with a GP set diagnosis, since we felt this would more accurately reflect the reality in primary care.

The participants made two visits, 2-3 months apart, without systematic changes in treatment between visits. If needed, the participants were advised and allowed to change their medication after the first visit though.

We used three questionnaires in this study: the SF-36, SGRQ, and the CCQ. The questionnaires were completed in this order on both visits. The participants were allowed a maximum of 60 min to complete all questionnaires. After having completed the questionnaire, the participants were not allowed to go back to change or check answers. At the second visit, the GP or a nurse, according to

local routines, estimated if and how the patients' clinical status had changed compared to visit 1.

Paper III – Asthma outcome study

In this study the sample consisted of 141 participants with an asthma diagnosis, aged 18-87, from 19 primary care centers in the Stockholm region.

The study was designed as a prospective, cluster-randomized trial and intended to measure the effect of structured information and monitoring by diary on treatment outcome of asthma. Study centers were randomized either to follow their local routine (controls) or to add extra structured written and verbal information and monitoring the patients by an asthma diary (intervention).

We used two asthma-specific PRO's in this study: the ACQ and the MiniAQLQ. Change in the ACQ score between visits was the primary outcome variable, and change in the MiniAQLQ score between visits was a secondary outcome in the study, along with lung function, number of emergency visits, number of additional/unanswered questions about asthma, changes of drug treatment, patient-perceived benefit and costs of asthma treatment.

Paper IV – Individual QoL in COPD

In this study, eligible patients were those who had a COPD diagnosis. The final study sample consisted of 20 participants with COPD. They were recruited through one primary care center and a hospital chest clinic. All patients received written and oral information about the study before deciding whether or not they wished to participate.

The participants were interviewed with the SEIQoL-DW[78, 79], which is derived from the full Schedule for the Evaluation of the Individual Quality of Life (SEIQoL)[80]. The SEIQoL and SEIQoL-DW is administered in the form of a semi-structured interview. The interviewer first elicits five areas of life considered most important by the respondent in determining his/her QoL. The level of satisfaction/functioning in each area is then recorded, followed by the SEIQoL-DW task, which allows the interviewer to determine the relative importance of each QoL area using a disk designed for this purpose[78].

In this study, we used the extended version of the instrument, including a generic and health-related part[81]. The interviews were carried out by the first author in the homes of the participating patients. Before conducting the interviews the interviewer was trained in the technique. The interviews took on average 40 minutes to complete.

Statistics & analysis

Paper I - Asthma Validation study

This study was aimed at validating the MiniAQLQ and the ACQ for use in primary care. As the validity of any instrument in any setting hinges on the instrument's reliability, this was where we started.

Reliability in terms of internal consistency was estimated by calculating the Cronbach's alpha coefficient[44] for the instruments in the study. Reliability in terms of ability to provide stable measurement was evaluated by calculation of ICC's of the overall scores and subscale scores of all instruments in the study. In addition to this we also evaluated the test-retest reliability by calculating test-retest correlations.

In evaluation of the validity of the instruments we used a criterion-related approach. To evaluate the concurrent validity of the MiniAQLQ and ACQ we postulated that if the MiniAQLQ measures the same construct as the AQLQ(S), and the ACQ measures the same construct as the symptoms domain of AQLQ(S), these should correlate reasonably well. The same reasoning applies to the change in scores between visits: if the same construct is measured with the MiniAQLQ as with the AQLQ(S) and the ACQ measures the same construct as the symptoms domain of AQLQ(S), then the changes in both of these should correlate reasonably well. In the paper we referred to the latter as longitudinal validity and the former as cross-sectional validity.

Responsiveness was evaluated in two ways. Firstly, we determined whether the instruments could detect differences between patient groups that were stable, improved, or deteriorated according to their AQLQ(S) scores using the Kruskal-Wallis test and post hoc multiple comparisons. The patients that had change scores larger than the MID (0.5) in the positive direction, were categorized as improved, those with change scores larger than the MID in the negative direction were categorized as deteriorated. Those that had change scores less than the $MID \pm 0.5$ were categorized as stable. Secondly, responsiveness was evaluated by calculating the effect sizes of the instruments. Finally, we checked for floor and ceiling effects.

Paper II - COPD Validation study

The statistical analysis in this study parallels the analysis made in the asthma validation study. There are some differences though: in this study all analyses were performed both for the entire study sample with clinical COPD ($n = 111$) and for the subgroup of patients with spirometry-verified COPD ($n = 83$) (i.e. correct diagnosis) which were the majority of the study population.

We evaluated reliability in terms of internal consistency and in terms of ability to provide stable measurement, in the same manner as in the asthma study.

In evaluation of the validity of the instruments we again used a criterion-related approach. To evaluate the concurrent validity, we postulated that if the SGRQ and CCQ measure the same construct, they should correlate reasonably well. The a priori expectations were that the total score of SGRQ as well as the symptoms and activity domain scores would correlate strongly with the total score of CCQ and with the corresponding domains of CCQ (symptoms and functional state) respectively. For the impacts domain of SGRQ and the mental health domain of CCQ, the expectation was that there would be a moderate correlation, since these domains only partially measure the same construct.

Responsiveness was not addressed directly in this paper but we analyzed floor and ceiling effects in all domains in both the CCQ and the SGRQ. This was done by calculating the proportion of subjects that had the highest possible score and the proportion of subjects that had the lowest possible score in each domain. In this text I have added a direct assessment of responsiveness, though. Responsiveness was examined by determining if the CCQ could detect differences between patient groups that were stable, improved, or deteriorated according to their SGRQ scores using the Kruskal-Wallis test and post hoc multiple comparisons. The patients that had change scores larger than the MID (± 4) in the positive direction, were categorized as improved, those with change scores larger than the MID in the negative direction were categorized as deteriorated. Those that had change scores less than the MID were categorized as stable.

Paper III - Asthma outcome study

The effect of the intervention was described by the change in ACQ scores and differences between study groups were tested for with weighted *t*-tests. We used means weighted by cluster size when comparing groups since we needed to account for possible cluster effects.

The Pearson Chi-square test was used to analyze for differences between groups on the categorical variables and adjusted Chi-square values were calculated to account for the clustering effect.

In the paper we did not mention any assessments of responsiveness; nonetheless, we calculated the standardized response mean (SRM)[82] for both the ACQ and MiniAQLQ. The SRM is calculated by dividing the change in score between visits with the standard deviation of the change scores. The SRM is a estimate of effect size and is usually interpreted using the criteria presented by Cohen[83]. These criteria identify an effect size of 0.2 or less as small, 0.5 as medium, and 0.8 or greater as large. We also did an analysis of floor and ceiling effects. This was done by calculating the proportion of subjects that had the highest possible score and the proportion of subjects that had the lowest possible score in each domain. This was done for both instruments.

Paper IV - Individual QoL in COPD

The results of the interviews with the extended SEIQoL-DW were further analyzed in both a quantitative and a qualitative fashion.

The slightly more qualitative approach began with an analysis of cue statements made by the respondents in the semi-structured interview in search of latent underlying constructs. The label that the respondents used for the cues was then

used to generate a higher level of abstraction. These “families” of cues were then labeled according to the content of the cues. This was done to reach a beforehand unspecified number of domains, that could be compared with the domains of some the standardized instruments in the area. In some ways, the method applied reminds of that of grounded theory[84].

The work on generating domains was initially done by the first author. Once a preliminary result was reached another of the authors (ALE) got involved in the process and critically reviewed the domains. This was done by questioning whether or not a certain cue label actually referred to some aspect of the domain it was placed in. This resulted in revisions of cue placing as well as a change in the number of domains. The work was considered complete when both authors felt that they could accept the results. The quantitative analysis consisted of counting frequencies, calculating weights and satisfaction ratings.

Results

Paper I – Asthma Validation study

Reliability in terms of internal consistency was estimated by calculating the Cronbach’s alpha coefficient for the instruments in the study. The Cronbach’s alpha values were generally good for the overall scores, ranging between 0.93 and 0.89. The subscales in AQLQ(S) and MiniAQLQ had lower alpha values, but the pattern was consistently similar.

The reliabilities of the MiniAQLQ and the ACQ, in terms of temporal stability, were determined in the group of patients who were categorized as stable according to AQLQ(S) ratings. The ICC and test-retest reliability coefficients were good for the “gold standard” instrument, the AQLQ(S). The ICC’s and test-retest reliability coefficients for the MiniAQLQ were good but consistently

lower in the overall score and all domains of the MiniAQLQ. The ICC for the ACQ was lower than for the ICC for the overall and symptoms domain scores of the AQLQ(S). The test-retest reliability coefficient of the ACQ was 0.89, indicating good reliability.

In order to evaluate concurrent validity we postulated that the MiniAQLQ and AQLQ(S) scores should correlate well and the ACQ should correlate well with the symptoms domain of the AQLQ(S). The (cross-sectional) overall correlation between the MiniAQLQ and AQLQ(S) was strong ($r = 0.95$), with the highest r value for the symptoms domain, and somewhat lower r values for the other domains. The correlation between the ACQ and the AQLQ(S) symptoms domain was strong ($r = -0.89$) and so was the correlation between the overall scores ($r = -0.88$).

We also postulated that the change scores of the AQLQ(S) and the MiniAQLQ should correlate well and that the ACQ change scores should correlate well with the symptoms domain of the AQLQ(S). The correlation between MiniAQLQ and AQLQ(S) overall change scores was 0.85. The correlations of change scores of the subscales were lower, and only moderate for the emotions and environment domains. The ACQ overall change score correlated well with the AQLQ(S) overall change score ($r = -0.78$), and even better with the symptoms domain change scores ($r = -0.81$).

The MiniAQLQ and ACQ detected differences between groups of patients that had been categorized as stable, improved, or deteriorated ($p < 0.001$) according to AQLQ(S) ratings. The effect sizes for all three instruments were similar, range 0.19-0.21, indicating similar responsiveness of the questionnaires. The ACQ had floor effects but no ceiling effects. The AQLQ(S) and the MiniAQLQ did not suffer from any floor effects and had only negligible ceiling

effects (<5%) in the overall and symptom domain scores. The three remaining domains had moderate ceiling effects in both questionnaires.

Paper II - COPD Validation study

The reliabilities of the SGRQ and the CCQ were assessed using data only from patients categorized as stable according to change in SGRQ scores. The ICC's were good for both instruments at the overall and domain levels. The ICC values ranged between 0.92 and 0.80 for the SGRQ and between 0.86 and 0.74 for the CCQ. The ICC's for the CCQ were consistently lower than those for SGRQ. The test-retest reliability coefficients showed a pattern to that of the ICC.

Cross-sectional correlations between the SGRQ and the CCQ were good. The total scores of the two questionnaires correlated best: $r = 0.88$. The correlations between domains in the SGRQ and CCQ ranged between 0.84 and 0.63. The correlation of the total change scores of the CCQ and the SGRQ was 0.52. The correlations of the domain change scores were poor, $r < 0.4$ for all domains.

Table 1 - Comparison of group differences in change score

Instrument Group	Deteriorated (n=23)	Stable (n=48)	Improved (n=40)	P-value
CCQ				
Total	0.23	-0.18	-0.73	<0.001
Symptoms	0.13	-0.18	-0.89	<0.001
Mental state	0.33	-0.27	-0.67	0.009
Functional state	0.30	-0.14	-0.62	<0.001

Mean change score (difference between visit 2 and visit 1) for each of the domains in CCQ. Group differences compared with Kruskal Wallis test with following post hoc multiple comparisons. Groups created on the basis of SGRQ scores.

It was expected that some of the domains would correlate poorly, since these domains measure very different aspects of health status.

The CCQ consistently failed to differentiate deteriorated and stable patients defined by SGRQ, with regard to both the total score and the domains (Table 1). In the mental state domain it also failed to differentiate between improved and stable.

Floor and ceiling effects in the total and symptom domain scores of the CCQ were negligible. In the functional and mental state domains, floor and ceiling effects were present. In the entire population 3.6% had optimal functional state scores at visit 1 and 7.2% at visit 2. In the mental state domain 14.4% of the patients scored optimally at visit 1 and 16.2% at visit 2. The SGRQ did not suffer from floor or ceiling effects.

Paper III - Asthma outcome study

One hundred and forty-one participants completed the study, of these, 64 participants were in the intervention group and 77 in the control group.

The changes in ACQ scores differed significantly, $t(137) = 3.51$, $p = 0.01$ between the control group ($M = -0.29$, $SD = 0.31$) and the intervention group ($M = -0.45$, $SD = 0.23$). However, the difference in mean change was less than the Minimal Important Difference (MID) of $\approx \pm 0.5$ in the control group.

Both groups improved their disease-specific quality of life during the study. The magnitude of change was $M = 0.28$, $SD = 0.31$ in the control group and $M = 0.53$, $SD = 0.18$ in the intervention group ($t(137) = -5.72$, $p < 0.05$ for the group

difference). The magnitude of change exceeded the threshold for the MID (0.5) in the intervention group.

The ACQ SRM for the intervention group was 0.53 and for the controls 0.32. The MiniAQLQ SRM for the intervention group was 0.70 and for the controls 0.33, indicating a medium effect in the intervention group and a small effect in the control group on both outcomes. The ACQ suffered from ceiling (best possible score) effects in the intervention group, but no floor effects were present (Table 2). Considerable ceiling effects for both groups, negligible floor effects for the control group and none for the intervention group were present on the MiniAQLQ (Table 2).

Table 2. Floor and ceiling effects of the MiniAQLQ

	Control		Intervention	
	Floor (%)	Ceiling (%)	Floor (%)	Ceiling (%)
Total	0	0	0	0
Symptoms	0	1.3	0	3
Activities	0	6.5	0	23.4
Emotions	1.3	16.9	0	10.9
Environment	1.3	14.3	0	18.8
ACQ	0	1.3	0	7.8

Paper IV – Individual QoL in COPD

The participants made a total of 99 statements with regard to the generic part and 78 regarding the disease-specific part. These statements were categorized in 27 areas labeled under five domains: physical health, mental health, social life, economy and other.

With the generic SEIQoL-DW the most frequently nominated cue area was the subject's own health, followed by physical activity. With the disease-specific extended SEIQoL-DW the most frequently nominated cue areas were worries

about health, and fatigue, which were nominated by 40% of the subjects. The second most frequently nominated area was efficient treatment, nominated by 30% of the subjects. In third place was a cluster of areas all nominated by 20% of the subjects.

When one takes into account the weights attached to the cue areas elicited with the generic version, the order of importance changes. The subject's own health remains the most important area of life, whereas physical activity and relation to family/partner switch places. If one considers the weights attached to the cue areas elicited with the disease-specific extended version, the pattern also changes. Independence then appears as the second most important area, as weighted by the subjects.

The cue areas elicited with the SEIQoL-DW were physical health, mental health, social life, economy, and others. When one compares these cue areas and the content of standardized disease-specific questionnaire, differences become apparent on the item level. The symptom areas are well covered by the standardized questionnaires, whereas several other areas of life nominated by the COPD patients are not. The standardized questionnaires do not address independence, isolation, disappointment, passivity or worries about the future. Within the mental health domain, specific fear of exacerbations is addressed (CCQ), but not unspecific, generalized fear. Likewise, worries about health are only partly addressed by the health expectations items (SGRQ).

Discussion & Conclusions

Improvement of the patient's HRQoL is a major goal in treatment of both asthma [2] and COPD [4]. To reach this treatment goal it is necessary to incorporate routine assessment of HRQoL or related constructs into clinical routines just as other treatment outcomes are monitored. The reality of current long term asthma management is disappointing. Even though we have the treatment options needed to keep the disease under control for most patients [53], we continuously fail to achieve this, with diminished HRQoL as a result [85]. When it comes to COPD, the treatment options do not hold as much promise as those for asthma. Nevertheless, we may alleviate symptoms and slow disease progression[3]. Just like asthma patients, COPD patients have a generic HRQoL (measured by SF-36) which is lower than the national reference norm, as we showed in paper II, and there are studies showing diminished HRQoL in COPD patients when compared to other patient groups as well [24].

To include and understand the patient perspective in disease management has been pointed out as one potential remedy to the failure to reach treatment goals in asthma [86]. This reasoning can easily be translated to the COPD context as well. It is too often implicitly assumed that a general improvement in clinically relevant physiological outcomes is a guarantee for increased HRQoL, but this assumption is only partly correct. A study on patients with COPD has shown that lung function is moderately correlated to patient perceived physical functioning, and weakly correlated with psychosocial and emotional function[87]. Thus, specific monitoring of HRQoL is needed to assess this treatment goal and cannot be replaced by other routine clinical assessments.

Since HRQoL questionnaires have hitherto not been used to a large extent in primary care, health care professionals may be discouraged from using them out

of fear that the questionnaires are complicated, developed for research purposes and require special education of the staff. However, the results of the validation studies described in papers I and II showed that with brief questionnaires, such assessments are feasible in primary care under conditions similar to everyday care with minimal training of the staff.

Lack of instruments developed for monitoring on an individual level is sometimes mentioned as a reason for not measuring HRQoL in clinical practice. In asthma the standardized PRO's that we assessed in papers I & III, could based on the results be incorporated into clinical practice. The PRO's exhibited good reliability. Total scores in both the MiniAQLQ and the ACQ exceeded the requirements for use on an individual level (reliability coefficients > 0.90) set by the Medical Outcomes Trust [88]. The validity of the instruments was acceptable. The responsiveness of the ACQ and the MiniAQLQ, estimated as effect sizes, was small in study I, and in study III the effect sizes were medium in the presence of an intervention. However, in both studies the ACQ was plagued by ceiling effects that might prevent improvement in scores. The MiniAQLQ had negligible ceiling effects on the total score in study I and III, but considerable ceiling effects in the domain scores in study III. Thus, one could conclude that – at least in terms of total scores – the MiniAQLQ and the ACQ have measurement properties that give them enough precision and responsiveness to be used on individual level in clinical practice. The domains in MiniAQLQ do not have the precision required and there is a problem with the ceiling effects.

The CCQ that was assessed in study II had good reliability: the coefficients ranged between 0.80 and 0.75. The validity of the instrument was also good. However, the ability to detect change had a bias against detecting change in the positive direction. The instrument performed worst in the mental health domain,

in which it could not detect change in any direction, but then again this domain was the one that was troubled by ceiling effects. The conclusion from study II is that the CCQ is not suitable for use on an individual level in clinical practice. It could be that additional items in the mental health domain could remedy its poor measurement performance. In the version we assessed this domain contained only two items, versus four items in the two domains that performed well. Including two additional items in one domain hardly seems like an excessive price to pay, if it could improve the overall performance of the instrument. Still, the relative “shortness” of CCQ is one of its advantages. The “gold standards” in both studies I and II (SGRQ and AQLQ(S)) we considered too time-consuming (too many items) and too complex to score (calculate total and domain scores from raw scores) to qualify for routine use. However, it is good that the CCQ addresses the domain of mental health as this appears to be a very important area for patients with COPD. In study IV the most frequently nominated cue area in the disease-specific extended SEIQoL-DW was worries about health, and it was also weighted as most important. In the study, other areas that relate to mental health also came up: isolation, disappointment, passivity and fear. Thus, from a patient perspective, this domain deserves to be taken seriously.

The incorporation of QoL assessment into clinical routine should be accompanied with an idea of how the result should be used. Is it to assist clinicians in medical decision making? Is it to facilitate doctor–patient communication? Or is it a combination of both? Given that there is only weak to moderate correlation between HRQoL domains and physiological measures, maybe the last-mentioned would be the most appropriate. Possible clinical applications need to be evaluated, since they should only be implemented if they can improve treatment outcome and/or patient satisfaction at a reasonable cost. The evaluated brief questionnaires for asthma (paper I) are ready for this step. In paper III we showed that the effect of a simple intervention could be evaluated

on a group level. The next step will be to evaluate the use of these questionnaires for guiding individual therapeutic decisions.

There are those that argue that the IRT approach is superior to that of CTT[89] that was used in this study. They do not necessarily argue that the clinical practice setting is one of the areas where IRT might prove its superiority. However, it is easy to be seduced by the potential benefits of IRT applications. One of the chief potential applications of IRT lies in the realm of computerized adaptive testing. A computerized adaptive test is an instrument that is administered via the computer and is “tailored” to the individual examinee so that the items are neither too difficult nor too easy. An additional advantage to this is that the computerized adaptive tests usually contain fewer items than conventional tests.

However, there are major drawbacks with IRT as well. First of all, sample sizes (both study subjects and items) needed to get acceptable estimates are large. For example, it has been shown that items with 5-point response formats do not reach acceptable item parameter estimates until sample sizes are 500 and more[90]. Such an approach would thus not have been possible in primary care in the Stockholm area. Secondly, IRT, like many other “modern” methods, is conceptually simple but technically highly complex. To gain a fair understanding of the models that underlie the IRT applications a person will probably need to have relatively deep understanding of statistics.

Future research

Several obstacles and barriers surrounding the clinical use of disease-specific questionnaires remain to be dealt with, response shift being one of them[91]. The term response shift refers to a phenomenon that occurs spontaneously: individuals change with time and the basis on which they make QoL judgements

may also change. For instance, the individual may change his or her internal standards, values, and/or conceptualization on the target construct as a result of external factors such as a treatment or a change in health status. This has important implications for assessing the effects of treatments, since a change in QoL may reflect a response shift, a treatment effect, or a complex combination of both. To my knowledge, no studies have investigated this in asthma and it has only partly been investigated in COPD[92]. It is a necessity to have at least an idea if and to what extent this phenomenon is present in asthma. In COPD it seems as though response shift does not cause value reorientation [92] but it is unclear whether it causes reconceptualization of target constructs or recalibration of scale.

Another equally important aspect that needs attention is the cost of incorporating routine assessment of HRQoL into primary care. How much does it cost to incorporate assessment of HRQoL into a clinical practice setting? Are the costs balanced by the benefits of incorporating HRQoL assessments into these settings and, if so, how? These questions need to be answered in order to justify the additional effort and resources.

Acknowledgements

I början av min forskarutbildning, var det en professor som hälsade oss nya studenter välkomna, han talade varmt om forskning och kunskapssökande i allmänhet. I slutet av sitt anförande talade han om hur nya vetenskapliga upptäckter byggde på tidigare forskargenerationers ansträngningar. Nya vetenskapliga höjder nåddes genom att unga forskare klättrade upp och stod på tidigare generationers axlar för att nå högre. Han uppmanade oss att klättra så gott vi kunde. Vad han glömde nämna var att tidigare generationer var giganter och att det gällde att inte få svindel och falla ner.

Jag vill gärna tacka alla de suveräna, briljanta, intelligenta, ibland älskvärda och vid tillfällen helt avskyvärt besvärliga människor som hjälpt och stöttat mig i min klättring. Det här avhandlingsarbetet skulle aldrig ha blivit klart om det inte vore för er!

Ett stort tack till min huvudhandledare, Eva Wikström Jonsson, giganten bland giganter, för stöd och uppmuntran i allt som rört det vetenskapliga. Men även för alla intressanta diskussioner om allt och inget, men kanske mest för ditt tålamod med mina påhitt.

Mina bihandledare Ann Langius-Eklöf och Lennart Högman ska också ha ett stort tack för insiktsfull vägledning och tålamod.

Nuvarande och tidigare föreståndare för CFA Sven-Erik Dahlén, Gunilla Hedlin, Lars Gustafsson och Bengt Björkstén (den glömske professorn), för möjligheten att få bedriva forskarstudier.

Gunilla Jacobsson Ekman och Anne Renström för gott samarbete och framförallt intressanta diskussioner.

CFA doktoranderna i första och andra kullen, speciellt Lydia Bennedich Kahn, Cecilia ”Cia” Moberg och Marianne Heibert Arnlind, och givetvis även alla andra CFA:are.

Mina medförfattare Per Olof Ehlers, Björn Stållberg, Paul Hjemdahl, Lennart Forslund och Ingvar Krakau för gott samarbete och möjligheten att få lära av er.

Ett stort tack även till Michael Runold och Per-Olof Ehlers, utan er hjälp hade aldrig den sista delstudien varit möjlig.

Alla på avdelningen för Klinisk farmakologi vid Karolinska sjukhuset i Solna. Personal och forskarstudenter vid Akademien för hållbar samhälls- och teknikutveckling på Mälardalens högskola. Ett tack även till personalen på Söderskolan, ingen nämnd ingen glömd.

Jag vill även ta tillfället iakt och tacka mina nära och kära.

Till min underbara fru Malgorzata ”Gosia” Nokela, min son Martin och vår jytte Ludde, tack för att ni orkade stå ut. Nu blir det inga mer ”jag ska bara skriva klart det här...” på ett tag.

Jag tackar mina syskon Stefan, Sara och Maarit och självklart min mor och min far för stöd och uppmuntran.

Sedan vill jag även speciellt tacka Barbara & Stig Karlsson.

Slutligen, ett stort tack till ”folkbildaren” Ingemar Svensson och övriga på Åsa Folkhögskola som fick mig att våga tro på min egen förmåga.

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