
THE VALIDITY OF QUALITY OF LIFE
QUESTIONNAIRES IN CAPTURING
PEOPLE'S EXPERIENCE OF LIVING WITH
ASTHMA

CHRISTIAN JOACHIM APFELBACHER

PHD

2012

Abstract

At least six asthma-specific measures of health-related quality of life (HrQoL) exist. It is unclear what concepts of “quality of life” these instruments assess, how they compare psychometrically and what patients think of them.

A structured review of six of these questionnaires found that they differ in almost all criteria considered (conceptual model, reliability, validity, interpretability, patient burden, translations).

A mini version of the Juniper Asthma Quality of Life Questionnaire (Mini AQLQ-J) and the Sydney Asthma Quality of Life Questionnaire (AQLQ-S) were psychometrically analysed, using data from an adult asthma trial (n=146). Strong correlations with asthma symptoms and asthma control suggest that the measures may not measure a distinct quality of life construct.

Semi-structured interviews were conducted in Germany and the UK to elicit adult asthma patients' (n = 32) views on three of the reviewed questionnaires (AQLQ-J, AQLQ-S, and the Living with Asthma Questionnaire (LWAQ) or its German adaptation) and analysed in thematic content analysis.

The findings demonstrate that the number of response options should be kept to a maximum of five, the layout should be set out in a clear way and some items should be amended to increase comprehensibility or specificity. A tension between missing content and irrelevant content emerged from the interviews. However, co-morbidities such as allergies or infections, asthma control and asthma management were widely mentioned as missing. Despite the diversity of views expressed, the AQLQ-S was perceived to be the most appropriate questionnaire and was situated between the AQLQ-J as a ‘medical’ questionnaire and the LWAQ as an ‘emotional’ questionnaire.

The absence of explicit conceptual frameworks underpinning the existing measures, their differing foci and the findings from qualitative work with patients call for the development of a second-generation asthma-specific quality of life measure.

Table of contents

1	Introduction	15
1.1	Asthma	15
1.1.1	Disease definition	15
1.1.2	Prevalence, incidence and mortality	16
1.1.3	Determinants of asthma	17
1.2	Health-related quality of life	18
1.2.1	Patient-reported outcomes measures (PROMs)	18
1.2.2	The concept of health-related quality of life	20
1.2.3	Measuring health-related quality of life	21
1.3	Measurement properties	21
1.4	Aim of thesis	25
2	A structured literature review of asthma-specific quality of life measures	26
2.1	Background	26
2.2	Methods	27
2.3	Results	31
2.3.1	Juniper Asthma Quality of Life Questionnaire (AQLQ-J)	31
2.3.2	Sydney Asthma-Quality of Life Questionnaire (AQLQ-S)	34
2.3.3	Living With Asthma Questionnaire (LWAQ)	35
2.3.4	St George’s Respiratory Questionnaire (SGRQ)	37
2.3.5	Quality of Life for Respiratory Illness Questionnaire (QOL-RIQ)	39
2.3.6	Rhinasthma	41
2.3.7	Summary of information relating to review criteria	42
2.3.8	Quantitative quality assessment	67
2.3.9	Strengths and weaknesses of the questionnaires	69
2.4	Discussion	71
2.4.1	Conceptual model and questionnaire content	71
2.4.2	Variation in methodological development	73
2.4.3	Choosing a questionnaire	74

2.5	Strengths and limitations of the literature review.....	77
2.6	Conclusion.....	77
3	Psychometric validation study of two common asthma-specific quality of life questionnaires: Juniper Mini Asthma Quality of Life Questionnaire (mini AQLQ-J) and Sydney Asthma Quality of Life Questionnaire (AQLQ-S).....	79
3.1	Background.....	79
3.2	Methods.....	80
3.3	Results.....	86
3.3.1	Patient characteristics.....	86
3.3.2	Internal consistency.....	87
3.3.3	Correlation of mini AQLQ-J and AQLQ-S with symptoms, lung function, asthma control, asthma bother and generic quality of life.....	89
3.3.4	Relationship of mini AQLQ-J and AQLQ-S to patient characteristics (age, gender, asthma severity).....	94
3.4	Discussion.....	98
3.5	Conclusion.....	100
4	Validity of three asthma-specific quality of life questionnaires: the patient's perspective.....	101
4.1	Background.....	101
4.2	Methods.....	102
4.2.1	Patient recruitment.....	102
4.2.2	Questionnaires.....	104
4.2.3	Data collection.....	108
4.2.4	Data analysis.....	111
4.2.5	Ethics.....	112
4.3	Results from the German interviews.....	114
4.4	Results from the UK interviews.....	125
4.5	Discussion.....	174
4.5.1	Summary of findings.....	174
4.5.2	Differences and similarities between the two parts of the study.....	175
4.5.3	Ideas for improving the questionnaires.....	178

4.5.4	Lost items	180
4.5.5	Strengths and weaknesses of this research	181
4.5.6	Similarity to other published work	184
4.5.7	Implications	185
5	Discussion of thesis	187
	References.....	198

List of tables

Table 1: Definitions of domains, measurement properties, and aspects of measurement properties	22
Table 2: Citation counts for six common asthma QoL measures obtained from Scopus (February 2008)	28
Table 3: Key characteristics of six asthma specific Quality of Life Questionnaires.....	43
Table 4: Validity of the six asthma-specific QoL measures.....	50
Table 5: Results from quantitative quality assessment	68
Table 6: Strengths and potential weaknesses of the six asthma-specific QoL measures	69
Table 7: Number of items and content of the mini AQLQ-J and the AQLQ-S	82
Table 8: Distribution of scores and internal consistency of AQLQ-J and AQLQ-S	88
Table 9: Relationship of domain and total scores of AQLQ-J and AQLQ-S (correlation matrix)	91
Table 10: Relationship of spirometry parameters with domain and total scores of AQLQ-J and AQLQ-S	93
Table 11: Median score (interquartile range) of AQLQ-J and AQLQ-S according to patient characteristics.....	95
Table 12: Ordering of German questionnaires given to the interviewees...	109
Table 13: Topics covered in the interview topic guide.....	110
Table 14: Themes, codes and illustrative quotes (German sample)	118

Table 15: German patient ratings of quality of life questionnaires (from 1=best to 3=worst)	124
Table 16: Demographic characteristics of participants.....	125
Table 17: Codes and illustrative quotes relating to theme “Response format/response options” (UK sample)	129
Table 18: Codes and illustrative quotes relating to theme “Missing content” (UK sample)	136
Table 19: Codes and illustrative quotes relating to theme “Redundant/similar content” (UK sample)	142
Table 20: Codes and illustrative quotes relating to the theme “Irrelevant content” (UK sample)	147
Table 21: Codes and illustrative quotes relating to the theme “Confusing content” (UK sample)	153
Table 22: Codes and illustrative codes relating to the theme “Irritating content” (UK sample)	157
Table 23: Codes and illustrative quotes relating to the theme “Layout” (UK sample)	160
Table 24: Codes and illustrative quotes relating to the theme “general perception” (UK sample)	165
Table 25: Illustrative quotes relating to theme “Comparative aspects” (UK sample)	172

List of figures

Figure 1: Example items from the AQLQ-S, English version	104
Figure 2: Example items from AQLQ-S, German version	105
Figure 3: Example items from the LWAQ.....	106
Figure 4: Example items from the FLA.....	107
Figure 5: Example items from the AQLQ-J, English version	107
Figure 6: Example items from the AQLQ-J-s, German version.....	108

List of abbreviations

ISAAC: **I**nternational **S**tudy of **A**sthma and **A**llergies in **C**hildhood

MAS: **M**ulticentre **A**llergy **S**tudy

WHO: **W**orld **H**ealth **O**rganization

WHOQOL: **W**orld **H**ealth **O**rganization **Q**uality of **L**ife Assessment

FDA: **F**ood and **D**rug **A**dministration

PRO: **P**atient-reported **O**utcome

PROM: **P**atient-reported **O**utcome **M**easure

ICF: **I**nternational **C**lassification of **F**unctioning, **D**isability and **H**ealth

QoL: **Q**uality of **L**ife

HrQoL: **H**ealth-related **Q**uality of **L**ife

SF-36: **S**hort-form **36** Health Survey

NHP: **N**ottingham **H**ealth **P**rofile

EQ-5D: **E**uro**Q**o**L**-**5** **D**imensions

COSMIN: **C**onsensus-based **S**tandards for the Selection of Health **M**easurement **I**nstruments

MOT: **M**edical **O**utcomes **T**rust

AQLQ-J: **J**uniper **A**sthma **Q**uality of **L**ife **Q**uestionnaire

AQLQ-S: **S**ydney **A**sthma **Q**uality of **L**ife **Q**uestionnaire

LWAQ: **L**iving **W**ith **A**sthma **Q**uestionnaire

SGRQ: **S**t **G**eorge's **R**espiratory **Q**uestionnaire

QOL-RIQ: **Q**uality of **L**ife in **R**espiratory **I**llness **Q**uestionnaire

AQ20: **A**irways **Q**uestionnaire – **20**

SIP: **S**ickness **I**mpact **P**rofile

MID: **M**inimal **I**mportant **D**ifference

ICC: **I**ntraclass **C**orrelation **C**oefficient

FVC: **F**orced **V**ital **C**apacity

FEV1: **F**orced **E**xpiratory **V**olume in **1** **S**econd

ECSC: **E**uropean **C**oal and **S**teel **C**ommittee

GP: **G**eneral **P**ractitioner

6MWD: **6**-**M**inute **W**alk **D**istance

MRC: **M**edical **R**esearch **C**ouncil

CNSLD: **C**hronic **N**on-**S**pecific **L**ung **D**isease

COPD: **C**hronic **O**bstructive **P**ulmonary **D**isease

HIV: **H**uman **I**mmunodeficiency **V**irus

AERA: **A**merican **E**ducational **R**esearch **A**ssociation

APA: **A**merican **P**sychological **A**ssociation

RCT: **R**andomised **C**ontrolled **T**rial

WED: **W**ritten **E**motional **D**isclosure

ACT: **A**sthma **C**ontrol **T**est

ABP: **A**sthma **B**other **P**rofile

A&E: **A**ccident & **E**mergency

SD: **S**tandard **D**eviation

DAAB: **D**eutscher **A**llergie- und **A**sthmabund

CAQDAS: **C**omputer **A**ssisted **Q**ualitative **D**ata **A**nalysis **S**oftware

NHS: **N**ational **H**ealth **S**ervice

BSMS: **B**righton and **S**ussex **M**edical **S**chool

R&D: **R**esearch and **D**evelopment

REC: **R**esearch **E**thics **C**ommittee

IRAS: **I**ntegrated **R**esearch **A**pplication **S**ystem

PIC: **P**articipant **I**dentification **C**entre

N/A: **N**ot **A**pplicable

ACQ: **A**sthma **C**ontrol **Q**uestionnaire

ACT: **A**sthma **C**ontrol **T**est

ATAQ: **A**sthma **T**herapy **A**ssessment **Q**uestionnaire

OHS: **O**xford **H**ip **S**core

THR: **T**otal **H**ip **R**eplacement

POMG: **P**atient-reported **O**utcome **M**easurement **G**roup

NIH: **N**ational **I**nstitutes of **H**ealth

PGI: **P**atient **G**enerated **I**ndex

SEIQoL: **S**chedule for the **E**valuation of **I**ndividual **Q**uality of **L**ife

PROMIS: **P**atient **R**eported **O**utcomes **M**easurement **I**nformation **S**ystem

DLQI: **D**ermatology **L**ife **Q**uality **I**ndex

IRT: **I**tem **R**esponse **T**heory

DIF: **D**ifferential **I**tem **F**unctioning

List of appendices

German questionnaires used for qualitative study

1. Fragebogen zur Lebensqualität von Asthmapatienten – Version mit standardisierten Taetigkeiten (AQLQ(S))
2. Fragebogen zur Lebensqualität von Asthmapatienten (Marks AQLA)
3. Fragebogen zur Lebensqualität bei Asthma (FLA)

English questionnaires used for qualitative study

4. Juniper Asthma Quality of Life Questionnaire, English version
5. Sydney Asthma Quality of Life Questionnaire, English version
6. Living With Asthma Questionnaire, English version

Statement of contribution

Parts of the research for this thesis were done in collaborative work. Qualitative interviews in Germany were conducted by a master's student in Public Health which I co-supervised with Dr Adrian Loerbroks of the Mannheim Institute of Public Health. I developed the idea for the study, was responsible for the study design, coded the data and discussed the emerging framework with the research team. The data for the Written Emotional Disclosure (WED) trial were collected by Alice Theadom and Dr Christina Jones of the Department of Public Health and Primary Care, Brighton and Sussex Medical School. Prof Helen Smith acted as Principal Investigator for this study. I developed the idea for the psychometric analysis, analysed the data and discussed the interpretation within the research team. I was also a member of the Scientific Advisory Board throughout the period of this trial.

Acknowledgements

I would like to express my thanks to the people who have enabled me to write this PhD thesis through their knowledge, guidance and support.

Firstly I would like to express my gratitude to my supervisors Professor Helen Smith (Brighton and Sussex Medical School) and Professor Paul Stenner (Open University London) for their continued support and encouragement without which this thesis would not have been possible. I would further like to thank colleagues and staff in the Division of Public Health and Primary Care at the Brighton and Sussex Medical School and in particular would like to acknowledge Dr Christina Jones for her time and support.

I am indebted to the research team at the Mannheim Institute of Public Health for managing the first phase of the study in Germany: Dr Adrian Loerbroks, Melanie Weiss and Dr Joachim Saur. I am grateful for the support by Professor Anthony Frew of the Royal Sussex County Hospital, Brighton, who was very helpful in the second phase of the qualitative study in the United Kingdom. I am furthermore grateful to Professor Julika Loss, Medical Sociology, at the University of Regensburg who was supportive of the research periods I spent in the UK for the empirical part of this work.

I would like to express my sincere thanks to the patients who participated in this study and hope that the findings will help to improve quality of life assessment for those who suffer from asthma.

I am grateful to the European Academy of Allergy and Clinical Immunology (EAACI) for providing a platform for the dissemination of this research.

Finally I wish to thank my parents Karl and Christine Apfelbacher and friends who encouraged me throughout the PhD process.

Declaration

I declare that the research contained in this thesis, unless otherwise formally indicated within the text, is the original work of the author. The thesis has not been previously submitted to these or any other university for a degree, and does not incorporate any material already submitted for a degree.

Signed

Dated

1 Introduction

1.1 Asthma

1.1.1 Disease definition

Asthma is a chronic inflammatory disease with variable airway obstruction, characterized by episodes of coughing, wheezing, breathlessness and chest tightness. The elaborate working definition of the National Heart, Lung and Blood Institute (United States) states:

“Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role: in particular, mast cells, eosinophils, neutrophils (especially in sudden onset, fatal exacerbations, occupational asthma, and patients who smoke), T lymphocytes, macrophages and epithelial cells. In susceptible individuals, this inflammation causes recurrent episodes of coughing (particularly at night or early in the morning), wheezing, breathlessness, and chest tightness. These episodes are usually associated with widespread but variable airflow obstruction that is often reversible either spontaneously or with treatment.” (1).

The British guideline on the management of asthma states that no standardised definition exists of the type, severity or frequency of symptoms, nor the findings on investigation (2). According to the guideline, the presence of both symptoms (more than one of the following symptoms: wheeze, breathlessness, chest tightness and cough) and variable airflow obstruction is key to all definitions. More recent definitions also include airway hyper-responsiveness and airway inflammation .

‘Reversible airflow obstruction’ has been established as the cardinal feature of asthma as early as 1959 (3). It has then been elaborated by the American Thoracic Society and the feature of ‘hyperreactivity of the airways’ was introduced. Airway hyperresponsiveness denotes the exaggerated narrowing of the airways after the inhalation of various stimuli (4). It is assessed by airway challenges, but comparability is hampered because there are various

different challenge tests, measuring for instance response to histamine (5), cold air (6), methacholine (7) or exercise (8).

'Chronic inflammatory disorder' has been added as a defining component in 1992 by the International Consensus Report on the Diagnosis and Treatment of Asthma (3). No single instrument can be used to assess asthma with certainty (4). For epidemiological studies, questionnaires are often used asking whether people have experienced asthma symptoms (9) or whether they were diagnosed with asthma by a physician (10).

1.1.2 Prevalence, incidence and mortality

The burden of asthma varies hugely around the globe. Data from phase three of the International Study of Asthma and Allergies in Childhood (ISAAC) showed the prevalence of asthma (measured as symptom prevalence of wheeze in the past 12 months) to vary from 3.5% (Indonesia) to 34.8% (Costa Rica) in 6- to 7-year-olds, and from 3% (Albania) to 32.3% (Isle of Man) in 13- to 14-year-olds (11).

Evidence concerning asthma prevalence in adults stems from the World Health Survey (12). Mean prevalence of asthma was found to be highest in the richest countries (9.4%), followed by the poorest countries (8.2%) and the middle-income countries (5.2%).

It is estimated that around 300 million people worldwide suffer from asthma and that asthma accounts for about one in every 250 deaths globally (13). By 2025 there may be 100 million people with asthma more. The number of disability-adjusted life years (DALY) lost to asthma is comparable to the DALYs lost for diabetes, cirrhosis of the liver, or schizophrenia.

A recent systematic review investigated whether the prevalence of asthma is declining (or has plateaued) and concluded that there are now signs that the prevalence of asthma is declining overall. (14). However, asthma prevalence is still rising in many parts of the world at the same time.

1.1.3 Determinants of asthma

Various factors have been implied as determinants of asthma, amongst which is exposure to tobacco smoke (15, 16). The association with air pollution is less clear, and there seems to be little association of ambient particulate matter with aerodynamic diameter less than 10 μm (which is the component of air pollution small enough to penetrate the intrathoracic respiratory tract), abbreviated to PM_{10} , with the prevalence of childhood asthma (17). However, long-term exposure to air pollution, measured as annual nitrogen dioxide (NO_2) level, has been linked to asthma hospitalisations in older adults (18).

The role of allergic sensitisation in the aetiology of asthma is elusive. No association between early exposure to house-dust mite and cat allergens and the development of asthma was found in the German Multicentre Allergy Study (MAS) (19). However, the exposure to allergens indoors may contribute to the persistence of an impaired lung function in children with allergic asthma (20). Evidence has accumulated linking obesity and asthma. A meta-analysis of prospective epidemiological studies found that overweight and obesity are associated with incident asthma in both men and women in a dose-dependent manner (21). A German study also looked at effect modification by gender, and found that the association between obesity and asthma may be present in women, but not in men (22).

Attempts have been made to investigate the role of diet for asthma (23, 24), but dietary intake is difficult to measure and prone to information bias. A recent study in rural regions of Germany, Austria and Switzerland looked at farm milk consumption and found reported raw milk consumption (in particular the whey protein fraction of the milk) to be inversely associated with asthma (25). Evidence suggests that breastfeeding is not associated with childhood wheezing (26, 27).

In the context of the 'hygiene hypothesis', a lack of exposure to infections and microbial products early in life have been discussed as aetiological factors involved in the development of asthma (4). Exposure to environments

rich in microbes such as stables and barns of farms has been inversely associated with asthma (28). Furthermore, farming animals may play an important role in this context (29).

1.2 Health-related quality of life

1.2.1 Patient-reported outcomes measures (PROMs)

The measurement of patient assessed health outcomes as opposed to physician-assessed outcomes has seen a massive expansion. A systematic bibliographic study of patient assessed health outcome measures identified 3921 reports on the development and testing of patient assessed measures of health outcome by the year 2000 (30). These reports cited 1275 identifiable measures. From 1990 to 1999 the number of new reports relating to development and evaluation of patient assessed health outcome measures increased from 144 to 650 per year. The bibliographic study concludes that there is little standardisation and calls for concurrent evaluation of measures as well as structured reviews to guide the selection of patient assessed measures of health outcomes.

When examining the literature, it becomes evident that the terminology used to describe different patient assessed health outcomes is confusing. This was first noted by Guyatt et al. in 1992:

„The health status measurement literature is a jungle. Students of the area (whether fledgling graduate students or experienced researchers) must hack through an underbrush of confused terminology and contradictory conceptualizations. Many get lost; some, presumably consumed by large carnivores, are never heard from again.“ (31)

In order to simplify matters, the U.S. Food and Drug Administration (FDA) has devised a guidance document for use in medical product development to support labelling claims, published as draft guidance in 2006 (32) and as final guidance three years later (33), and proposed the umbrella term “patient-reported outcome”, abbreviated to “PRO”. According to this, a PRO

is defined as “any report of the status of a patient’s health condition that comes directly from the patient, without interpretation of the patient’s responses by a physician or anyone else” (33). This definition actually focuses on the source of information but does not tell us how to conceptualise outcome measures. In the literature, often the abbreviation “PROM” (rather than “PRO”) is found which stands for “patient-reported outcome measure”.

Several attempts have been made to classify health outcome measures, including the FDA guidance document (32, 34-42). However, like all previous classification attempts, the FDA classification has not been linked to any valid model of health outcomes. Valderas & Alonso have attempted to provide a classification system of PRO instruments which is based on a valid conceptual model of health outcomes (43). The model represents an integration of the model proposed by Wilson and Cleary (44) with the theory underpinning of the International Classification of Functioning, Disability and Health (ICF) (45).

The Wilson & Cleary model is a bio-psycho-social model for health outcomes, whilst the ICF is a classification system of health states proposed by the WHO which considers disability along the whole functioning continuum. As both differentiate health related variables and contextual factors (further splitting these into environmental and individual characteristics) they could be integrated into one model. Valderas & Alonso distinguish three axes to classify patient reported outcome measures: construct, population and measurement. The axes are subdivided further as follows:

- *Construct*: symptoms, functional status, health perceptions, health related quality of life, other health related constructs (satisfaction with care, disadvantage, resilience, environmental)
- *Population*: age (all ages, children, adolescents, adults, seniors), gender (all genders, female, male), disease, culture (country and language dyads)

- *Measurement:* metric (psychometric, econometric, clinimetric, other metrics), dimensionality (index, profile, index and profile), adaptability (completely standardised, partially individualised, completely individualised)

The classification system serves as an aid for researchers, clinicians, administrators and policy makers in the selection of a PRO instrument for a particular purpose. Compared to previous classification systems it is based on current conceptual models of health outcomes and is a simplified system at the same time.

1.2.2 The concept of health-related quality of life

Health-related quality of life (HrQoL) is among the most frequent PROMs but is also referred to as health status, perceived health or simply 'quality of life' (43). To date, no single concept has been universally adopted (34, 46, 47). The World Health Organisation's international collaborative Quality of Life Group (WHOQOL) has developed a definition of the concept according to which quality of life is an "individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards and concerns" (48). The group developed a comprehensive quality of life assessment with six domains: physical, psychological, level of independence, social relationships, environment and spirituality/religion/personal beliefs (49).

A systematic review of health-related quality of life models concluded that quality of life was not defined by at least 25% of authors (50). One attempt to define 'quality of life' is to conceptualise it as subjective well-being, comprising cognitive judgement, positive affect and negative affect (45, 51).

1.2.3 Measuring health-related quality of life

There are – in principle – two ways of measuring HrQoL. One approach attempts to measure generic HrQoL (examples include the SF-36 (52), the Nottingham Health Profile (53) or the EuroQoL 5D (54)), the other approach attempts to measure disease-specific HrQoL (examples include disease-specific instruments for a large variety of diseases). Disease-specific instruments have been developed because different aspects of HrQoL are more or less salient for specific conditions. Their advantage is that they are more sensitive to change for particular conditions compared to generic instruments. Generic instruments, in contrast, are less sensitive for particular conditions but allow comparing findings across conditions.

The quality of a quality of life measure, i.e. its adequacy and robustness, crucially depends on its measurement properties, i.e. how well (validity) and robust (reliability) a measure measures what it purports to measure.

1.3 Measurement properties

A lack of consensus on taxonomy, terminology and definitions in relation to measurement properties has led to an international Delphi study involving 43 experts who finally reached consensus (COnsensus-based Standards for the selection of health Measurement Instruments, COSMIN) (55). Four domains are distinguished (reliability, validity, responsiveness and interpretability) with related measurement properties and aspects of measurement properties. These are listed in table 1 (adapted from (55)).

Table 1: Definitions of domains, measurement properties, and aspects of measurement properties

Domain	Measurement property	Aspect of a measurement property	Definition
Reliability			The degree to which the measurement is free from measurement error
Reliability (extended definition)			The extent to which scores for patients who have not changed are the same for repeated measurement under several conditions: for example, using different sets of items from the same HR-PROs (internal consistency), over time (test-retest) by different persons on the same occasion (inter-rater) or by the same persons (i.e., raters or responders) on different occasions (intrarater)
	Internal consistency		The degree of interrelatedness among the items
	Reliability		The proportion of total variance in the measurements which is because of “true” ^a differences among patients
	Measurement error		The systematic and random error of a patient’s score that is not attributed to true changes in the construct to be measured
Validity			The degree to which an HR-PRO instrument measures the

			construct(s) it purports to measure
	Content validity		The degree to which the content of an HR-PRO instrument is an adequate reflection of the construct to be measured.
		Face validity	The degree to which (the items of) an HR-PRO instrument indeed looks as though they are an adequate reflection of the construct to be measured.
	Construct validity		The degree to which the scores of an HR-PRO instrument are consistent with hypotheses (for instance with regard to internal relationships, relationships to scores of other instruments, or differences between relevant groups) based on the assumption that the HR-PRO instrument validly measures the construct to be measured
		Structural validity	The degree to which the scores of an HR-PRO instrument are an adequate reflection of the dimensionality of the construct to be measured
		Hypothesis testing	Idem construct validity
		Cross-cultural validity	The degree to which the performance of the items on a translated or culturally adapted HR-PRO instrument are an adequate reflection of the performance of the items of the original version of the HR-PRO

			instrument
	Criterion validity		The degree to which the scores of an HR-PRO instrument are an adequate reflection of a “gold standard”
Responsiveness			The ability of an HR-PRO instrument to detect change over time in the construct to be measured
	Responsiveness		Idem responsiveness
Interpretability ^b			The degree to which one can assign qualitative meaning – that is, clinical or commonly understood connotations – to an instrument’s quantitative scores or changes in scores

Abbreviations: HR-PROs, health related patient-reported outcomes; CCT, classical test theory

^a The word “true” must be seen in the context of the CCT, which states that any observation is composed of two components – a true score and error associated with the observation. “True” is the average score that would be obtained if the scale were given an infinite number of times. It refers only to the consistency of the score and not to its accuracy (56).

^b Interpretability is not considered a measurement property but an important characteristic of a measurement instrument.

1.4 Aim of thesis

With the proliferation of the development of HrQoL measures often many measures are now in use for single disease entities such as asthma. When several measures are available the question arises how the relative validity of the measures can be assessed and if there is a 'most valid' measure. It is the aim of this thesis to explore the validity of asthma-specific quality of life questionnaires in capturing the quality of life of people living with asthma, using multiple approaches.

The thesis includes three studies with distinct objectives:

- i. to review the literature on six commonly used asthma-specific quality of life measures in a structured way, the Juniper Asthma Quality of Life Questionnaire (AQLQ-J) (57, 58), the Sydney Asthma Quality of Life Questionnaire (AQLQ-S) (59, 60), the Living With Asthma Questionnaire (LWAQ) (61), the St George's Respiratory Questionnaire (SGRQ) (62, 63), the Quality of Life for Respiratory Illness Questionnaire (QOL-RIQ) (64) and the RHINASTHMA questionnaire (65)
- ii. to investigate the construct validity of two common asthma-specific quality of life measures (the AQLQ-S (59, 60) and the mini version of the AQLQ-J (66)) using data from an asthma intervention trial
- iii. to explore format and content validity of three common asthma-specific quality of life measures from the patient's perspective in a German and a UK setting, the AQLQ-J (57, 58) or standardized AQLQ-J (AQLQ-J-s) (67), the AQLQ-S and the LWAQ or its German adaptation, the *Fragebogen zur Lebensqualität bei Asthma* (FLA)(68)

2 A structured literature review of asthma-specific quality of life measures¹

2.1 Background

In the 1990s, several asthma-specific QoL instruments were published as well as two for patients with fixed or reversible airway obstruction (57-63, 69). These instruments have later undergone refinement (70) including adaptation for different age groups (71, 72), standardisation (67), reduction in length (66, 73) and one instrument has been developed specifically for patients with both asthma and rhinitis (65).

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 scepticism and confusion has been expressed about the measurement of QoL (74). Eight years ago, a bibliographic study of the development and evaluation of QoL measures identified the need for a structured review to guide users (30). A standard review on subjective health outcome measures for diabetes addressed validity, reliability and responsiveness to change (75) 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 (76). Similarly, the US Food and Drug Administration has emphasised the importance of identifying concepts and domains that are important to patients and of developing a conceptual framework for patient-reported outcome instruments (32).

The aim of this structured review is to review published QoL measures designed for use in adults with asthma.

¹ Apfelbacher CJ, Hankins M, Stenner P, Frew AJ, Smith HE. Measuring asthma-specific quality of life: structured review. *Allergy*. 2011 Apr;66(4):439-57.

2.2 Methods

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 paediatric asthma. Derivatives of original questionnaires such as short versions or versions adapted for particular groups (e.g. for patients with acute exacerbations of asthma) were excluded. As in a recent quality-assessment of disease-specific QoL questionnaires for rhinitis and rhinosinusitis (77), studies reporting measurement properties as secondary outcomes (for example within a trial) were excluded.

The literature search was not guided by the application of a systematic search algorithm as it was initially undertaken as an exploratory exercise to familiarise myself with the field and to set the context for future work. It was rather inspired by discussions with experts at the annual meeting of the European Academy of Allergy and Clinical Immunology (EAACI) in Gothenburg 2007 and by presentations relating to the topic. I had also visited Elisabeth Juniper, the author of the most widely cited asthma-specific HrQoL measure, for informal discussion in 2006. Following these discussions, citation counts were obtained from Scopus (www.scopus.com), the world's largest abstract and citation database. This was done to confirm that the measures under consideration were actually frequently used.

Scopus citation counts as of February 2008 are shown in table 2. Total citation counts are shown as well as citation counts for the three years prior to 2008 to show more recent citation counts. The measures selected represent the most frequently cited asthma-specific QoL questionnaires and are therefore considered as the measures most frequently used.

Six QoL measures were thus identified: the Asthma Quality of Life Questionnaire (AQLQ-J) (57, 58), the Asthma Quality of Life Questionnaire (AQLQ-S) (59, 60), the Living With Asthma Questionnaire (LWAQ) (61), the St George's Respiratory Questionnaire (SGRQ) (62, 63), the Quality of Life for Respiratory Illness Questionnaire (QOL-RIQ) (64) and the RHINASTHMA questionnaire (65).

Table 2: Citation counts for six common asthma QoL measures obtained from Scopus (February 2008)

Measure	Citation count	Citation count after 2005
Development paper AQLQ-J (57)	432	81
Validation paper AQLQ-J (58)	405	69
Development paper AQLQ-S (59)	187	32
Validation paper AQLQ-S (60)	91	11
Development paper LWAQ (61)	113	8
Paper describing validation studies LWAQ (69)	58	6
Development/validation paper SGRQ(62)	311	86

Validation paper SGRQ (63)	731	190
Development paper QOL-RIQ (64)	56	9
Development/validation paper RHINASTHMA (65)	24	11

Our data extraction and critique were guided by the attributes and criteria suggested by the MOT for reviewing health status and QoL measures (76), but unlike the approach taken by the MOT, responsiveness was incorporated into validity (78). The seven aspects considered are:

- 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)
Reliability assessment includes internal consistency (the homogeneity of the scale's items at one point in time, often measured by Cronbach's alpha (79)) 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. Points were assigned according to the following criteria which were developed following discussion within the research team:

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), 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)

The scoring yielded a maximum total score of either 25.5 or 26.5 because a point for separate validation studies for different administration formats could only be given if different administration formats (interviewer-administered, self-administered) had in fact been developed.

2.3 Results

2.3.1 Juniper Asthma Quality of Life Questionnaire (AQLQ-J)

The Asthma Quality of Life Questionnaire (57, 58) (AQLQ-J) was developed in Canada.

No formal statement is made about the conceptual model, but several assumptions are alluded to: 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 (80) 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 (81). Patients can choose from a list of 26 activities the five most important to them. Later, the questionnaire was standardised with a fixed activity list (67) replacing the five individualised 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 (58). 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

(82), Sickness Impact Profile (SIP) (83)) 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 (84), using a modified version of the AQLQ-J with a three-day recall period. Correlations between the SIP and AQLQ-J 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 (85).

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 (86). The MID is derived by comparing QoL score changes to global ratings of change. For the AQLQ-J (87), the MID was found to be around 0.5 (range 0.42-0.58) for overall QoL and for individual domains.

The AQLQ-J was initially developed for interviewer administration and pre-tested 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, Lyon, France (<http://www.mapi-research.fr/>).

A French version of the AQLQ-J was used in a study comparing occupational with non-occupational asthma which found that patients with occupational asthma experienced greater impairment of QoL than matched controls (88). A detailed description of the translation/back translation process into Spanish is available (89). A separate validation study of the Spanish version was carried out later in 116 patients (90). This study found the AQLQ to show high internal consistency (Cronbach’s alphas: 0.78 to 0.96) and a high 2-week reproducibility (ICC: 0.82 to 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 dyspnoea moderate to strong and between AQLQ and FEV1 (Forced Expiratory Volume in 1 Second) weak to moderate. There was a significant difference in changes in AQLQ scores between patients who either improved or deteriorated in comparison to 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) (91), 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 (Forced Expiratory Volume in 1 Second/Forced Vital Capacity). QoL was better in men and worse in those with high school education or less.

When validated in Serbo-Croat (92) 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.

2.3.2 Sydney Asthma-Quality of Life Questionnaire (AQLQ-S)

The Asthma Quality of Life Questionnaire-Sydney (AQLQ-S) (59) 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 make-up, 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; overall sense of well-being. These aspects are considered the minimum standards for judging the content validity of health measures by Ware (93).

From these three sources, a 69 statement questionnaire, relating to the past four 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 multi-collinearity 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 varied with domain.

Construct validity was assessed in a community sample by correlating AQLQ-S scores with medical markers of disease severity. Weak, non-significant 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 four months in AQLQ-S scores in a group of 19 persons with improving asthma and 20 persons 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 anticipated.

Formal validation studies have been carried out for American English (94), Spanish (95) and German versions of the AQLQ-S (96).

2.3.3 Living With Asthma Questionnaire (LWAQ)

The Living with Asthma Questionnaire (LWAQ) was developed in the UK in 1993 for adults with asthma (61, 69).

The original paper emphasises 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 emphasise that QoL is multi-domain “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 behaviour 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. 77 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 loadings were made positive, assuming that their negativity had led to problems in comprehension. The revised questionnaire consisted of 43 negative and 29 positive items which 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 to 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), dysphoric states and attitudes (over one third of items)'. 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 males and was lower in participants recruited through the Asthma Society compared to those recruited through general practitioners (GPs). Further evidence of validity comes from positive correlations with the Sickness Impact Profile ($r=0.66$) and negative correlations with peak flow ($r=-0.44$) (69). In another study, QoL correlated with steroid prescribing ($r=0.35$)(97).

Responsiveness of the LWAQ has not been reported in separate validation studies, only in the context of clinical trials (98).

The LWAQ has been validated in Norwegian (99). An unvalidated Bulgarian version is available from the website of the research group “Psychology of Holistic Health” (<http://www.psychhealth.org.uk/questionnaires.html>).

2.3.4 St George’s Respiratory Questionnaire (SGRQ)

The St George’s Respiratory Questionnaire (SGRQ) was developed in 1991 for adults with chronic airflow obstruction/limitation aged >20 years (62, 63).

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 (100). The development of the SGRQ was inspired by an established measure of general health, the Sickness Impact Profile (SIP) (83), which was being used in patients with chronic airflow limitation (101) 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 organised in 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 three months’ (102)), activities (causing

or limited by breathlessness), and impacts (social functioning impairment and psychological disturbances resulting from airways disease). It is stated that anxiety and depression items were not included in the SGRQ because established measures existed for these constructs (63).

Each item in the SGRQ has an empirically derived weight (range 0-100) (100). 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) (102), so the scores for the domains as well as the total score range from zero to 100%. Demographic and disease characteristics had only minimal effects on the weights (100, 103).

Validity of the SGRQ was established by a comparison with other measures of disease activity and general health (63). 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-minute walking distance test (6MWD) and the MRC dyspnoea grade. The correlations with the SGRQ impacts section and the total score were more evenly distributed and included anxiety, walking distance, dyspnoea and wheeze. Significant correlations of the SGRQ with FEV1, FVC, 6MWD, dyspnoea, anxiety and depression (measured by the Hospital Anxiety and Depression Scale (104)) were similar compared to the correlations with the SIP. However, the regression slopes against the reference measures were greater when the SGRQ was used as outcome compared to the SIP (63). 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 one year ($n > 120$), significant correlations were found between change in SGRQ total score and changes in FVC, anxiety and dyspnoea (62). 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 one 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 (63). 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 (www.mapi-institute.com) or Health Research Associates (www.hrainc.net).

Spanish (105), Swedish (106), American English (107), Polish (108) and Chinese (109) versions of the SGRQ have been formally validated, but only the Polish and Chinese validation studies included patients with asthma.

2.3.5 Quality of Life for Respiratory Illness Questionnaire (QOL-RIQ)

The Quality of Life for Respiratory Illness Questionnaire (QOL-RIQ) was developed in 1997 for use in chronic non-specific lung disease (CNSLD), i.e. asthma and COPD (64, 110).

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 (111). Second, that the development should encompass the stages described by Guyatt et al. (112).

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; schooling/training.

Factor analysis was used to reduce the item pool to 55 items grouped in 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; social activities, relationships and sexuality.

Construct validity was assessed by analysing correlations between the total score and its seven sub-scales with illness severity indicators (degree of dyspnoea, 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 which 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 above (113). 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 SF-36 domains. This study also provided evidence for responsiveness in that domains and total QoL-RIQ score changed significantly over time.

An 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 (114). The QoL-RIQ questionnaire is available in English and Dutch.

2.3.6 Rhinasthma

The RHINASTHMA instrument was developed for adults with rhinitis and/or asthma (65) to reflect the united airways disease hypothesis (115, 116).

Assessing the subjective point of view of the patient is considered “to offer a more comprehensive description of the impact of both disease and its therapy on everyday life”(65), as compared to the physician-defined concept of health status. It is emphasised that the new instrument includes the “functional, physical and emotional problems experienced by adult patients with respiratory allergy”(65).

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 x mean importance). Based on this composite score, 12 items were deleted.

For validation, 104 patients with respiratory allergy (rhinoconjunctivitis alone: n=42, asthma and rhinoconjunctivitis: n= 62), completed the RHINASTHMA questionnaire and the SF-36. Scores of patients with rhinitis were compared to scores of patients with asthma and rhinitis in order to assess criterion validity. 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 assessed to investigate the ability of the 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 assessed in 27 patients suffering from respiratory allergy (persistent rhinitis plus intermittent asthma) who were evaluated at baseline and then after three weeks treatment with cetirizine. 18

items of the RHINASTHMA showed a significant difference after three weeks. One formal validation study of RHINASTHMA has been conducted in German (117).

2.3.7 Summary of information relating to review criteria

A full summary of the information relating to the review criteria is presented in tables 2 and 3. 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.

Table 3: Key characteristics of six asthma specific Quality of Life Questionnaires

Characteristic	AQLQ-J	AQLQ-S	LWAQ	SGRQ	QOL-RIQ	Rhinasthma
Country of Origin	Canada	Australia	UK	UK	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 non-specific 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: pre-structured focus groups (n=8); clinical experience of investigators; interviews with asthma nurse educators	101 items sources: 6 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	42 items sources: published literature on HrQoL questionnaires & symptom scores; expert discussions (allergists, pulmonologists); unstructured interviews with outpatients (n >

					interviews (11 patients)	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)
Item content areas (domains)	32 items in 4 domains: <ul style="list-style-type: none"> •Activity limitation •Symptoms •Emotional functioning •Exposure to environmental stimuli 	20 items in 4 domains: <ul style="list-style-type: none"> •Breathlessness •Concerns •Mood •Social 	68 items in 11 domains: <ul style="list-style-type: none"> •Social/leisure •Sport •Holidays •Sleep •Work & other activities •Colds •Mobility •Effects on others •Medication usage 	50 items in 3 domains: <ul style="list-style-type: none"> •Symptoms (frequency & severity) •Activities (causing or limited by breathlessness) •Impacts (social functioning impairment & psychological disturbances) 	55 items in 7 domains: <ul style="list-style-type: none"> •Breathing problems •Physical problems related to chest problems •Emotions related to chest problems •Problems with general activities •Situations that 	30 items, grouped into three factors which are not labelled

			<ul style="list-style-type: none"> •Sex •Dysphoric states & attitudes 	<p>resulting from airways disease)</p> <p>[recall period: past 12 months, past month, past three months; 'these days' for part of the items in different versions of the SGRQ]</p>	<p>might trigger or enhance breathing problems</p> <ul style="list-style-type: none"> •Daily & domestic activities •Social activities, relationships & sexuality 	
	[recall period: 2 weeks]	[recall period: 4 weeks]	[recall period: current time point of assessment]		[recall period: 12 months]	[recall period: 2 weeks]
Response format & scoring	7 point Likert scale Responses to each of the 32 items are added together & divided by	5 point Likert scale Item scores are added up for total & the respective domain items; lower scores	3 point Likert scale with 'not applicable' option Values of each negative item (1-3) are added to the values of each positive item	Mostly binary (true/ false), some items have three, four or five response options Each item in questionnaire has empirically derived weight; scores are	7 point Likert scale with 'not applicable' option Scoring not described in the public domain	5 point Likert scale Responses to each of the 32 times are added and divided by 32 (same applies for

	32 (same applies for domains); higher scores indicate better QoL	indicate better QoL	reversed in polarity (3-1), sum is divided by number of positive & negative items; higher scores indicate better QoL	calculated as % of summed weights of positive items relative to summed weights of all items (for each component & in total); score range for domains & total 0-100% (where 100% = worst possible health status)		domains); higher scores indicate worse QoL
Reliability	<p><i>Juniper 1993 Am Rev Respir Dis</i></p> <p>Test-retest reliability (intra-class correlation coefficient, ICC)</p> <p>Total 0.92 activities: 0.93, symptoms:</p>	<p><i>Marks 1992 J Clin Epidemiol</i></p> <p>Test-retest reliability (ICC)</p> <p>Breathlessness 0.61 (0.44, 0.74) Mood 0.78 (0.67,</p>	<p><i>Hyland 1991 J Psychosom Research</i></p> <p>Test-retest reliability (correlation coefficient r)</p> <p>0.95</p>	<p><i>Jones 1992 Am Rev Respir Dis</i></p> <p>Test-retest reliability in patients with asthma (n=40) or COPD (n=20)</p> <p>Coefficient of variation 19% for total score (same</p>		<p><i>Baiardini 2003 Allergy</i></p> <p>Test-retest reliability [Pearson correlation coefficient r] N=31 stable patients, one week apart</p> <p>r=0.70 - 0.92 for 25 items, r= 0.61</p>

	0.89 emotions: 0.91 environment: 0.94	0.86) Social 0.78 (0.67, 0.86) Concerns 0.80 (0.69, 0.87) Total 0.80 (0.70, 0.88)		for asthma and COPD); intraclass correlation r=0.91 for asthma, r= 0.92 for COPD; intraclass correlation according to domains: Symptoms: r=0.91 Activity: r=0.87 Impact: r=0.88 (combined data for asthma & COPD)		- 0.69 for remaining 5 items
	Internal consistency not reported	Internal consistency [Cronbach's alpha] <i>Outpatient sample (n=77)</i> Breathlessness: 0.89 Mood: 0.82 Social: 0.88 Concerns: 0.84 Total: 0.92 (Item-total	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	Internal consistency [Cronbach's alpha] $\alpha > 0.70$ for all 30 items

		<p>correlations ranged from 0.41-0.72)</p> <p><i>Community sample (n=87)</i> Total: 0.92 Subscales: 0.87 - 0.94 (Item-total correlations ranged from 0.44-0.78)</p>			<p>Emotions: 0.88</p> <p><i>Van Stel 2003 Qual Life Res</i> (108 patients with moderate to severe asthma or COPD)</p> <p>Intraclass correlation of change for total score: 0.90</p>	
Interpretability	Minimal important difference ~ 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 ~ 0.5	Not reported
Burden of administration	10-15 minutes	5 minutes	15-20 minutes	10 minutes	Not reported	Not reported*
Administration format	Self-administration,	Self-administration	Self-administration,	Supervised self-administration	Self-administration	Self-administration

	interviewer-administration		interviewer-administration			
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	www.goltech.co.uk	-	http://www.psychhealth.org.uk/	-	-	-

*completion time of 5-10 minutes reported in the German validation study (117)

Table 4: Validity of the six asthma-specific QoL measures

Table 3a - AQLQ-J	
<i>Juniper 1993 Am Rev Respir Dis</i>	
<i>(39 patients with symptomatic asthma)</i>	
Cross-sectional correlations	
<ul style="list-style-type: none"> <li data-bbox="181 595 2101 635">• <i>Asthma QoL and clinical asthma</i> 	
FEV1 % predicted (activities: $r=0.06$ (not significant (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))	
<ul style="list-style-type: none"> <li data-bbox="181 834 2101 874">• <i>Asthma QoL and generic QoL</i> 	
Sickness Impact Profile (SIP)	
-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: $r=0.07$ (ns), symptoms: $r=0.19$ (ns), emotions: $r=0.27$ ($p<0.05$), environment: $r=0.00$ (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 : $r=0.36$ (<0.05))

-emotional domain (activities : $r=0.34$ (<0.05), symptoms : $r=0.31$ (<0.05), emotions : $r=0.30$ (<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 to changes in 13 patients with stable asthma ($p<0.001$) for overall QoL, activities, symptoms, emotions; $p=0.007$ for environment)

Table 3b - 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)

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)

Table 3c - LWAQ

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 : $r=0.41$ ($p<0.01$)

Table 3d - 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, $p < 0.0001$)
- *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, $p < 0.0001$), Sa_{o2}, 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^s: $SS=1077$ ($p=0.02$); 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 one 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 one 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 dyspnoea grade: 3455 (p=0.0001)

Change in anxiety score: 1043 (p=0.002)

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

Table 3e - 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)
- *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 dyspnoea (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)

- *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)

**Table 3f -
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

(27 patients with respiratory allergy (persistent rhinitis and intermittent asthma) assessed at baseline and three weeks after treatment with cetirizine).

18 items showed significant difference after three 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 (118); magnitude of responsiveness index signifies the relative utility in distinguishing improved from stable subjects

#Asthma Symptom Checklist (119, 120)

§arterial oxygen saturation

\$6-minute walking distance

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 rigour 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 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.

2.3.8 Quantitative quality assessment

In the quantitative quality assessment the highest score was achieved by the AQLQ-S and the lowest score was achieved by the SGRQ, as illustrated in table 4.

Table 5: Results 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%

2.3.9 Strengths and weaknesses of the questionnaires

Strengths and potential weaknesses of the measures are listed in table 5.

Table 6: Strengths and potential weaknesses of the six asthma-specific QoL measures

Questionnaire	Strengths	Potential weaknesses
AQLQ-J	<p>Specifically designed for asthma</p> <p>Linguistically validated in many languages</p> <p>Validation studies in a number of languages</p> <p>Potentially fine discrimination (7 response options)</p> <p>Idiographic component of the original version</p> <p>Widely used</p>	<p>Contains a symptom list</p>
AQLQ-S	<p>Specifically designed for asthma</p> <p>Quick to complete (20 items)</p> <p>Response format (5 options) compromise between ease of completion and accuracy</p>	<p>Few linguistic validations</p>
LWAQ	<p>Specifically designed for asthma</p> <p>Has “not applicable” option</p> <p>Compensates for acquiescence bias</p>	<p>Lengthy questionnaire (68 items)</p> <p>Few linguistic validations</p>
SGRQ	<p>Combines questions on current problems with questions on problems in recall period (4 weeks, 3 months, 12 months)</p> <p>Linguistically validated in many</p>	<p>Rather long questionnaire (50 items)</p> <p>Contains a symptom list</p> <p>Designed for asthma</p>

	<p>languages</p> <p>Weights are applied to obtain domain and summary scores</p> <p>Widely used (but mainly in COPD)</p>	<p>and COPD</p> <p>Complex calculation of scores (weights need to be applied)</p>
QOL-RIQ	<p>Has “not applicable” option</p>	<p>Rather long questionnaire (55 items)</p> <p>Designed for chronic non-specific lung disease</p> <p>Role of symptom items unclear</p> <p>Few linguistic validations</p>
Rhinasthma	<p>Good for patients who suffer from both asthma and rhinitis</p>	<p>Limited evidence for validity (in use for only a few years)</p> <p>Potentially decreased sensitivity in patients who suffer from either rhinitis or asthma</p> <p>Few linguistic validations</p>

2.4 Discussion

2.4.1 Conceptual model and questionnaire content

The ideal stages in HRQoL questionnaire development are as follows, according to the FDA guidance document (32):

- I. Hypothesise Conceptual Framework
 - A. Outline hypothesised concepts and potential claims
 - B. Determine intended population
 - C. Determine intended application/characteristics (type of scores, mode and frequency of administration)
 - D. Perform literature review/expert review
 - E. Develop hypothesised conceptual framework
 - F. Place PROs within preliminary endpoint model
 - G. Document preliminary instrument development
- II. Adjust Conceptual Framework and Draft Instrument
 - A. Obtain patient input
 - B. Generate new items
 - C. Select recall period, response options and format
 - D. Select mode/method of administration/data collection
 - E. Conduct patient cognitive interviewing
 - F. Pilot test draft instrument
 - G. Document content validity
- III. Confirm Conceptual Framework and Assess Other Measurement Properties
 - A. Confirm conceptual framework with scoring rule
 - B. Assess score reliability, construct validity, and ability to detect change
 - C. Finalise instrument content, formats, scoring, procedures and training materials
 - D. Document measurement development

- IV. Collect, Analyse, and Interpret Data
 - A. Prepare protocol and statistical analysis plan (final endpoint model and responder definition)
 - B. Collect and analyse data
 - C. Evaluate treatment response using cumulative distribution and responder definition
 - D. Document interpretation of treatment benefit in relation to claim
- V. Modify Instrument
 - A. Change wording of items, populations, response options, recall period, or mode/method of administration/data collection
 - B. Translate and culturally adapt to other languages
 - C. Evaluate modifications as appropriate
 - D. Document all changes

The development of a PRO instrument is described as iterative, so (I) to (V) represent stages in a circular process. 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. The underlying conceptual models can only be inferred from the domains in which the items are grouped and are hence implicit rather than explicit.

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 (121). A systematic review looked at concept and definition of PROs relating to physical activity and found that the development of these PROs was not based on a conceptual framework of physical activity in any of the 103 studies included for review (122). A lack of conceptual framework has also been identified in relation to health-related consequences of living with HIV (123).

Besides the aforementioned review criteria and attributes and the FDA draft guidance, the importance of embedding constructs of interest in conceptual frameworks is also stressed in the *Standards for Educational and*

Psychological Testing of the American Psychological Association (APA) (124). The lack of a conceptual framework may lead to measurement error (information bias) which may hamper the detection of intervention effects.

The lack of clear definitions of QoL in asthma-specific questionnaires and the fact that it is operationalised in a number of ways was first noted in a review of empirical studies published between 1980 and 1994 (125). 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). Whilst symptom scores do have a place in the assessment of patients with asthma (126) their inclusion in a QoL measure is questionable. HrQoL is a multi-dimensional concept representing the “patient’s overall perception of the impact of the illness and its treatment” (32). 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 which captures the frequency of symptoms would exaggerate the impairment of QoL.

2.4.2 Variation in methodological development

Whilst 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 (127). 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.

2.4.3 Choosing a questionnaire

Formal review/scoring system

The formal review process generates a lot of data which is 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 towards good science (128) because strong validation studies cannot compensate for a lack of conceptual modelling at the start of a questionnaire development procedure. Elements from the validation studies are thus overrepresented in a scoring system.

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 (129), whilst 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) (130). 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 FEV1) was weaker with the LWAQ (Spearman correlation coefficient $r = -0.23$) compared to 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.

In another study using data from a trial comparing inhaled salmeterol with inhaled salbutamol (131), the AQLQ-J was again found to be more responsive compared to 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 weak for the LWAQ (Spearman rank correlation coefficient: -0.05 , n.s.), but not for the AQLQ ($r = 0.32$, $p < 0.001$). 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)) (132). 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 of the relative strengths of asthma specific questionnaires.

Horses for courses

Beyond empirical grounds, the choice of instrument most 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, LWAQ). Of these asthma-specific questionnaires, the LWAQ is the most comprehensive one: it 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 is not suitable for this purpose, because it has an idiographic component and hence would not yield comparable results. The standardised version of the AQLQ-J, however, is suitable for large cross-sectional studies.

In the quantitative quality assessment we conducted (table 4), the AQLQ-S obtained the highest score. However, for use in multinational studies, it might be most convenient to choose those questionnaires which have been linguistically validated in many languages (AQLQ-J, SGRQ). It is very important that questionnaires are culturally and linguistically adapted, recognising individuals are likely to interpret scale items of a QoL measure in the light of culturally available subjective constructs of QoL (81). As it is specific for asthma, the AQLQ-J would be preferable compared to the SGRQ in multi-national studies.

2.5 Strengths and limitations of the literature review

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.

A limitation of this review is that it is restricted to published literature and to studies which reported measurement properties as primary outcomes, however this approach is similar to that taken in other rigorous reviews (77). We also acknowledge that other groups might develop different criteria for the review of questionnaires. Finally, it was a pragmatic review: it did not begin with a systematic literature search but I used a standardised approach to the papers selected based on use and popularity. Asthma-specific measures of HrQoL will have been missed, for examples the review does not include the Asthma Bother Profile (ABP)(99), the Asthma Impact Survey(133) or the Asthma Short Form(134), all of which were included in a subsequent review conducted in the US(135).

In the future I would be wary of performing anything other than a full systematic review because it is important to gain a comprehensive and complete understanding of all the questionnaires available even if they are not widely used or not popular.

2.6 Conclusion

It cannot be assumed that all questionnaires that are used to measure QoL in asthma measure the same thing. We recommend choosing 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 multi-national 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 experiences. 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 lead to a de novo development of a new questionnaire.

3 Psychometric validation study of two common asthma-specific quality of life questionnaires: Juniper Mini Asthma Quality of Life Questionnaire (mini AQLQ-J) and Sydney Asthma Quality of Life Questionnaire (AQLQ-S)

3.1 Background

The validation of a test is a continuous process as evidence needs to accumulate to increase the confidence in the reliability and validity of a measure (124). Estimates of reliability and validity are always sample-dependent (i.e. the coefficients obtained are expected to vary from sample to sample) (136), hence it is important to publish the respective coefficients so a clear picture of the performance of the questionnaires in a particular population can be built up. We therefore studied the internal consistency and validity (construct validity and discriminative ability) of the AQLQ-S and the AQLQ-J (mini version) in a sample of people with mild to moderately severe asthma in the UK.

Furthermore, few studies have been conducted which look at quality of life measures used for asthma in a comparative manner (131, 137, 138). This is important to get a sense of the relative validity and conceptual structure of PROMs which claim to measure the same thing. As a secondary objective, we therefore compared the psychometric properties of the AQLQ-S and the mini AQLQ-J.

3.2 Methods

First, the study population was characterised by means of descriptive statistics. Second, measures of internal consistency were calculated for the mini AQLQ-J and the AQLQ-S.

Third, we investigated how the two measures related to:

- each other
- symptom score
- lung function
- asthma control
- asthma bother
- generic quality of life

Finally, the discriminative ability of the two asthma-specific measures with respect to age, gender, health care utilisation (GP visits) and perceived asthma severity was examined.

Data source

Data were drawn from the baseline assessment of a double blind randomised controlled trial (RCT) investigating the effects of a written emotional disclosure (WED) intervention in adult patients with asthma in the UK. One hundred forty-six adults (18–45 years) with a diagnosis of asthma requiring regular inhaled corticosteroids were recruited into this trial. Participants were allocated to receive either WED or non-emotional writing instructions and asked to write for 20 minutes over three consecutive days. Spirometry, health care utilisation, asthma-specific and generic quality of life, rhinoconjunctivitis and asthma symptoms, subjective asthma control and asthma bother were documented. The participants' lung function was

measured using a Vitalograph Micro spirometer. The remaining constructs were assessed using self-administered questionnaires (the questionnaires were sent to participants and completed prior to the visit by the researcher, i.e. prior to the administration of the intervention). The questionnaires were administered in the same order each time: Rhinoconjunctivitis and Asthma Symptom Score, Asthma Control Test, mini AQLQ-J, AQLQ-S, Profile of Mood States, EuroQoL Current Health status, Significant Other Scale and Asthma Bother Profile. It must be noted that we used the mini version of the AQLQ-J because this and not the original version was included in the randomised controlled trial (RCT) from which the data was drawn. The Profile of Mood States and the Significant Other Scale were not considered for this paper.

The trial was registered with www.controlled-trials.com, registration number ISRCTN82986307. Ethical approval was obtained from the Brighton and Mid Sussex Research Ethics Committee (reference number 04/Q1907/91).

Using the data from this RCT was opportunistic. Conducting a secondary analysis on the data already available enabled me to address this research issue within the timeframe of my PhD, whereas the conduct of a separate validation study would have been beyond the resource and duration of the PhD.

Quality of life measures

The AQLQ-J was developed in Canada and comprises 32 items in four domains with a two-week recall period (57, 58). Higher ratings denote less impairment (better quality of life). Later, a shorter and simpler questionnaire with 15 items in the same domains was developed (mini AQLQ-J) (66). There are five items in the domain 'Symptoms', four items in the domain 'Activity Limitations', three items in the domain 'Emotional Function' and three items in the domain 'Environmental Stimuli'. Higher scores indicate better quality of life. This questionnaire showed good measurement properties, but they were not quite as strong as for the original AQLQ-J (66).

The minimal important difference of quality of life score per item has been reported to be very close to 0.5 (range 0.42-0.58) for the original AQLQ-J (87).

The AQLQ-S was developed in Australia and comprises 20 items with a four-week recall period (59, 60). Lower ratings indicate less impairment (better quality of life). Items are grouped into four domains (breathlessness: five items, mood: five items, social: seven items, concerns: three items). The content of the questionnaires is illustrated in Table 6. For the AQLQ-S, a minimal important difference has not been reported.

Table 7: Number of items and content of the mini AQLQ-J and the AQLQ-S

Domain	Number of items	Content
AQLQ-J symptoms	5	Feeling short of breath as a result of asthma, feeling bothered by coughing, experiencing a feeling of chest tightness or chest heaviness, having difficulty getting a good night's sleep as a result of asthma, experiencing a wheeze in the chest
AQLQ-S breathlessness	5	Having been troubled by episodes of shortness of breath, having been troubled by wheezing attacks, having been troubled by tightness in the chest, having been restricted in walking down the street on level ground or doing light housework because of asthma, having been restricted in walking up hills or doing heavy housework because of asthma
AQLQ-J environment	3	Feeling bothered by or having to avoid dust in the environment, feeling bothered by or having to avoid cigarette smoke in the environment, feeling bothered or having to avoid going outside because of weather or

		air pollution
AQLQ-S concerns	3	Having been worried about asthma shortening the life, having felt dependent on asthma sprays, having been worried about present or future life because of asthma
AQLQ-J emotions	3	Feeling frustrated as a result of asthma, feeling afraid of not having asthma medication available, feeling concerned about having asthma
AQLQ-S Mood	3	Having felt tired or a general lack of energy, having been unable to sleep at night, having felt sad or depressed, having felt frustrated with oneself, having felt anxious, under tension or stressed
AQLQ-J activities	4	Having been limited in doing strenuous activities (such as hurrying, exercising, running up stairs, sports) as a result of asthma; having been limited in doing moderate activities (such as walking, housework, gardening, shopping, climbing stairs) as a result of asthma, having been limited in doing social activities (such as talking, playing with pets/children, visiting friends/relatives), having been limited in doing work-related activities* (tasks you have to do at work)
AQLQ-S social	7	Having felt that asthma is preventing one from achieving what one wants in life, asthma having interfered with one's social life, having been limited in going to certain places because they are bad for one's asthma, having been limited in going to certain places because of having been afraid if getting an asthma attack and not being able to get help,

		having felt generally restricted, having been restricted in the sports, hobbies, or other recreations one can engage in because of one's asthma, having felt asthma is controlling one's life
--	--	---

*these should be activities which one has to do most days if not employed or self-employed

The EuroQoL Current Health Status Scale (CHS) is a generic, preference-based measure of health status and consists of five items (mobility, self-care, usual activities, pain/discomfort, anxiety/depression)(139). Higher scores indicate better quality of life.

Lung function measurement

The following parameters were measured in spirometry: forced vital capacity (FVC) in litres [l], forced expiratory volume in one second (FEV1) in litres [l], peak expiratory flow (PEF) in litres per minute [l/min]. The European Coal and Steel Community (ECSC) prediction equations were used to calculate what participant's optimum lung function should be based on age, height and gender (140, 141). This reading was used with FEV1 scores to determine FEV1, % predicted scores.

Rhinoconjunctivitis and Asthma Symptom Score

The Rhinoconjunctivitis and Asthma Symptom Score has 21 items which are rated on a five point Likert scale (142, 143). Patients are asked how much they have been disturbed by symptoms during the last week. The rhinitis module of the score asks about symptoms of irritation, congestion and discharge in the eyes, the nose and the sinuses. The asthma module asks about daytime and night-time symptoms of cough, wheeze, sputum production and shortness of breath.

Asthma Control Test (ACT)

The Asthma Control Test (ACT) consists of five questions pertaining to the past 4 weeks (144, 145). The brief questionnaire assesses asthma symptoms (daytime and nocturnal), use of rescue medications, and the effect of asthma on daily functioning. The total score is obtained by summing the scores for each item and ranges from 5 (poor control of asthma) to 25 (complete control of asthma).

Asthma Bother Profile (ABP)

The Asthma Bother Profile (ABP) is a 15 item measure of asthma distress(146). Patients are asked how much their asthma bothers them in the different areas of their life and they are given six response options (no bother, minor irritation, slight bother, moderate bother, a lot of bother, makes my life a misery) and one 'not applicable' option. Higher scores indicate greater distress.

Statistical analysis

To describe the characteristics of the sample, counts and percent were calculated for categorical variables and means with standard deviations (SD) were calculated for continuous variables.

In order to analyse the distribution of domain and total scores for the two asthma-specific quality of life measures mean, median, SD, percentage of participants with missing items, observed range, the percentage of participants with the worst possible score ('floor') and percentage of participants with the best possible score ('ceiling') were calculated. Standardised Cronbach alpha coefficients were computed as a measure of internal consistency (79).

Correlational analyses were performed to analyse the relationship between scores where appropriate. Spearman rank-order correlations, nonparametric measures of association based on the ranks of the data values, were

calculated because the scores of the measures of interest (AQLQ-J and AQLQ-S) were not normally distributed.

In order to analyse the relationship between the domain and total scores of the AQLQ-J and the AQLQ-S, a correlation matrix was computed. Correlations were considered as absent if $\rho < 0.20$, poor if $\rho = 0.20-0.34$, moderate if $\rho = 0.35-0.50$ and strong if $\rho > 0.50$ (147). In order to compare scores between categories (gender, GP visits, perceived severity), non-parametric tests were used (Wilcoxon rank sum two sample test for comparison between two groups and Kruskal-Wallis test for comparison between more than two groups). Missing data in the questionnaires were dealt with by imputing mean values where more than half of the responses to a subscale were present.

All analyses were performed using SAS 9.2 for Windows.

3.3 Results

3.3.1 Patient characteristics

One hundred forty-six people with asthma (average disease duration: 21.4 years (SD : 11.5 years)), aged 18–45 years and with a mean age of 36.1 years (SD : 7.0 years), participated in the study. Most of the participants were female (76.7%), in employment (82.2%) and of white ethnicity (97.3%). Their asthma was perceived as mild by 48.0%, moderate by 45.9% and severe by 3.4%. About one quarter (25.3%) of all patients reported consulting their GP because of their asthma during the past four months (excluding asthma review appointments), 3.4% reported they had visited Accident & Emergency (A&E) because of their asthma during the past four months but none reported having been admitted to hospital in the same time period.

The distribution of the questionnaire scores is displayed in table 7. The mean AQLQ-J score was 5.4 (SD 1.0, minimum 1.7, maximum 7.0), the mean

AQLQ-S was 0.8 (*SD* 0.6, minimum 0.1, maximum 3.4). About one quarter of the responses in the 'activity limitation' domain of the AQLQ-J and the 'social' domain of the AQLQ-S were the best possible scores (ceiling effect).

Mean Rhinoconjunctivitis and Asthma Symptom Score was 45.2 (*SD*: 13.9, median: 44.5, range: 20.0-89.0, *N*= 136). For the asthma module, mean symptom score was 20.4 (*SD*: 7.6, median: 19.0, range: 9.0 - 42.0, *N*= 137) and for the rhinitis module, mean symptom score was 24.8 (*SD*: 8.1, median: 25.0, range: 11.0-48.0, *N*= 136).

The following spirometry results were observed (*N* = 145): mean FVC was 3.72 l (*SD* 1.03, range: 1.37-7.35), mean FEV1 was 2.82 l (*SD* 0.77, range: 0.74-4.95), mean FEV1, % predicted was 87.5% (*SD*: 20.5, range: 24.8 - 167.3) and mean PEF was 427.4 l/min (*SD*: 132.2, range: 117.0-847.0).

3.3.2 Internal consistency

Cronbach's alpha values for the total and the domain scores of both QoL measures are also displayed in table 7.

For the subscales of the AQLQ-J, all Cronbach's alpha values were ≥ 0.61 and for the subscales of the AQLQ-S, all Cronbach's alpha values were ≥ 0.83 . Cronbach's alpha was 0.92 for the total AQLQ-J score and 0.93 for the total AQLQ-S score.

Table 8: Distribution of scores and internal consistency of AQLQ-J and AQLQ-S

	AQLQ-J					AQLQ-S				
	Symptoms	Environ- mental stimuli	Emotional Function	Activity Limitation	Total	Breath- lessness	Mood	Social	Con- cerns	Total
Items [n]	5	3	3	4	15	5	5	7	3	20
Mean	5.06	5.38	5.18	5.97	5.39	0.83	0.99	0.52	0.76	0.80
Median	5.20	5.67	5.33	6.25	5.60	0.60	0.80	0.29	0.57	0.70
SD	1.15	1.24	1.48	1.12	1.04	0.60	0.76	0.68	0.66	0.58
Participants with missing items [%]	4.79	4.79	5.48	5.48	6.16	5.48	5.48	4.79	5.48	5.48
Theoretical range	1-7	1-7	1-7	1-7	1-7	0-4	0-4	0-4	0-4	0-4
Observed range	1.80-7.00	1.33-7.00	1.00-7.00	1.50-7.00	1.67-7.00	0-3.0	0-3.80	0-4.0	0-3.57	0.05-3.35
'Floor' [%]*	0	0	1.45	0	0	0	0	0	0	0
'Ceiling' [%]**	1.44	10.79	10.87	25.36	0.73	5.80	10.90	26.62	12.32	0
Cronbach's alpha	0.85 (N=139)	0.61 (N=139)	0.82 (N=138)	0.89 (N=138)	0.92 (N=137)	0.83 (N=138)	0.85 (N=138)	0.91 (N=139)	0.77 (N=139)	0.93 (N=138)

*Percentage of participants with worst possible score

** Percentage of patients with best possible score

3.3.3 Correlation of mini AQLQ-J and AQLQ-S with symptoms, lung function, asthma control, asthma bother and generic quality of life

Correlation of AQLQ-J and AQLQ-S

A correlation matrix of the two measures is shown in table 8. The total scores of the AQLQ-J and AQLQ-S correlated strongly with each other ($\rho = -0.80$, $p < 0.0001$). The domain scores of the AQLQ-J and AQLQ-S showed weaker, but still strong ($0.5 \leq \rho \leq 0.8$) correlations with each other. The only exception was the 'mood' domain of the AQLQ-S which correlated moderately ($\rho < 0.5$) with the 'environmental stimuli', the 'emotional function' and the 'activity limitation' domain of the AQLQ-J.

Correlation of AQLQ-J and AQLQ-S with Rhinoconjunctivitis and Asthma Symptom Score

Both QoL measures were significantly correlated with the Rhinoconjunctivitis and Asthma Symptom Score, but the correlation of the AQLQ-J with the symptom score was stronger ($\rho = -0.62$, $p < 0.0001$, $N = 134$) compared with the correlation of the AQLQ-S ($\rho = 0.46$, $p < 0.0001$, $N = 135$). For both QoL measures, correlations with the symptom score asthma module (AQLQ-J: $\rho = -0.69$, $p < 0.0001$, $N = 135$; AQLQ-S: $\rho = 0.50$, $p < 0.0001$, $N = 136$) were stronger compared with the total symptom score and the symptom score rhinitis module (AQLQ-J: $\rho = -0.41$, $p < 0.0001$, $N = 134$; AQLQ-S: $\rho = 0.31$, $p = 0.0002$, $N = 135$).

Correlation of AQLQ-J and AQLQ-S with lung function

As shown in table 9, the AQLQ-J total score and all domain scores except 'emotional function' were significantly correlated with FVC, but only the association with environmental stimuli was of moderate strength. Regarding the AQLQ-S, a significant, but weak correlation with FVC was found for the

'breathlessness' domain. The AQLQ-J total score and the domains 'environmental stimuli' as well as 'activity limitation' showed significant, but weak correlations with FEV1 and PEF.

Neither the total score nor any domain score of the AQLQ-S were significantly correlated with FEV1. There were, however, significant correlations of the AQLQ-S domains 'breathlessness' and 'social' with PEF. The correlation with 'breathlessness' qualified as absent, while the correlation with 'social' classified as weak. No significant correlation of either QoL measure at total or domain level was observed with FEV1, % predicted.

Correlation of AQLQ-J and AQLQ-S with asthma control

Both AQLQ-J total score ($\rho=0.68$, $p<0.0001$, $N=136$) and AQLQ-S total score ($\rho=-0.61$, $p<0.0001$, $N=137$) were significantly correlated with asthma control.

Correlation of AQLQ-J and AQLQ-S with Asthma Bother Profile (ABP)

Both QoL measures correlated significantly with the ABP to the same degree (AQLQ-J: $\rho=-0.73$, $p<0.0001$, $N=130$; AQLQ-S: $\rho=0.73$, $p<0.0001$, $N=131$).

Correlation of AQLQ-J and AQLQ-S with EuroQoL CHS

Both AQLQ-J ($\rho=0.35$, $p<0.0001$, $N=134$) and the AQLQ-S ($\rho=-0.40$, $p<0.0001$, $N=135$) correlated significantly with the EuroQoL CHS Scale.

Table 9: Relationship of domain and total scores of AQLQ-J and AQLQ-S (correlation matrix)

	AQLQ-J					AQLQ-S				
	Symp- toms	Environ- mental stimuli	Emotion -al Function	Activity Limita- tion	Total	Breath- less- ness	Mood	Social	Con- cerns	To- tal
AQLQ-J										
Symptoms	-	0.54	0.68	0.60	0.90					
Environmental Stimuli		-	0.52	0.47	0.73					
Emotional Function		0.52	-		0.82					
Activity Limitation		0.47	0.51	-	0.78					
Total					-					
AQLQ-S										
Breathlessness	-0.74	-0.42	-0.54	-0.61	-0.72	-				
Mood	-0.57	-0.36	-0.46	-0.42	-0.58	0.57	-			
Social	-0.52	-0.54	-0.53	-0.70	-0.68	0.56	0.41	-		
Concerns	-0.59	-0.45	-0.65	-0.53	-0.68	0.59	0.61	0.68	-	

Total	-0.73	-0.52	-0.66	-0.66	-0.80	0.81	0.80	0.76	0.88
-------	-------	-------	-------	-------	-------	------	------	------	------

Spearman's rank correlation coefficients, all correlation coefficients showed p values < 0.0001;

Correlations between AQLQ-J and AQLQ-S scores are negative because the respective scores run in opposite direction

Table 10: Relationship of spirometry parameters with domain and total scores of AQLQ-J and AQLQ-S

	AQLQ-J					AQLQ-S				
	Symptoms (N=138)	Environment- al Stimuli (N=138)	Emotional Function (N=137)	Activity Limitation (N=137)	Total (N=136)	Breathless ness (N=137)	Mood (N=137)	Social (N=138)	Concerns (N=137)	Total (N=137)
FVC	0.24 (p=0.005)	0.36 (p<0.0001)	0.17 (p=0.05)	0.33 (p<0.0001)	0.33 (p<0.00 01)	-0.22 (p=0.01)	-0.12 (p=0.15)	-0.16 (p=0.05)	-0.11 (p=0.19)	-0.17 (p=0.05)
FEV1	0.15 (p=0.07)	0.20 (p=0.02)	0.08 (p=0.38)	0.23 (p=0.007)	0.20 (p=0.02)	-0.16 (p=0.07)	-0.05 (p=0.56)	-0.07 (p=0.39)	-0.06 (p=0.50)	-0.09 (p=0.31)
PEF	0.13 (p=0.13)	0.26 (p=0.002)	0.12 (p=0.17)	0.32 (p=0.0001)	0.24 (p=0.00 6)	-0.18 (p=0.04)	-0.09 (p=0.32)	-0.22 (p=0.01)	-0.09 (p=0.32)	-0.14 (p=0.09)
FEV1, % predicted	0.15 (p=0.08)	0.09 (p=0.32)	0.10 (p=0.25)	0.17 (p=0.05)	0.16 (p=0.06)	-0.17 (p=0.05)	-0.01 (p=0.88)	-0.09 (0.31)	-0.10 (p=0.26)	-0.09 (p=0.29)

Spearman's rank correlation coefficients

3.3.4 Relationship of mini AQLQ-J and AQLQ-S to patient characteristics (age, gender, asthma severity)

Neither measure correlated with age ($\rho=0.01$, $p=0.92$, $N=137$ for the AQLQ-J and $\rho=-0.03$, $p=0.77$, $N=138$ for the AQLQ-S). As shown in table 10, there was no significant difference between male and female in total AQLQ-J scores, but a significantly better QoL score was observed in the male group for the domains 'environmental stimuli' and 'activity limitation'. No significant difference between male and female was observed for the AQLQ-S total and in the domains.

Scores were significantly worse for those patients who reported having visited their GP during the past four months for the AQLQ-J total and the 'symptom' and 'activity limitation' domains. They were also significantly worse for the AQLQ-S total as well as the 'breathlessness', 'mood' and 'concerns' domains.

The relationship between median quality of life scores and perceived asthma severity was significant for the 'symptoms' and 'emotional function' domain scores of the AQLQ-J as well as the total AQLQ-J score. The relationship between median quality of life scores and perceived asthma severity was also significant for the 'breathlessness', 'mood', 'concerns' domains and the total score of the AQLQ-S.

Table 11: Median score (interquartile range) of AQLQ-J and AQLQ-S according to patient characteristics

	AQLQ-J					AQLQ-S				
	Symptoms	Environmental Stimuli	Emotional Function	Activity Limitation	Total	Breathlessness	Mood	Social	Concerns	Total
Gender										
Female	5.20 (4.20-6.00) N=105	5.67 (4.67-6.00) N=105	5.33 (4.00-6.33) N=105	6.25 (5.25-6.75) N=104	5.50 (4.57-6.07) N=104	0.80 (0.40-1.20) N=104	0.80 (0.40-1.40) N=104	0.29 (0.00-0.86) N=105	0.57 (0.29-1.14) N=104	0.70 (0.35-1.10) N=104
Male	5.10 (4.60-6.00) N=34	6.00 (5.33-7.00) N=34	5.67 (4.33-6.33) N=33	6.63 (5.75-7.00) N=34	5.93 (5.27-6.20) N=33	0.60 (0.40-1.00) N=34	0.90 (0.40-1.40) N=34	0.14 (0.00-0.71) N=34	0.64 (0.29-1.00) N=34	0.63 (0.45-0.95) N=34
<i>P value*</i>	0.58	0.003	0.61	0.03	0.10	0.48	0.70	0.39	0.74	0.69
Health care usage (GP visit) during the past four months										
Yes	4.20 (3.60-	5.33 (4.00-	5.00 (4.00-	6.00 (4.25-	4.93 (4.40-	1.00 (0.60-	1.20 (0.80-	0.29 (0.00-	0.86 (0.43-	0.90 (0.55-

	5.20) N=35	6.00) N=35	6.33) N=35	6.75) N=35	5.93) N=35	1.60) N=35	1.80) N=35	1.29) N=35	1.43) N=35	1.55) N=35
No	5.40 (4.60-6.10) N=104	5.67 (4.67-6.33) N=104	5.67 (4.33-6.67) N=103	6.25 (5.75-7.00) N=103	5.77 (5.13-6.20) N=102	0.60 (0.40-1.00) N=103	0.80 (0.40-1.20) N=103	0.29 (0.07-0.71) N=104	0.57 (0.29-1.00) N=103	0.55 (0.35-0.95) N=103
<i>P value*</i>	0.0009	0.05	0.09	0.04	0.003	0.002	0.0003	0.51	0.01	0.002
Perceived asthma severity										
No symptoms	6.10 (5.40-6.20) N=4	6.00 (5.50-6.50) N=4	6.00 (5.50-6.67) N=4	6.88 (6.38-7.00) N=4	6.27 (5.73-6.53) N=4	0.30 (0.20-0.50) N=4	0.40 (0.10-0.70) N=4	0.14 (0.07-0.50) N=4	0.00 (0.00-0.43) N=4	0.23 (0.15-0.48) N=4
Mild	5.40 (4.60-6.20) N=67	5.67 (4.67-6.00) N=67	6.00 (4.67-6.67) N=67	6.50 (6.00-7.00) N=66	5.80 (5.20-6.33) N=66	0.60 (0.40-0.80) N=66	0.80 (0.40-1.20) N=66	0.14 (0.00-0.71) N=67	0.43 (0.29-1.00) N=66	0.53 (0.35-0.90) N=66
Moderate	5.00 (3.90-5.80) N=64	5.67 (4.67-6.33) N=64	5.00 (4.00-6.00) N=63	6.25 (5.13-6.75) N=64	5.33 (4.53-5.93) N=63	0.80 (0.60-1.40) N=64	0.98 (0.50-1.40) N=64	0.29 (0.00-0.86) N=64	0.71 (0.43-1.21) N=64	0.73 (0.45-1.28) N=64

Severe	3.50 (2.60-4.10) N=4	4.17 (2.67-5.33) N=4	3.50 (2.17-5.33) N=4	4.50 (3.63-5.88) N=4	4.20 (2.93-4.93) N=4	1.70 (1.30-2.20) N=4	1.70 (1.60-2.80) N=4	1.38 (0.29-2.93) N=4	1.43 (0.71-2.79) N=4	1.58 (1.03-2.65) N=4
<i>P value</i> **	0.003	0.28	0.01	0.05	0.004	0.0002	0.007	0.29	0.008	0.002

*Wilcoxon rank sum two sample test (normal approximation, including continuity correction)

**Kruskal-Wallis test

3.4 Discussion

Overall, mild quality of life impairment was observed in a sample of adult patients with asthma recruited in Southern England, as measured by the mini version of the Juniper Asthma Quality of Life Questionnaire (AQLQ-J) and the Marks Asthma Quality of Life Questionnaire (AQLQ-S). Like in a previous Dutch study (137), this may be explained by the fact that all patients were recruited through primary care.

Missing item-level data were imputed as the mean of at least 50% of the subscale items. Ordinarily this might be expected to reduce the precision of calculated statistics. However, in this context imputation of values from at least 50% of subscale items is acceptable, since the subscale items were highly correlated with each other (as should be expected for items on a common subscale). Hence it was reasonable to infer a given missing item value from the mean value of the completed items. In fact, the highest percentage of missing data among all the scales used was 9.6% for the ABP.

Acceptable internal consistency ($\alpha > 0.7$) was found for both asthma-specific quality of life measures at total and domain level, except for the 'environmental stimuli' domain of the AQLQ-J.

Both measures correlated strongly with each other at the total score level. This was also true for most domain-domain correlations. Similarly strong domain-domain and domain-total as well as total-total correlations were found in a Spanish study which compared the performance of the full version of the AQLQ-J and the St George's Respiratory Questionnaire (SGRQ) (129).

Correlations with the symptom score, particularly the asthma module of the symptom score, were strong for the AQLQ-J and moderate for the AQLQ-S.

The strength of the correlation of the AQLQ-J ($\rho=0.69$) with asthma symptoms we found was comparable to that found in the Dutch study ($\rho=0.65$) (137). Taking the perspective of van der Molen et al. (137) this

may be interpreted as evidence for (cross-sectional) construct validity, although we have taken the stance before that not symptoms per se, but the impact of symptoms is influencing asthma-specific quality of life (148). Hence, the strong correlation of the AQLQ-J with the symptom score may raise the question of overlap between the symptom score construct and the quality of life construct as operationalised in the AQLQ-J.

The stronger correlation of the AQLQ-J compared to the AQLQ-S with the symptom score seems plausible in the light of the fact that the AQLQ-J has more symptom-related items compared to the AQLQ-S.

The finding that correlations of both measures (at total and domain level) with lung function measures were weak, if not absent, was expected. It corroborates previous findings (137, 138).

The AQLQ-J showed more and stronger correlations with lung function measures. This was expected because the AQLQ-J has more symptom-based items. The findings for lung function contrasted with the strong correlations found for asthma bother and asthma control. Taking the moderate strength of the correlations with generic quality of life into account, we interpret the findings from these correlational analyses as supporting evidence for construct validity of both measures.

The relationships of the AQLQ-J and AQLQ-S with health care utilisation as measured by GP visits and with perceived asthma severity were as expected and support the discriminative ability of both measures. The observed gender difference is less clear. There are few studies looking into gender differences in asthma-specific quality of life. A very recent study from India found that women reported poorer quality of life, especially in the symptoms and emotional domains of the AQLQ (149). The findings point in a similar direction to our findings, however we found significant differences in the “environmental stimuli” and “activity limitation” domains.

Any findings however, from this psychometric study, need to be interpreted with caution, as the study was not primarily designed as a validation study.

The sampling frame was that of an RCT and there was no a priori power calculation for any of the analyses relating to reliability or validity.

3.5 Conclusion

This study provides evidence for the validity of the mini AQLQ-J and the AQLQ-S in a British population of adults with asthma who are managed in primary care. The correlations with lung function and symptoms were different for the two measures and stronger for the mini AQLQ-J compared to the AQLQ-S, reflecting partly the different content of the questionnaires. Both the mini AQLQ-J and the AQLQ-S are able to discriminate between patients with differing levels of asthma severity.

4 Validity of three asthma-specific quality of life questionnaires: the patient's perspective

4.1 Background

The literature review reported in chapter 2 concluded that the questionnaires reviewed differ in almost all the criteria used to review them (conceptual and measurement model, reliability, validity, interpretability, burden, administration format and number of linguistic validations/translations) (148). In particular, a lack of explicit conceptual models was noted. The underlying conceptual models can only be inferred from the domains in which the items are grouped and hence are implicit rather than explicit. Therefore it cannot be assumed that the instruments which are currently in use to measure asthma-specific quality of life measure the same construct. From these observations, the question arises as to which sets of items best reflect the lived experience of people with asthma. To date, no attempt has yet been made to explore this question from the patient's perspective. Qualitative research methods are suitable to identify such perspectives by highlighting common themes and differences (150, 151). They allow an in-depth exploration of patients' views and experiences, in order to reach an understanding of how they perceive the relevance of the questionnaires in the context of living with asthma.

It was the aim of this study to capture the views that people affected by asthma have with respect to the existing asthma-specific quality of life questionnaires. The study used three asthma-specific quality of life questionnaires which are internationally among the most widely used measures of asthma-specific quality of life. They are included in a comprehensive structured review of patient-reported outcome measures for people with asthma that has been reported to the Department of Health in England (152). Furthermore, they are also suggested by the German national guideline for asthma monitoring (153).

If HrQoL is conceptually about the impact of a disease on an individual's position in life (rather than functional limitations, symptoms or health status) then perceptions take centre stage. As perceptions are shaped by culture, language and more specifically by health care systems, studies looking at measures of HrQoL need to be culturally sensitive. In the following, a two-stage qualitative study exploring patients' perceptions on asthma-specific measures of HrQoL is described.

4.2 Methods

4.2.1 Patient recruitment

The study had two phases: one sample of patients was recruited in Germany, and sequentially a second sample was recruited in the UK. An a priori power calculation was deemed to be inappropriate as the study was qualitative in nature. Recruitment continued until enough data were obtained in order to formulate meaningful comparisons in relation to the research objective. Patients were eligible for the study if they reported a physician-diagnosis of asthma, did not have serious difficulties with the German or English language and did not have severe mental health difficulties. Written informed consent was sought from each study participant.

German sample

A convenience sampling strategy was used between mid-September and mid-November 2010 to identify potential participants living in the German cities of Mannheim or Heidelberg and in surrounding communities in Germany. Individuals with asthma were recruited through posters in waiting rooms of GPs and pulmonologists, through the pneumology unit of the University Hospital Mannheim, through advertisement in a regional newspaper and at an information event for patients organised by the local branch of the German Allergy and Asthma Association (DAAB, website: www.daab.de).

Ten individuals with asthma participated in Germany: two patients contacted the study centre in response to the posters in their GP's or specialist's practice, four patients were recruited at the University Hospital Mannheim, one patient participated in response to the newspaper advertisement and three individuals with asthma were recruited at the information event. All interviews were carried out at a place chosen by the patients. Four patients were interviewed in their homes, three at the Mannheim Institute of Public Health, and the remaining three at the University Hospital Mannheim, the patient's office or a public place, respectively.

An information package was sent to potential participants upon their request (in response to posters at GP offices or the newspaper advertisement) or was handed over to them at the pneumology unit or the information event. The package contained information about the study, the consent form and a basic demographic questionnaire which covered age, gender, nationality, marital status and whether the participant lived with a partner. Participants were asked to take the completed questionnaire along to their interview.

UK sample

The second part of the study was conducted using National Health Service (NHS) sites in Brighton and Hove, UK. Data were collected in August 2011 and March 2012. Letters explaining the study's aim were sent to respiratory consultants at the Royal Sussex County Hospital and the Princess Royal Hospital as well as to GP practices in Brighton and Hove. An advertisement poster which contained information on the study in lay language and contact information was included with each letter. Doctors were asked to put up the poster on noticeboards. Personal contacts with respiratory consultants were also established.

Dates and times for the interviews were arranged when patients called in, sent e-mails or when their contact details were passed on by doctors following expression of interest to participate. Interviews took place in full privacy at the Brighton and Sussex Medical School, the Royal Sussex

County Hospital or in private homes. 22 individuals with asthma participated in the UK.

4.2.2 Questionnaires

Patients were asked to evaluate the following questionnaires:

Sydney Asthma Quality of Life Questionnaire (AQLQ-S)

The AQLQ-S has been developed in Australia as a 20-item self-administered questionnaire with a five-point Likert scale and a four-week recall period to measure quality of life in adults with asthma (59). The AQLQ-S consists of four subscales: breathlessness, mood disturbance, social disruption and concerns for health.

Figure 1: Example items from the AQLQ-S, English version

What follows is a series of statements describing the way in which asthma (or its treatment) affects some people. You are asked to tick (✓) the response to each statement which closely applies to you **over the past 4 weeks**.

	Not at all	Mildly	Moderately	Severely	Very severely
I have been troubled by episodes of shortness of breath	<input type="checkbox"/>				
I have been troubled by wheezing attacks	<input type="checkbox"/>				
I have been troubled by tightness in the chest	<input type="checkbox"/>				
I have been restricted in walking down the street on level ground or doing light housework because of asthma	<input type="checkbox"/>				

A linguistically equivalent German language version of the AQLQ-S has been produced in Switzerland following sequential backward and forward translation (96).

Figure 2: Example items from AQLQ-S, German version

	Nie	Selten	Manchmal	Häufig	Sehr häufig
1	Es kommt vor, dass ich vorübergehend unter Kurzatmigkeit leide				
	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
2	Es kommt vor, dass es beim Atmen plötzlich stark pfeift				
	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
3	Es kommt vor, dass ich unter Engegefühl im Brustkorb leide				
	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
4	Ich werde durch Asthma-beschwerden oder <input type="checkbox"/> Kurzatmigkeit eingeschränkt, wenn ich draußen geradeaus gehe oder im Haushalt leichte Arbeit verrichte				
	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Living with Asthma Questionnaire (LWAQ) and Fragebogen zur Lebensqualität bei Asthma (FLA)

The "Living with Asthma Questionnaire (LWAQ)" has been developed in the UK and comprises 68 items in eleven domains (social/leisure, sport, holidays, sleep, work and other activities, colds, mobility, effects on others, medication usage, sex, dysphoric states, attitudes) (61). It has a three-point

Likert scale and consists of both positive and negative items, thus compensating for acquiescence bias. Of the three questionnaires used, the LWAQ is the only questionnaire which has a 'not applicable' (n/a) option.

Figure 3: Example items from the LWAQ

Begin here . . .

Sample Markings

Wrong

Right

		Untrue of me	Slightly true of me	Very true of me
1. I can take part in any sport I want.	Not applicable <input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. When invited round to a friend's house, I worry that there may be something there which sets off an attack.	Not applicable <input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Having asthma restricts the sort of holiday I can take.	Not applicable <input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. I am a sound sleeper.	Not applicable <input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

The *Fragebogen zur Lebensqualität bei Asthma* (FLA) (68) represents the German revision of the "Living with Asthma Questionnaire (LWAQ)" (61). It comprises 40 items in three domains which were categorised on the basis of theoretical considerations into "physical symptoms", "psychological distress" and "functional status". Like the original LWAQ, the FLA has a three-point Likert scale and an n/a option, and consists of both positive and negative items.

Figure 4: Example items from the FLA

	<i>stimmt genau</i>	<i>stimmt in etwa</i>	<i>stimmt nicht</i>	<i>nicht anwendbar</i>
1. Bei privaten Einladungen befürchte ich, daß irgendetwas in der dortigen Umgebung einen Atemnot- oder Hustenanfall auslösen könnte.	1	2	3	4
2. Aufgrund meines Asthmas sind meine Urlaubsmöglichkeiten beschränkt.	1	2	3	4
3. Ich habe einen gesunden Schlaf.	1	2	3	4
4. Es fällt mir leicht, meine Einkäufe zu tragen.	1	2	3	4

Juniper Asthma Quality of Life Questionnaire (AQLQ-J) and Standardized Juniper Asthma Quality of Life Questionnaire (AQLQ-J-s)

The AQLQ-J has been developed in Canada and is a questionnaire with an idiographic component, i.e. patients can choose the five items most important to them from a list of activities (57). It comprises 32 items in four domains (activity limitation, symptoms, emotional functioning, exposure to environmental stimuli) and uses a seven-point Likert scale and a two-week recall period. The AQLQ-J was used in the study in the UK.

Figure 5: Example items from the AQLQ-J, English version

IN GENERAL, HOW MUCH OF THE TIME DURING THE LAST 2 WEEKS DID YOU:

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	Hardly Any of the Time	None of the Time
7. Feel CONCERNED ABOUT HAVING ASTHMA?	1	2	3	4	5	6	7
8. Feel SHORT OF BREATH as a result of your asthma?	1	2	3	4	5	6	7
9. Experience asthma symptoms as a RESULT OF BEING EXPOSED TO CIGARETTE SMOKE?	1	2	3	4	5	6	7
10. Experience a WHEEZE in your chest?	1	2	3	4	5	6	7

The AQLQ-J-s (67) is a standardized version of the original AQLQ-J in which the five individualized activities were replaced with five generic activities (strenuous, moderate, social, work-related, and sleeping). The AQLQ-J-s comprises 32 items in four domains (activity limitation, symptoms, emotional functioning, exposure to environmental stimuli). It uses a seven-point Likert scale and a two-week recall period. A linguistically equivalent German version of the AQLQ-J-s was used in the German study.

Figure 6: Example items from the AQLQ-J-s, German version

ALLES IN ALLEM, WIE OFT IN DEN LETZTEN 2 WOCHEN:

	Immer	Meistens	Oft	Manchmal	Selten	Fast nie	Nie
7. Haben Sie sich SORGEN WEGEN IHRES ASTHMAS gemacht?	1	2	3	4	5	6	7
8. Waren Sie wegen Ihres Asthmas KURZATMIG?	1	2	3	4	5	6	7
9. Haben Sie Asthmabeschwerden bekommen, WEIL SIE ZIGARETTENRAUCH AUSGESETZT WAREN?	1	2	3	4	5	6	7
10. Haben Sie ein PFEIFEN in Ihrer Brust bemerkt?	1	2	3	4	5	6	7

4.2.3 Data collection

Data were collected through in-depth interviews to gain insight into people's subjective narratives of how the content of the questionnaires used related to their experience of living with asthma. Prior to the interviews, participants were asked to complete the three different asthma-specific quality of life questionnaires as a prompt for the subsequent interviewing. Following completion, they were asked to reflect on the process of completing the questionnaires. They were then asked to talk freely about aspects of their

asthma that were bothersome to them and whether the questionnaire items covered those aspects.

Table 11 illustrates that the questionnaires were given to participants in one of six different sequences in Germany, with the intention to avoid the potential for the order of questionnaire presentation to influence patient's perceptions. Since no ordering effect could be observed, questionnaires were not administered in different sequences in the UK.

Table 12: Ordering of German questionnaires given to the interviewees

Participant	AQLQ-J-s	AQLQ-S	FLA
P1	1	2	3
P2	3	2	1
P3	2	1	3
P4	3	1	2
P5	1	3	2
P6	2	3	1
P7	1	2	3
P8	3	2	1
P9	2	1	3
P10	3	1	2

A topic guide was used as an aide memoir in order to ensure that the interviews did not deviate too much from the prime aims of the study (table 12). The topic guide was developed based on the structured literature review (148) and discussions within the research team. Interviews were audiorecorded and transcribed verbatim by a Master's student in Public

Health in Germany and transcribed by an experienced commercial transcriber in the UK.

Table 13: Topics covered in the interview topic guide

General impression of the questionnaires: What were your feelings/thoughts when completing the questionnaires?
Length of the questionnaires: How did you feel about the length of the questionnaires?
Layout/visual clarity: How did you feel about the looks/the layout of the questionnaires?
Format of the questions/response options: How did you feel about the options that were given to choose from when responding to each question?
Comprehensibility: How understandable were the questions to you?
Burden: How strenuous was it for you to answer the questions?
Redundancy of questions: are there any questions which are repeated or very similar?
Need for specification of question wordings: are there any questions which should be phrased in a more specific manner?
Adequacy/validity of questionnaires in relation to situation of living with asthma: How much did you feel the questions in the questionnaires covered the issues you are concerned with because of your asthma? Do important aspects of living with asthma lack in the questionnaires?
Suggestions for improvement: do you have any suggestions to improve the questionnaires?

Preference: Did you like one of the questionnaires better than the other/others? Could you tell a preference? If questionnaires should be judged as insufficient: which questionnaire is still the most adequate?

Extension for interviews in the UK

Preference: Would you recommend one of the questionnaires?

We are very interested in all of your views and impressions, so in this last section please feel free to add any other comments you feel are relevant to the ways asthma influences quality of life.

Whereas patients brought the demographic questionnaire along when the interview took place in Germany as described above, basic demographics (age, gender, year of asthma diagnosis and years spent in full time education) were noted by the interviewer at the beginning of each interview in the UK.

4.2.4 Data analysis

The focus of the data analysis was on illuminating patient views with respect to the asthma-specific quality of life questionnaires described above. Thematic content analysis was performed by coding the data material and then grouping the codes into thematic categories (154). The method is suitable in investigating the pre-set objectives of this exploratory study. The thematic framework was pre-structured by the topics included in the topic guide. Open coding according to grounded theory would not have been feasible within the scope of this PhD. Theory generation was also not a desired outcome of the study. We expected themes to emerge around missing, redundant and irrelevant content and also expected themes to

emerge around layout and format. These expectations are reflected in the topic guide.

Data were coded using the computer assisted qualitative data analysis software (CAQDAS) ATLAS.ti, version 6.2 (155, 156). Data was summarised using the respondents' own words to code the material. Main themes found in the verbatim transcripts were categorised according to frequency and relevance and then interpreted. The analysis aimed to find patterns and similarities between the respondents by contrasting and comparing the material. The emerging analysis was discussed regularly within the research team and credibility of the findings (how well categories actually represent data) was established by seeking agreement among co-researchers (157). The thematic framework that emerged from the German sample was applied to the textual data from the UK sample and substantially extended.

Codes and categories that had emerged from the German sample were cross-translated into English together with illustrative quotes from the participants.

4.2.5 Ethics

Interviews in Germany

The study was reviewed and approved by the ethics board (EK-II) of the Medical Faculty Mannheim, Heidelberg University, Germany (reference number 2010-289E-MA).

Interviews in the UK

Research governance was obtained from the Brighton and Sussex Medical School (BSMS), Brighton, UK who took on the role of the Research sponsor for the duration of the study (R&D reference number 10/022/SMI).

An application to the Brighton East Research Ethics Committee (REC) was made using the web-based Integrated Research Application System (IRAS), accessible via <https://www.myresearchproject.org.uk/>. Ethical approval was obtained, following one revision of the original documents (REC reference number: 10/H1107/38).

R&D approval was obtained from Brighton and Sussex University Hospitals NHS Trust (R&D reference number 10/022/SMI). The sites covered by the approval included the Royal Sussex County Hospital and the Princess Royal Hospital. Permission was obtained from the Sussex NHS Research Consortium to access Participant Identification Centres (PICs) in the NHS Brighton and Hove (ID 1415/NOCI/2011).

4.3 Results from the German interviews

A total of ten patients (four women, six men) with asthma participated in Germany. Their mean age was 29 years, ranging from 18 to 46 years. Two participants were married, one was divorced and seven were single. Two participants had nine years, three had ten years and five had 13 years of school education. The mean time since asthma diagnosis was 11 years, ranging from two to 21 years.

Patients spoke about a range of diverse aspects pertaining to the questionnaires, which were grouped into the following main themes: response format, missing content, redundant or similar content, irrelevant content, layout, and diverse issues. These categories are presented as broad headings with subthemes (codes) grouped under them. Table 13 gives a summary of categories, codes and illustrative quotes.

A. Response format

Not applicable (n/a) option

Patients often found the n/a option (which is solely a feature of the FLA) confusing. However, one patient (P3) had a distinctly different view. The FLA has one item which pertains to an asthma attack. Since he had never had an asthma attack he appreciated having an n/a option.

Number of response options

Patients' views differed with respect to the optimal number of response options. Patients expressed that three or five response options were sufficient, and in a number of interviews, seven options were judged as too many; however, one patient also expressed a preference for seven response options because this allowed more choice.

Specification of response options

A desire for more specification of the meaning of the various options was expressed. For instance, one interviewee was unclear what 'a little of the time', 'some of the time', 'most of the time' actually meant.

Recall period

Patients considered recall periods of two and four weeks as in the AQLQ-J-s and the AQLQ-S difficult and more appropriate for stable rather than acute or fluctuating asthma.

B. Missing content

Coughing from cold or coughing from asthma

Interviewees found it problematic that there was no question to distinguish whether the patient currently suffered from a cold besides the asthma.

Environmental trigger factors

Patients very often found that the questionnaires lacked coverage of environmental trigger factors or causes of their asthma. Pets, allergies, weather/climate and odours were specifically mentioned.

Medication/medication needs

Patients felt that the questionnaires did not cover medication and the limitations arising from ongoing dependence on medication. In connection

with medication, patients also spoke about having had previous asthma education as missing in the questionnaires.

C. Redundant or similar content

Patients often spoke about questions being similar or even redundant. This was a general impression, but was specifically noted for items in each questionnaire. The different questions about impairment in the AQLQ-S were mentioned. In the AQLQ-J-s, the questions about *feeling one had to avoid a situation or environment because of an exposure* (such as strong odours/perfumes or cigarette smoke) and *experiencing asthma symptoms as a result of being exposed to that exposure* were mentioned as redundant. The use of positive and negative items in the FLA was also perceived as creating unnecessary replications.

D. Irrelevant content

Beyond issues of redundancy or similarity, patients also found particular items in the questionnaires irrelevant. They mentioned shortness of breath in the AQLQ-S, being sexually frustrated in the FLA and being sad or depressed in both the AQLQ-S and FLA.

E. Layout

Participants judged the layout of the AQLQ-S in a positive way, and contrasted it with the layout of the FLA and the AQLQ-J-s. Participants often emphasised that the varying writing in small and capital letters in the AQLQ-J-s was confusing to them.

F. Diverse issues

Some participants perceived scales as inadequate means to assess quality of life in the first place. A desire for having space for free text was expressed.

One interviewee contextualised space for free text within asthma control (P3).

“(...) because asthmatics are often relatively well controlled and surely always tick off ‘never’ in the questionnaire; there are however things or situations which are not captured then, which nonetheless impair quality of life.” (P3)

There was also a perception that the questionnaires were a test of psychological wellbeing.

Furthermore, interviewees mentioned that some of the items needed a clearer specification. One interviewee (P7) contrasted the environmental exposure stemming from a particular activity with the activity itself (dust from decorating vs. decorating). With regard to sports-related questions which ask about physical activity in general (item 13 in the FLA, item 15 in the AQLQ-S), one interviewee (P1) said that swimming or indoor sports were not a problem, but running was. One participant expressed a preference for statements (as in the FLA or AQLQ-S) as opposed to questions.

Table 14: Themes, codes and illustrative quotes (German sample)

Theme	Code	Illustrative Quote
RESPONSE FORMAT	<i>Not applicable (N/A) option</i>	<p>“And this ‘not applicable’; it’s not clear what this is supposed to mean.” (P6)</p> <p>“What I liked was that there is ‘not applicable’” (P3)</p>
	<i>Number of response options</i>	<p>“(…) well there’s a range of five options here. I think that is enough.” (P3)</p> <p>“(…) seven distinctive features: that’s just too much.” (P8)</p> <p>“Regarding the choices in the FLA, I would definitely say ‘grade E’. AQLQ-J on the other hand, grade A. You have more choices that could apply, which [you don’t have with FLA].” (P5)</p>
	<i>Specification of response options</i>	<p>“A definition of the frequency is lacking in all of them a little bit.” (P3)</p> <p>“Practically if one defines what ‘a little of the time’, ‘some of the time’, ‘most of the time’ means” (P3)</p>
	<i>Recall period</i>	<p>“In general, I found the AQLQ-J very difficult, because it really just pertains to the last two weeks and this actually doesn’t make sense for chronic asthmatics who have asthma regularly or else always during a certain peak phase.” (P1)</p>
MISSING CONTENT	<i>Coughing from cold or coughing from asthma</i>	<p>“And that something like this isn’t asked - whether you have a cold at the same time – this isn’t very realistic”. (P6)</p>
	<i>Environmental trigger</i>	<p>“Well they ask a lot about activities, but never [about] the environment” (P4)</p>

	factors, for example	
	Pets	“And animals – if I remember correctly – were somehow not mentioned anywhere, and I find that important because animal hair plays a role again and again for almost any asthmatic.” (P2)
	Allergies	“That you are asked, do you have allergies or do you not? I didn’t see that in any [questionnaire]“ (P9) “There are some foods, for example, [which] asthmatics cannot eat, for instance again related to the allergies. This is also very limiting. “ (P9)
	Weather/climate	“Well it’s really not always about sports or work. It also has something to do with weather or food.” (P9)
	Odours	“What I realized is that in the FLA and AQLQ-S questionnaires odours are not even addressed, one can be exposed to when short of breath. And me for instance I am a person who reacts very strongly to odours.” (P8)
	Medication/medication needs	“What about when I haven’t got my asthma spray with me and I am out somewhere. Well I think this issue is not covered very well.” (P1) “The most important question for me would be whether the patient has already had asthma education, yes or no. Because one often makes mistakes applying the inhalers wrongly“ (P5) “How often do I need the medications or how often do I need my emergency inhaler? I didn't read anything about this so far, when it comes to medications.”

		(P9)
REDUNDANT OR SIMILAR CONTENT	General	“I find they are strongly repetitive. Well in general I think this could be reduced to - (...) six, seven questions. And the remainder are variations of those questions. That was my feeling somehow. (...)“ (P10)
	AQLQ-S	“Well I find it starts here already [points to AQLQ-S questionnaire] whether I am impaired when doing housework, in my hobbies, whether I am generally impaired...” (P1)
	AQLQ-J	“(...) this AQLQ-J asked about perfume and other odours twice: once because of asthma itself and once whether I feel rather limited by those [perfume/odours] (...). And I find it unnecessary to ask about this twice. And else...AQLQ-J does this quite often in general: it always asks about asthma complaints and then again separately whether I feel impaired there, or had avoided it, to go there. “ (P2)
	FLA	“(...) well in the FLA I find very many redundancies. Here I have ‘I have a sound sleep’ and ‘I sleep poorly because of my asthma.’ So precisely the direct opposite question. Or here another one ‘I can climb up the stairs without stopping’ and then again ‘I can only climb the stairs if I have one or several breaks’. Well here I really noted it, that often the same is asked for“ (P1)
IRRELEVANT CONTENT	FLA	“Well in the FLA I really had to think twice about the question about what asthma has to do with sexual frustration. Well, this would be one of those questions I

		would consider unnecessary.” (P2) “Well whether asthma has any influence on where to go for one’s holiday vacation or influence on travelling possibilities. Well I thought this was ridiculous. “ (P10)
	FLA and AQLQ-S	“(…) [participant pointing to questions in the FLA and AQLQ-S] Sad or depressed because of asthma? Why should I be sad? I have got it; I have to live with it, ok. I accept it, but depressed or sad? “ (P5)
	AQLQ-S	“And the first question in the AQLQ-S is relatively unnecessary because that one is short of breath when having asthma is logical. “ (P7)
LAYOUT		“Well I found the layout of the FLA weird because I didn’t have any clue where to make the mark; it was the same with the AQLQ-J. And this one [AQLQ-S] I found rather well done; here you are supposed to mark such a circle and that was relatively clear. “ (P6) “And the AQLQ-J questionnaire, this one’s (layout) needs to be totally redone, this one is really absolutely confusing. “ (P8)
DIVERSE ISSUES	<i>Inadequacy of scales to assess quality of life</i>	“Because quality of life is not necessarily captured with words and sentences that are just checked off. I rather find that certain questions should be better adapted to every respondent, (...). “ (P5) “Because you cannot say [with] a scale of one to seven or of one to ten “I am doing so and so”, I think.” (P9) “Well maybe there should be an open-text field in the questionnaires themselves

		where you can reveal things that are important, which are not covered in them. (...) But a [questionnaire] certainly doesn't cover everything that could occur or everything that you would want to say, (...)“ (P2)
	<i>QoL questionnaires as a means of psychological testing</i>	“(…) it appears to me that the whole thing [is] kind of a psycho test. That’s my impression. Because there are questions in it [which] actually, in my opinion, [have] nothing do with asthma at all.” (P5)
	<i>Desire for better specification/better examples</i>	<p>“(…) there were items [in the FLA] like ‘for example decorating’. Well I cannot imagine that someone gets asthma problems particularly while decorating. I think when you are doing housework, when you’re drilling a hole, and thereby create a lot of dust. Such things! They are more likely to impair, I think. And decorating I don’t think is impaired when you have asthma! “ (P7)</p> <p>“Well I don’t have any limitations when it comes to swimming. Because this is not a problem at all for a person with allergies, while a 1000-meter run is a sport where there are limitations. Erm, or also indoor sports are always do-able, or at least more do-able compared to something outdoors. So, there is a difference here and a little more specification would definitely yield more precise results here. “ (P1)</p>

G. Comparative aspects

7/9 participants rated the AQLQ-S first, 7/9 participants rated the FLA second and 7/9 participants rated the AQLQ-J-s last. The rating of each individual patient is detailed in table 14. Participants compared the questionnaires in many ways, and emphasised the clarity of the AQLQ-S and that it was a very compact questionnaire.

“Personally I would consider the AQLQ-S best. Simply because it covers a relatively broad spectrum with not too many questions and still follows a logical structure.” (P1)

The AQLQ-J-s was criticised for its lack of clarity and that there was a perceived overlap of the questions.

“(…)and I found the AQLQ-J worst, firstly because it is so poorly structured, there were quite a few overlaps in the questions and because it was a lot about resilience.” (P3)

However, preferences were not uniform, and despite the majority favouring the AQLQ-S, contrasting views were also expressed.

“(…) well in my view the options to answer the questions I think are best here [AQLQ-J] with the options from one to seven. (...) There are a number of questions – 32 – this is OK. Well I would judge the AQLQ-J best of all.” (P5)

“Well best in terms of the question and most adequate, where I could make the greatest number of statements, was in fact the FLA.” (P3)

**Table 15: German patient ratings of quality of life questionnaires
(from 1=best to 3=worst)**

Participant	AQLQ-S	FLA	AQLQ-J-s
P1	1	2	3
P2	1	2	3
P3	2	1	3
P4	1	2	3
P5	3	2	1
P6	1	2	3
P7	1	2	3
P8	1	2	3
P9	1	3	2
P10	Missing		
Mean rank (SD)	1.33 (0.71)	2.00 (0.50)	2.67 (0.71)

4.4 Results from the UK interviews

Participants' demographic characteristics are displayed in table 15.

Table 16: Demographic characteristics of participants

Participant	Age	Gender	Years of full time education	Age of asthma diagnosis
P1	52	Male	Left school at age 16	age 34/35
P2	20	Female	Ongoing	age 2
P3	57	Female	16 years	age 46
P4	53	Female	18 years	age 2
P5	21	Female	Ongoing	age 11
P6	49	Male	19 years	age 10
P7	19	Female	Ongoing	age nine months
P8	46	Female	16 years	age 22/23
P9	54	Female	14 years	age 28
P10	22	Male	Expelled from secondary school	age 2/3
P11	38	Male	17 years	age 12
P12	49	Male	18 years	age 3
P13	25	Female	14 years	age 18 months
P14	35	Female	16 years	age 8
P15	38	Female	18 years	age 11
P16	43	Female	16 years	age 8
P17	31	Female	16 years	age 9
P18	25	Male	16 years	age 2
P19	68	Male	10 years	age 7 (asthma disappeared at age 14/15 and came back in 30s)
P20	33	Male	17 years	age 26
P21	40	Female	21 years	age 2
P22	43	Female	21 years	age 8

Participants spoke about wide ranging issues in relation to the three questionnaires. The issues were grouped into the following main themes: response format, missing content, redundant or similar content, irrelevant

content, confusing/difficult content, irritating content, layout, general perceptions as well as comparative aspects. Subthemes (codes) are presented with illustrative codes in tables 16 to 24 under the respective theme.

A. Response format

Not applicable (n/a) option

Participants generally thought that having an n/a response option (a feature that only the LWAQ has) was good. An n/a option was perceived as a “let-out” and it was pointed out that having such an option might make it easier to complete the questionnaires. In contrast to this, some participants also said that an n/a option was not necessary because one could always leave a question blank or go for a “not true” or “not at all” option.

Number of response options

Participants were ambiguous in relation to the number of response options and expressed diverse views. A recurring theme was that seven options as in the AQLQ-J were too many, the reason for this being the fact that grading between being bothered/impaired and not being bothered/impaired becomes more difficult with more options.

“I found the range of one-to-seven, I didn’t really know where to put myself in that range.” (P17)

On the contrary, a view was expressed that the more choices the better and that hence seven options would be the preference.

“Whereas the Juniper one there was so many options I could select how I actually felt.” (P5)

A number of participants expressed a preference for five options but some also preferred three. One participant (P20) said that an uneven number of response options was better because of the middle ground but others thought that having a middle ground hindered committed decisions.

Specification of response options

Participants' judgements about response options were not solely based on the number of options but also on their specification. A preference for rating severity rather than time (as in the AQLQ-J) was expressed. In a more general sense, the subjectivity of the interpretation of the response options was emphasised, and a fear of misinterpretation was mentioned.

Ticking a box vs. filling a circle

Many participants preferred ticking a box (such as in the AQLQ-J or AQLQ-S) over filling a circle (such as in the LWAQ) because the latter seemed to be more burdensome.

“I found that a bit of a nuisance - where you have to colour in the ... umm ... the circles. And if you go out of it what does that mean? Yeah I found that a bit of a nuisance.” (P17)

Recall period

Interviewees felt that using a time frame narrowed the perspective and made it impossible to fully capture the experience of living with asthma. A time frame was also felt to be inadequate in the light of the fluctuating nature of asthma where one might be symptomatic in one week and then have little problems the following week. In particular, reporting activity limitations with respect to a narrow time frame was felt to be problematic as one may not have done any of these activities in the respective time frame (such as gardening).

“(...) for some asthmatics, like myself, I can be very well for quite a number of weeks or even months. And then I can go through a patch of being very unwell. So I think that using a particular time frame isn't necessarily always helpful” (P2)

A preference for four weeks over two weeks was expressed, and an even wider time frame was suggested. A preference for no time frame, like in the LWAQ, was also expressed.

Table 17: Codes and illustrative quotes relating to theme “Response format/response options” (UK sample)

Code	Illustrative Quote
Not applicable (N/A) option	
Not applicable (N/A) option, positive view	<p>“You know: it is quite good to let people have a let-out you know.” (P1)</p> <p>“Yes, because sometimes things are not applicable. Yes, sometimes ... like one of the questions was ‘if I am in a smoky restaurant it is really bad’. I can’t ever remember sitting in a smoky restaurant eating dinner and worrying about my asthma so it is not applicable, because I haven’t done it.” (P15)</p> <p>“Yes I must admit I think it is always useful to have a ‘not applicable’ option for them. So, umm ... you know for example question 12 in the ‘Living with Asthma’ questionnaire says ‘I can run like other people’ and this questionnaire (I presume whoever gives it out vets it) but you might have someone who is disabled and completely unable to run, but it is nothing to do with their asthma, and I guess they would write ‘not applicable’.” (P21)</p>
Not applicable (N/A) option, negative view	<p>“I mean - a lot of them don’t really - didn’t particularly apply to me. So instead of saying ‘they don’t apply’ - I just said they ‘are not true.’” (P1)</p> <p>“Well they kind of - I know it says ‘not applicable’ but it kind of - but it does cover ... it does cover it in the other questionnaires as well, because you have got the ‘not at all’ box. And ‘none of the time’ - so you could actually do it like that.” (P17)</p> <p>“Because what you ... yeah ... what I ... well I would try and answer all of them. But you don’t want people to just go ... no-no-no-no-no because that is not helpful for anybody.” (P17)</p>

Number of response options	
<i>Seven too many</i>	<p>“I found the range of one-to-seven, I didn’t really know where to put myself in that range.” (P17)</p> <p>“I think to be quite honest you don’t really ... umm ... tend to ... I think seven is too many. Because you are either looking at it one way ‘I don’t have this’ or ‘I do have this’ and I think to have six in between or five in between I am not sure I would actually, sort of ... umm ... actually sort of ... come to terms with that.” (P19)</p> <p>“Whereas the Juniper one there was so many options I could select how I actually felt.” (P5)</p>
<i>Preference for three options</i>	<p>“I preferred it - there were less options so it made it kind of easier to say ‘Yes’ ‘No’ or ‘Maybe’.” (P4)</p> <p>“I think ... well I was grateful that there were only 3 options in that context. Because however much you are enjoying filling in a questionnaire - there comes a saturation point.” (P8)</p> <p>“And I found that the three options (or the four effectively) were much easier to answer than the ‘Marks’.” (P17)</p>
<i>Preference for five options</i>	<p>“Because I think again, in the Marks Asthma thing, you have got five - and I think - there is two either side of one in the middle, which is a good balance isn’t it” (P11)</p> <p>“I think five points is just routine and people are comfortable with that and it is quite straight forward. (...) Because actually it is only a three point scale, I think in the eyes of the user - there is like maximum, minimum and middle and then the bit of a dither! And I think that is how people fill them in. Maximum, minimum, middle and then you have got this little bit of dither space, if you are not quite sure.” (P12)</p> <p>“And I suppose a format of four or five - yeah. Umm ... yeah I suppose in a way, now looking at it, that is the one that I ... that I prefer.” (P19)</p>
<i>Preference for seven options</i>	<p>“I found that, whereas in the previous questionnaires I was saying - ‘I am not particularly</p>

	<p>bothered about having asthma and it doesn't particularly affect me' - I found that because I had identified areas in which it did affect me, I was now say - 'yes I do have some concerns a little bit of the time', and the 7-point scale captured that. The shorter scale didn't." (P6)</p> <p>"Seven, because I think the more choices the better." (P22)</p>
<i>Preference for an even number of response options</i>	<p>"I prefer a 4-point Likert scale personally. Which makes you commit yourself one side of the average." (P8)</p> <p>"But sometimes I think, when you have got a middle ... a middle ground, I would be interested to know, but I probably haven't, but it makes you steer towards the middle ground if you are not quite sure. Rather than making a committed decision." (P21)</p>
Specification of response options	
<i>Preference for severity rather than time</i>	<p>"I just think, if I have had a really bad week, and I have had really severe tightness of the chest for a couple of days, then I find it easier to say - 'yes severely' - rather than - 'a little of the time' . But actually in that time it might have been really severe as well. So I think this kind of gives more of an idea of how serious things are or not serious how things are." (P4)</p>
<i>Subjectivity of interpretation</i>	<p>"I still think that having the three options ... because it is a 'true' or 'not true' or kind of a midway. And it is not a ... you don't have to think. Because everybody's perception of mild, moderate, severe and very severe, it can be quite different. So everybody has their own severity of how they are feeling." (P17)</p>
<i>Ticking a box vs filling a circle</i>	<p>"I found that a bit of a nuisance - where you have to colour in the ... umm ... the circles. And if you go out of it what does that mean? Yeah I found that a bit of a nuisance." (P17)</p> <p>"Yeah, the thing about ... if ... I didn't use a pencil, but if you do fill out the circles and you want to change your answer you would have to sort of cross it out. Whereas with a tick you can just to ... do a simple cross and then tick another box." (P18)</p>

Recall period	
<i>Narrow time frame problematic</i>	<p>“(…) and the questions didn’t have enough space in them for story, they just wanted very narrow time-frames” (P12)</p> <p>“But here - I have felt asthma controlling my life: again not really in the last four weeks. So I like the questions but again maybe the time-frame I couldn’t relate to it completely.” (P13)</p> <p>“(…) for some asthmatics, like myself, I can be very well for quite a number of weeks or even months. And then I can go through a patch of being very unwell. So I think that using a particular time frame isn’t necessarily always helpful” (P2)</p> <p>“Because things like you know, for example asking you to tick activities in the last 4 weeks such as - sorry in the last 2 weeks - in this one, this is the Juniper one in particular - umm - for example, you know gardening, walking, whatever, umm - (a) you may not have done any of these activities in the last two weeks (...)” (P2)</p> <p>“(…) with it being two weeks, and having had a very recent asthma attack, it has increased the severity, maybe, of some of my answers.” (P15)</p> <p>“Yeah. Yeah. Not to me because I couldn’t answer a question there and say ‘no’ in the last four weeks where in actual fact it has happened two months ago, you know, or something like that, you know.” (P19)</p>
<i>Preference for four weeks recall</i>	<p>“Well I don’t know, maybe four weeks is just a bit of a wider space to capture any fluctuations in people’s asthma or their experience of symptoms.” (P12)</p> <p>“I think four weeks, yes I think so. Especially, like I keep saying, especially at this time of year when there are lots of colds and coughs floating around. So yes, four weeks I think is fine.” (P13)</p> <p>“Actually if anything probably I have a wee bit more of an affinity with the ‘Marks’ because it was asking for a longer time period (...)” (P15)</p> <p>“Then I think four weeks, and like the ‘Juniper’ one for two weeks, is quite ... is a real limited time. You wouldn’t get a true picture.” (P17)</p>

<i>Preference for a wider time frame</i>	“I think it should be a minimum of one month. And then there should be another section that should try to get a sense of the patient over the last year. And that should tend to record some of that fluctuation and identify - are there peak times and are they common in other sufferers?” (P22)
<i>Preference for no time frame</i>	“I think I would tend to prefer the ‘Living with Asthma’ questionnaire in that sense, because you can think about how you are generally, rather than a particularly bad or good time. So yes, you can average it out.” (P21)

B. Missing content

General

Participants identified a number of content areas that they thought were missing in the questionnaires. They alluded to the need to seek health care, in particular the need to get medication or pay for it, the need to see a doctor or the need to go into hospital because of asthma.

“There are no questions relating to quality of life in ... with respect to hospital admissions... And having to go in-and-out constantly.” (P1)

It became apparent that participants believed there was a lack of coverage of asthma control and asthma management and that responses to the items would be different depending on how well the asthma was controlled.

“Well I have to say, like I said, the one thing that is missing, is the asthma management of an individual, because that will have a bearing on quality of life - if it is very badly managed.” (P15)

AQLQ-S

With respect to the AQLQ-S, participants specifically spoke about cough, sex life, the need to use medication (having to use an inhaler), family impact, asthma triggers and wheezing attacks as lacking content areas.

“Umm ... there was one questionnaire that talked about it is a nuisance having to take tablets - it is a nuisance having to use your inhaler. I think that is maybe missing from the ‘Marks’ because your quality of life quite often is affected by how many times you have to stop, use an inhaler. (...) That, actually probably affects my quality of life more than anything else.” (P15)

AQLQ-J

Regarding the AQLQ-J, participants named social life, hospitalisation due to asthma, mental well-being, asthma management and family impact as missing content areas.

“(...) if there was anything missing, it would be more about ... err ... how it affects your ... your mental state, your mental wellbeing and ... err ... you know ... it is not very personal I guess.” (P11)

LWAQ

Hospitalisation due to asthma, cough, allergies and environment were mentioned as missing areas with regard to the LWAQ.

“Umm - well there isn't really a lot about allergies, and my asthma is affected a lot by my allergies. And it is not ... it didn't really, sort of ... it was almost like it is for someone who has got asthma just all the time, you know. I do take preventative medicine in the mornings and in the evenings and stuff, but my asthma mainly occurs when I come in contact with animals or with tree pollen or the things that set me off, you see what I mean?” (P1)

Table 18: Codes and illustrative quotes relating to theme “Missing content” (UK sample)

Code	Illustrative Quotes
Missing – general	
Health care needs	<p>“None of them really addressed the fact that, umm - it is actually quite annoying when you are a busy person to have to go to the doctor and get your medication, or to be bothered enough to take it.” (P1)</p> <p>“There are no questions relating to quality of life in ... with respect to hospital admissions... And having to go in-and-out constantly.” (P1)</p> <p>“Paying for medication!” (P1)</p>
Asthma control/asthma management	<p>“(…) so I think maybe having questions on how well you feel your asthma is controlled at the time of the questionnaire is being asked, might be quite useful.” (P4)</p> <p>“Well I have to say, like I said, the one thing that is missing, is the asthma management of an individual, because that will have a bearing on quality of life - if it is very badly managed.” (P15)</p> <p>“Maybe ... if you incorporate ... maybe if you said at the beginning ... can you answer all these questions on the basis that you always have your inhaler.” (P18)</p>
Allergies	<p>“The only question as I went through it there, that hasn’t (and this is common to all three questionnaires) is that it hasn’t separated the allergy from the asthma.” (P12)</p>
Hay fever/sneezing	<p>“There wasn’t much about sneezing in any of the questionnaires, and that is something that I think that isn’t ... that I have a lot of problems with. And I think that is also quite symptomatic to asthma sufferers.” (P22)</p>
Peak flow measurement	<p>“You know ... or the Peak Flow - none of them talked about a peak flow. But actually it takes time to sit and do the best of three, and work it out and put it on the graph. Because that is the way that I know ... if my peak flow is dropping, a lot of the time I can avoid an asthma attack, by having more of the steroids. And that is almost influencing</p>

	the quality of life, and I think actually that has an impact on people. And the ability to be able to do a peak flow (<i>laughing</i>) and having the right equipment. And that really is not mentioned anywhere.” (P15)
Means to improve quality of life	“And also, it didn’t talk about ... fitness in terms of ... it talked about people being limited, but it doesn’t talk about what people do to improve their quality of life. They are all quite ... either it doesn’t affect your quality of life, but none of the questionnaires had anything to find out what people are doing to help.” (P15)
Triggers	“So, yes, that is the other thing: circumstantially another thing that might be useful would be an understanding of how much of it is asthma on its own, and how much of it is asthma caused by a cold or drop in temperature, or an increase in temperature, an infection, or ... or the numerous things that can cause asthma.” (P15) “Well you didn’t mention anything about umm ... food. You know, do you find any ... any ... food or drink affects your asthma. Would you have any ... do you find any ... anything that you know sort of triggers your asthma? Something like that.” (P19)
Top end of scale	“And it is as if gardening is really hard, and for someone like me who is very fit, I find I struggle at the top end of the scale. So if I run, or at the moment because it is winter, and obviously experiencing a bit of a cold, I start getting a tightness of chest if I run or I cycle.” (P20)
Missing AQLQ-S	
Cough	“(...) cough didn’t come up in that questionnaire. (...) Yes, yes because certainly at the moment, err, my cough is the main area in which I feel my life is restricted.” (P8)
Sex life	“(...) the only one that it didn’t have on there, which the other two did, was about sex life. I think maybe that should have been on there (...)” (P13)
Medication needs	“Umm ... there was one questionnaire that talked about it is a nuisance having to take tablets - it is a nuisance having to use your inhaler. I think that is maybe missing from the ‘Marks’ because your quality of life quite often is affected by how many times you have to stop, use an inhaler. (...) That, actually probably affects my quality of life more than anything else. Because I can get half way down the street, on my way to work, and then think ... I haven’t brought my

	orange inhaler! ” (P15)
Family impact	“And the ‘Marks’ and the ‘Juniper’ don’t really talk about the family impact which can then affect guilt.” (P15)
Asthma triggers	“It doesn’t touch on any other trigger of asthma, such as smoking, food, stress and things like that.” (P20)
Wheezing attacks	“The wheezing attacks: more about that. It was very, very brief.” (P22)
Missing AQLQ-J	
Social life	“It didn’t really cover much of the social things...(…) There is a lot of kind of social things that I find a bit difficult or, not embarrassing sometimes, I used to it; but things I don’t like because of it. (...) And I am not too keen on that. And that for me is much more of a problem than not being able to walk up a hill.” (P4)
Hospitalisation due to asthma	“it doesn’t really mention going to hospital, or like, time taken going to hospital appointments” (P5)
Mental well-being	“If there was anything missing, it would be more about ... err ... how it affects your ... your mental state, your mental wellbeing and ... err ... you know ... it is not very personal I guess.” (P11)
Asthma management	“But again, missing ... umm ... was the rest of the management that goes with the asthma. It is not just about a concern for the need for medication or anything like that, it is still avoiding the ... well actually it is quite time consuming to sit in the morning and do this-that-and-the-other and map your peak flow.” (P15)
Family impact	“And the ‘Marks’ and the ‘Juniper’ don’t really talk about the family impact which can then affect guilt.” (P15)

Missing LWAQ	
<i>Hospitalisation due to asthma</i>	“It didn’t really talk about going into hospital with an asthma attack” (P5)
<i>Cough</i>	“And again although the cough features here, it is - ‘I tend to cough at night’. Well I don’t. So it didn’t come out, how asthma is affecting me with the cough; that didn’t really get reflected. Umm ...” (P8)
<i>Allergies</i>	“Umm - well there isn’t really a lot about allergies, and my asthma is affected a lot by my allergies. And it is not ... it didn’t really, sort of ... it was almost like it is for someone who has got asthma just all the time, you know. I do take preventative medicine in the mornings and in the evenings and stuff, but my asthma mainly occurs when I come in contact with animals or with tree pollen or the things that set me off, you see what I mean?” (P11)
<i>Environment</i>	“And they are all very culturally specific. It doesn’t factor in, you know, where people live, if it is countryside or city, if there is more pollution or less pollution.” (P22)

C. Redundant or similar content

Participants perceived some of the items in each questionnaire as redundant or similar.

AQLQ-S

The AQLQ-S has two items asking whether the respondent has been *troubled by episodes of shortness of breath* (item 1) and has been *troubled by tightness in the chest* (item 3), respectively. These two items were thought of as belonging together by one participant. *Having been limited in going to certain places because they are bad for one's asthma* (item 13) and *having been limited in going to certain places because of being afraid of getting an asthma attack and not being able to get help* (item 14) was also perceived as very similar. Likewise the emotional items in the AQLQ-S to do with anger, frustration and worry were perceived as repetitive.

“There often seems to be questions about ... umm ... feeling angry and frustrated with your asthma, and worried and all that kind of thing. And for me they are quite easy questions and I will move on. But I don't know ... they are often repeated quite a lot.” (P21)

AQLQ-J

The AQLQ-J asks whether the respondent *experienced asthma symptoms as a result of being exposed to cigarette smoke* (item 9, or dust in another item) and then goes on to ask whether the respondent *felt having to avoid a situation or environment because of cigarette smoke* (item 11, or dust in another item). These items were perceived as redundant. The many activity items (e.g. doing home maintenance, mopping or scrubbing the floor) were also thought of as being very similar.

‘Washing cars’ ‘doing home maintenance’ ‘doing your house work’ ‘gardening’. I would have thought they could have been more lumped into

one. (...) 'Home maintenance' ... err ... doing home maintenance and doing housework, you know ... they seem very similar, you know." (P19)

LWAQ

With respect to perceived redundancies in the LWAQ, participants mentioned that being limited in where one goes (e.g. item 2 "*When invited round to a friend's house, I worry that there may be something there which sets off an asthma attack.*") to be very similar to being limited in where one goes on holiday (e.g. item 3 "*Having asthma restricts the sort of holiday I can take.*"). "Walking up a hill" (item 37 "*I can walk up a hill as fast as anyone else of my age.*") and "walking up stairs" (item 42 "*I can walk up a flight of stairs without stopping.*") were also perceived as similar as well as the various questions on colds (item 27 "*Because of my asthma I feel drained after a cold.*", item 36 "*Colds don't bother me much*", item 47 "*My colds last longer than other people's*"). The use of positive and negative items was contextualised in a discourse of redundancy (e.g. item 3 "*Having asthma restricts the sort of holiday I can take*" and item 25 "*I can go on the same kind of holiday as everybody else.*").

"So they are kind of asking you - well it is not the same thing twice, but it is obviously similar thing and it is talking about (*pause*) *umm...* 'I feel frustrated at being unable to engage in a sport' - 'I feel I have missed out because there are some sporting activities I cannot join in with'. 'I can run like other people'." (P14)

Table 19: Codes and illustrative quotes relating to theme “Redundant/similar content” (UK sample)

Code	Illustrative Quotes
Redundant/similar - AQLQ-S	
<i>Shortness of breath/tightness of breath</i>	“Well I don’t know what other people experience. Umm, but usually a shortness of breath is automatically accompanied by tightness. And it feels like it is the same question twice.” (P15)
<i>Being limited in going to certain places because they are bad for one’s asthma / being limited in going to certain places because one has been afraid of getting an asthma attack</i>	“I think for example, in this questionnaire, there is a question about - ‘being limited and going to certain places because they are bad for your asthma’ - and then ‘being limited in going because you are afraid of getting and asthma attack’. So they are both about socialising with asthma.” (P21)
<i>Feeling angry/frustrated/worried about asthma</i>	“There often seems to be questions about ... umm ... feeling angry and frustrated with your asthma, and worried and all that kind of thing. And for me they are quite easy questions and I will move on. But I don’t know ... they are often repeated quite a lot.” (P21)
Redundant/similar - AQLQ-J	
<i>Asthma symptoms as a result of dust exposure / avoidance behaviour because of dust</i>	“‘Experience symptoms as a result of being exposed to dust’ - ‘to avoid a situation or environment because of dust’ (P2)”

<p><i>Asthma symptoms as a result of cigarette smoke exposure / avoidance behaviour because of cigarette smoke</i></p>	<p>“Have you experienced asthma symptoms as a result of being exposed to cigarette smoke?’ - I suppose that they are good questions but, like I said, but then about avoiding a situation where there is cigarette smoke.” (P13)</p>
<p><i>Activities</i></p>	<p>“Yes - the activities at the beginning, they are kind of what you have done and been limited by: but at the end it is asking you what you have done and how much you have limited it by. (...)I just wasn’t sure why they were asking it again” (P4)</p> <p>“You see, ‘doing regular social activities’, I suppose yeah ... yeah ... and ‘shopping’. ‘Going for a walk’ and ‘playing sport’ ‘jogging or exercising’. (...)I would have thought they would ... a lot of them seem to be, you know, all ... all the same sort of things. ‘Washing cars’ ‘doing home maintenance’ ‘doing your house work’ ‘gardening’. I would have thought they could have been more lumped into one. (...) ‘Home maintenance’ ... err ... doing home maintenance and doing housework, you know ... they seem very similar, you know.” (P19)</p>
<p>Redundant/similar – LWAQ</p>	
<p><i>Being limited where one goes</i></p>	<p>“(…) there was a question about - ‘am I limited on where I go?’ (...) - and then - ‘am I limited where I go on holiday?’ But they were just in separate places in the questionnaire (...) And it is almost like ...I have already answered this. And I kept thinking as I was answering - ‘am I putting the same thing as I did for the last one?’ ‘Why are they asking me this twice?’ (...) And if, obviously they are measuring consistency, then that is a good option. (...) But it is quite annoying.” (P1)</p>
<p><i>Walking up a hill / walking upstairs and downstairs</i></p>	<p>“But ... (<i>humming</i>)... I think it was about going up and down stairs. Either walking up a hill or walking up and down stairs: the different formats in which the question is asked.” (P8)</p>

<i>Restriction in choice of holiday</i>	“Having asthma restricts the sort of holiday I can take’ - and then later on in the questionnaire it says - ‘I can go on the same kind of holiday as anybody else’.” (P14)
<i>Engaging in sports</i>	So they are kind of asking you - well it is not the same thing twice, but it is obviously similar thing and it is talking about (<i>pause</i>) <i>umm...</i> ‘I feel frustrated at being unable to engage in a sport’ - ‘I feel I have missed out because there are some sporting activities I cannot join in with’. ‘I can run like other people’.” (P14)
<i>Colds</i>	“I am trying to think. There were lots of questions about colds I think. ‘I tend to be more conscious than other people of the early symptoms of a cold’ ‘colds don’t bother me much’.” (P21)

D. Irrelevant content

AQLQ-S

Interviewees did not mention irrelevant content in the AQLQ-S.

AQLQ-J

The emotive wording in some of the items (especially 'feeling afraid') in the AQLQ-J was perceived as irrelevant by one participant who said that she did not get as emotional about her asthma as other people. In the light of the smoking ban, the items relating to cigarette smoke (item 9: *experiencing asthma symptoms as a result of being exposed to cigarette smoke*, item 11: *feeling having had to avoid a situation or environment because of cigarette smoke*) were also perceived as irrelevant. Having to avoid situations because of exposure to for instance perfume was not thought to be pertinent. The items relating to having sexual intercourse (one of the activities to choose from), air pollution, fighting for air, experiencing a feeling of chest heaviness as well as feeling bothered by heavy breathing were also mentioned as irrelevant.

“Err ... I never really get a heavy chest” (P18)

Finally, the activity items (from which participants can choose five items) were perceived as not offering the right choice.

LWAQ

With respect to the LWAQ, the item on smoky restaurants was mentioned as not being relevant any longer. Furthermore, carrying shopping, colds, taking tablets for asthma, the questions on holiday, walking up stairs and getting depressed about asthma were mentioned.

“There were a few questions on, on holiday, which I have never even ... I have never even contemplated not going anywhere on holiday and not going somewhere because of my asthma.” (P18)

One participant (P19) said that while he normally experienced no problems in walking up stairs there was one instance where he did (walking up long stairs in a stadium) and hence he was not quite sure how to respond to this question.

Table 20: Codes and illustrative quotes relating to the theme “Irrelevant content” (UK sample)

Code	Illustrative Quotes
Irrelevant - AQLQ-J	
<i>Emotive wording</i>	<p>“I think such emotive words - although they don’t really apply to me - I am not afraid of not having my medication or anything like that (...)(P1)</p> <p>“It is like - ‘am I concerned about having asthma?’ - and it is no I am not - because I have had it for the last 10 years, and it doesn’t bother me. It doesn’t worry me anymore.” (P4)</p>
<i>Smoking</i>	<p>“And of course it was out of date, because there is a great deal in here on cigarette smoke.” (P3)</p> <p>“I have never worried too much about cigarette smoke, and I have never noticed that that has bothered me, but that might be because the age, well up until I was twenty when I left home, my dad smoked at home and my dad smoked forty-a-day, and we just sat in rooms that were just full of smoke and had layers of cloud and smoke hanging in the air. (...)So, yes, I don’t really avoid anywhere because of cigarette smoke.” (P12)</p>
<i>Avoiding situations</i>	<p>“I don’t feel I have to avoid a situation because of my asthma.” (P4)</p> <p>“Do you have to avoid stuff ... and it doesn’t apply to me. I don’t really go places with strong smells of perfume.” (P10)</p>
<i>Sexual intercourse</i>	<p>“(…) one thing did make me laugh though, about all these things on the ... umm ... on these questions and then having sexual intercourse - no one is going to put having sexual intercourse! People just won’t do it! It is almost irrelevant how they get there” (P11)</p>
<i>Air pollution</i>	<p>“- ‘weather’ ‘air pollution’: I have never noticed bothering me” (P12)</p>

<i>Fighting for air</i>	<p>“Umm, I don’t ‘fight for air’ in the last two weeks.” (P12)</p> <p>“I have a feeling of fighting for air’ - I think ... umm, I don’t know ... I remember ... I have gone to A&E before and I had a peak-flow of 90 at it was horrible. But I guess when you have had it a long time you ... yes it is not nice but I have never been one of those people who needs a brown paper bag and is told to calm down. So that question I just think, well that doesn’t say anything about me really, because I don’t think I ... I don’t think it is relevant.” (P21)</p>
<i>Heavy chest</i>	<p>“Err ... I never really get a heavy chest” (P18)</p>
<i>Heavy breathing</i>	<p>“Umm, I feel bothered by breathing difficulties, you know. Or constricted breathing or something like that, you know, rather than heavy breathing. So yes, that was that.” (P19)</p>
<i>Activity items</i>	<p>“Yes, but they are not the choices that I would have ... they are not the things that I would have put down as choices. So I wasn’t really able to choose the right things, if that makes sense.” (P22)</p>
Irrelevant – LWAQ	
<i>Smoky restaurants</i>	<p>“(…) when they asked about being in a smoke-y restaurant, that doesn’t apply anymore, because you are not allowed to smoke in restaurants in this country.” (P1)</p> <p>“Like - ‘an evening out can be ruined if the restaurant is smoky’. It just doesn’t apply any more.” (P11)</p>
<i>Carrying shopping</i>	<p>“(…) carrying shopping doesn’t really come into it very much!” (P8)</p>
<i>Colds</i>	<p>“I wouldn’t ... as the ‘Living with Asthma’ questionnaire spoke a lot about colds ... a few questions are about colds. I have never really been affected by colds.” (P18)</p> <p>“And so ... I don’t ... that is ... I don’t feel ‘drained after a cold’ ... my cold just turns into a chest infection.” (P19)</p>

<i>Taking tablets for asthma</i>	“No. I don’t think so. I could relate to pretty much ... I think there was one maybe ... oh yes. I didn’t ... I don’t ever take tablets for asthma, so I didn’t ... I put in ‘not applicable’.” (P18)
<i>Holiday</i>	“There were a few questions on, on holiday, which I have never even ... I have never even contemplated not going anywhere on holiday and not going somewhere because of my asthma.” (P18)
<i>Walking up stairs</i>	“I didn’t like to sort of say, but that one ... I have only ever had one case, number 42: ‘I can walk up the stairs without stopping’. Well I put ... umm ... true because I can, I don’t stop. Except this one particular case... (..)” (P19)
<i>Sad/depressed</i>	“And I also don’t see, again, how relevant ... again it was number 60 - ‘I often get depressed about my asthma’” (P22)

E. Confusing/difficult content

AQLQ-S

The items “*I have felt that asthma has prevented me from achieving what I want in life*” (item 11), “*I have felt asthma is controlling my life*” (item 17) and “*I have been restricted in walking up hills and doing heavy housework because of my asthma*” (item 5) were perceived as confusing or not meaningful.

“And - ‘I have felt that asthma has prevented me from achieving what I want in life’ - I could have actually put ‘very severely’ or ‘not at all’ – equally.” (P3)

One participant (P20) mentioned that the word ‘troubled’ which is often used in the AQLQ-S was unclear, because it could mean emotional trouble or physical trouble caused by symptoms.

AQLQ-J

In the AQLQ-J, picking a few activities to assess was perceived as difficult by one participant. It was felt that item 23 *experiencing asthma symptoms as a result of the weather or air pollution outside* (as opposed to cold weather) was a difficult item as most people are not really aware of levels of air pollution.

“Umm, I think in the Juniper, one question I thought was slightly, umm, not exactly strange but ... difficult to answer. You know - ‘Are you ...?’ ‘Do you have ... have you experienced asthma symptoms as a result of weather or air pollution outside?’ - you know, most people aren’t really aware of air pollution (...) you don’t go out and think - ‘oh it is very polluted today’ - how could you answer that?” (P2)

The final two questions asking whether one was *limited in the overall range of activities that one would have liked to have done* (item 31) versus *whether one was limited in all the activities that one has done* (item 32) was perceived as confusing. The fact that activities were asked for at the beginning as well as at the end also caused confusion. The item asking whether one *felt afraid of not having one's asthma medication available* (item 21) was problematic because it was unclear what "asthma medication" referred to. One participant contrasted ventolin and seretide. The items *feeling afraid of getting out of breath* (item 27) and *feeling having had to avoid a situation or environment because of strong smells or perfume* (item 28) were also perceived as difficult. *Experiencing a wheeze in one's chest* (item 10) was perceived confusing because the symptomatology of asthma varies and not everyone with asthma gets a wheeze.

LWAQ

With respect to the LWAQ, *feeling angry with one's body* (item 9) was perceived as confusing like the item *whether one would get emotionally upset when puffy* (item 32). Participants mentioned that this item was not English to them and that they had no idea what this meant.

"I get emotionally upset when puffy' - and I had no idea what that meant (...) If it was in relation to maybe taking the inhaler or taking steroids and being ... I just thought it was quite ambiguous" (P5)

The item on worrying what *one's condition will be like in 10 years' time* (item 57) was perceived as very wordy by one participant. *Never feeling fed up because one has asthma* (item 20) was perceived as confusing because the precise reason for feeling fed up was perceived as unclear (fed up because one can't do activities, fed up because one has to take medicine). Patients were unsure about the item on *taking good care to avoid doing things which make one's asthma worse* (item 5) as well as the item on *having a good future ahead of oneself* (item 50). *Being able to walk up a flight of stairs*

without stopping (item 42) was perceived as problematic because one participant said this depended on the length/height of the stairs.

Table 21: Codes and illustrative quotes relating to the theme “Confusing content” (UK sample)

Code	Illustrative Quotes
Confusing - AQLQ-S	
<i>Having felt that asthma has prevented one from achieving what one wants in life</i>	“And - ‘I have felt that asthma has prevented me from achieving what I want in life’ - I could have actually put “very severely” or “not at all” – equally.” (P3)
<i>Having felt that asthma is controlling one’s life</i>	“I wasn’t sure whether or not that was saying, you know, it was saying - ‘having asthma is controlling my life’.” (P12)
<i>Having been restricted in walking up hills or doing heavy housework because of asthma</i>	“You see I didn’t answer that one: ‘I have been restricted walking up hills and doing heavy housework’. I suppose really ‘not at all’ unless you want me to include that one particular time. Put ‘not at all’” (P19)
<i>‘Troubled’</i>	“The word ‘troubled’ as well, I get concerned about the word troubled. Because that could be ‘I am troubled’ from a symptomatic perspective or is it having an emotional ‘troubled’ effect on me? So it doesn’t really define itself very well.” (P20)
Confusing - AQLQ-J	
<i>Choice of activities</i>	“Umm, the Juniper questionnaire, umm, I think picking a few activities is quite difficult, umm, in some respects” (P2)

<p><i>Experiencing asthma symptoms as a result of the weather or air pollution outside</i></p>	<p>“Umm, I think in the Juniper, one question I thought was slightly, umm, not exactly strange but ... difficult to answer. You know - ‘Are you ...?’ ‘Do you have ... have you experienced asthma symptoms as a result of weather or air pollution outside?’ - You know, most people aren’t really aware of air pollution (...) You don’t go out and think - ‘oh it is very polluted today’ - how could you answer that? (...)You would have no ... realising ... weather perhaps, you know if it is very cold sometimes you are more aware and it makes you cough a lot more etc. But I think air pollution is an almost impossible question to answer” (P2)</p>
<p><i>Being limited in the overall range of activities that one would have liked to have done</i></p> <p>vs.</p> <p><i>Being limited in all the activities that one has done</i></p>	<p>“And then at the end, they were asking you an overall - I think overall - I found this a little bit confusing: think of the overall range of activities that you would have liked to have done during the last two weeks. How much has your range of activities been limited?” (P14)</p> <p>“And 32 - and ‘overall among all the activities you have done, how limited have you been by asthma’. So I suppose everything you would have liked to do, and then everything that you actually did.” (P14)</p> <p>“And the ‘Juniper’ one, just these last questions, were a bit like ‘What?’ - questions 31 and 32.” (P14)</p> <p>“I found question 31 and 32 quite difficult to distinguish as well. I had to kind of really re-read them and think about the differences between those questions (...) Yes, 31 talks about thinking about the overall range of activities that you would like to have done during the last two weeks, and how much you have been limited by your asthma. And then it is saying, of the range of activities that you have done how limited were you? So that is what you would like to have done and that is what you have done. So initially that is quite similar.” (P21)</p> <p>“There was one where I found it difficult - this I found it ... you know, do you fill them both out ...? This is the ‘Juniper’ on 31 and 32.” (P22)</p>
<p><i>Feeling discomfort or distress as a result of chest tightness</i></p>	<p>“Yes, well again I was not quite sure what that question [about chest tightness] refers to. Does it refer to that sense of lung capacity be restricted and lung lining being irritated. Or does it refer to that kind of muscular experience of restriction in the chest,” (P12)</p>
<p><i>Feeling afraid of not having one’s asthma medication</i></p>	<p>“‘Afraid of not having your asthma medication available?’ I wasn’t quite sure what that refers to - which medication. Because I have a ventolin inhaler but I don’t even know where it is, it will be in a cupboard</p>

available	somewhere. So if that question relates to carrying ventolin then no I am not at all bothered about whether I have my ventolin with me. But if it is a question about seretide, then yes. And if I go away for a weekend and I don't have it with me, then I think - 'oh shit I haven't got it with me!'" (P12)
Feeling afraid of getting out of breath	"Do I feel afraid of getting out of breath?' Umm ... I kind of feel a little bit nervous about being around pets and things. But actually I get out of breath most days if I am cycling hard or something; so no I am not quite sure what that relates to." (P12)
Feeling having to avoid a situation or environment because of strong smells or perfume	"Do you feel that you have to avoid an environment because of strong smells or perfumes?' Umm - I am not quite sure what that question is. I do have to avoid environments that smell of cats and dogs, but I suspect that question means synthetic smells and perfumes and not quite sure what that question is." (P12)
Being limited by asthma	"How limited have you been by your asthma? Well I have been limited about where I can live, which seems quite substantial and significant, but I am not sure that is what that question is asking. I think it is asking about, you know, did it stop you running for a bus?" (P12)
Experiencing a wheeze in one's chest	"And they talk about it as if it is a wheeze? Not everybody has a wheeze with asthma. I don't get a wheeze I get chest heaviness." (P20)
Confusing – LWAQ	
Feeling angry with one's body	"(...) to feel angry with your body is quite a strange thing to say (...)" (P1) "I feel angry with my body' - I didn't ... I found those quite weird (...). It kind of off-put me a bit (...). But I have never put it down to my body, and I have never thought - not really angry - I just thought that was a really weird question to answer, it was really weird." (P5)
Getting emotionally upset	"I get emotionally upset when puffy" (P1) "I get emotionally upset when puffy' - and I had no idea what that meant (...). If it was in relation to maybe taking the inhaler or taking steroids and being ... I just thought it was quite ambiguous" (P5)

<i>when puffy</i>	<p>“I get emotionally upset when puffy’ - what does that mean?” (P11)</p> <p>“I get emotionally upset when puffy’ - well that doesn’t ... that is not English is it? That is not ... that doesn’t mean anything, really does it? ‘I get emotionally upset when puffy” (P19)</p>
<i>Worrying what the condition will be like in ten years’ time</i>	<p>“I worry about what my condition will be like in ten years’ time?’ - very wordy” (P1)</p>
<i>Feeling fed up because of having asthma</i>	<p>“I never feel fed up because I have asthma’ (...)and I didn’t understand if it meant for me, did it mean fed up because I can’t do activities, or do I feel fed up because I have got to take medicine, or do I feel fed up ... I didn’t understand what it was asking from me.” (P5)</p>
<i>Taking good care to avoid doing things which make one’s asthma worse</i>	<p>“Umm, I was a bit unsure about question 5: ‘I take good care to avoid doing things which might make my asthma worse’.” (P12)</p>
<i>Having a good future ahead of oneself</i>	<p>“Do I feel I have a good future of ... (<i>frustrated sigh</i>) ... like ... was it ... do I think I have a good future ahead of me. And it is almost like I said, with my career and my personal life I feel I do, but in the back of my head it is my asthma, so I do worry about that really.” (P13)</p>
<i>Being able to walk up a flight of stairs without stopping</i>	<p>“Well I suppose when they ask you ... umm ... what sort of ... umm ... well err ... hang on ... if you can walk up a flight of stairs. And then you realise that you did have a situation where you couldn’t walk up some stairs, but the reason was because they were extremely long and extremely high.” (P19)</p>

F. Irritating content

General

Questions around depression as in the AQLQ-S and the LWAQ were perceived as irritating and patronising by one participant.

LWAQ

The item asking whether one felt angry with one's body (item 9) which was already perceived as confusing by some participants also had an irritating effect. Likewise the item on sexual frustration (item 56) was felt to be irritating and invasive.

"The 'sexually frustrated because of my asthma' is a very invasive question. I didn't particularly care about it but I could see how some other people could find that very invasive and again wouldn't expect that." (P22)

Table 22: Codes and illustrative codes relating to the theme "Irritating content" (UK sample)

Code	Illustrative Quotes
Irritating – General	
Depression	"(...) the questions around depression are not what you would expect when you fill out an asthma questionnaire, because people again, get depressed for many different reasons. And I felt that was a bit patronising." (P22)
Irritating – LWAQ	
Feeling angry with one's body	"In the 'Living with Asthma' questionnaire is a really difficult one to ... to ... it is quite a ... one could feel angry with one's body for many different reasons and again, I felt that was too limiting and wasn't quite the right ... I was a bit put off by that. I found it a bit, you know, presumptuous." (P22)
Feeling sexually frustrated	"The 'sexually frustrated because of my asthma' is a very invasive question. I didn't particularly care about it but I could see how some other people could find that very invasive and again wouldn't expect that." (P22)

<i>because of one's asthma</i>	
---	--

G. Layout

AQLQ-S

Participants judged the layout of the AQLQ-S in a positive way. They emphasised that it was simple and clear and that there was just the right space between the boxes. They also liked the lines between the questions.

AQLQ-J

Participants did not particularly like the use of capital letters in the AQLQ-J. One participant also said that the use of bold words was not very clear. The repetition of the header on each page in the AQLQ-J was perceived as annoying by one participant. However, one participant said that the AQLQ-J was the most professional questionnaire in terms of layout.

LWAQ

The clarity of the AQLQ-S was contrasted with the layout of the LWAQ which was perceived as busy or even “noisy”. Filling in the circles was perceived as cumbersome and the font was perceived as too small. Some participants spoke of the LWAQ as being poorly presented overall.

Table 23: Codes and illustrative quotes relating to the theme “Layout” (UK sample)

Code	Illustrative Quotes
Layout AQLQ-S	
<i>Simplicity and clarity</i>	<p>“The ‘Marks’ one I thought was - I like its blank plain simplicity” (P12)</p> <p>“(…) and it is nice and open and it is easy to read.” (P15)</p> <p>“But other than that ... so in terms of ease of filling out the ‘Marks’ was the easiest to fill out and the clearest layout (…)” (P22)</p>
<i>Lining</i>	<p>“That one is favourite, that one on the Marks Asthma is my favourite because it is just, there are lines in between them as well, which makes it simpler. So you know which question goes where.” (P11)</p> <p>“And I like the layout of the ‘Marks’, just because it has a line under each one and you know where you are (…)” (P15)</p> <p>“Although I think the lines help in the ‘Marks’, having the lines there helps to distinguish the questions.” (P22)</p>
<i>Space</i>	<p>“There is nice spacing between the boxes.” (P11)</p>
Layout AQLQ-J	
<i>Bold words</i>	<p>“And the fact that they “bolded” some words actually, I found that some of the words that they bolded weren’t actually highlighting what I thought they wanted to highlight” (P1)</p>
<i>Use of capital letters</i>	<p>“And I didn’t like this going in and out of upper and lower case. I don’t even understand it.” (P12)</p> <p>“I found it was quite an odd, certain things, there was small writing and then it went to capital letters.” (P13)</p> <p>“I don’t know how much detail you want, but I really didn’t like the capital letters.” (P21)</p>
<i>Repetition of header</i>	<p>“The next one, which is the ‘Juniper’, it kind of annoyed me that all this information, this header, was there again and again. And I kind of almost wanted to start filling it in and - oh no it is that again. Why is that there over and over, it seems superfluous and it is just clutter on the page?” (P12)</p>

Professional layout	“Probably the one that looks the most professional from a user point of view, would be the ‘Juniper’, because you have got the first page which tells you what it is and it looks quite professional doesn’t it really?” (P15)
Layout LWAQ	
Busy	“But presented like that, it looks very different; it is all a bit noisy and cramped; way too much instruction too” (P12) “Umm ... it’s the ‘Living with Asthma’ questionnaire is just very busy on the eye. There is a lot of information presented on each page which is great because, you know, it condenses down and if you are going to stick it in a computer then that is absolutely fine.” (P15)
Circling cumbersome	“I am relatively young still, but if I were an older person I think I would really find it very difficult. I found it difficult to put the circles in properly, because you obviously have to put circles in.” (P22)
Poor presentation	“This questionnaire, umm, is very poorly presented” (P1) “And actually it is pretty horrible, and that might be partly (...) Partly because it is just a bit of a rough photocopy, and it has been forced onto two pages on to an A4. I don’t know if that was its original design. And it has got a lot of noise on it. I don’t know what -all these lines down the corner and on the side and some rubber stamp has been put on it. Maybe if it were a bit crisper in an A4 format that might have looked a lot more manageable, next to these.” (P12)
Small font	“I can’t read it - the print is too small” (P3) “(…) you know, the font is quite small, not very clear, so that is not maybe an ideal set out.” (P13) “This is very small, and I know I have lost my glasses, but I was a bit struggling. And you have got to imagine that a number of people of my age and above and below, have vision impairment of some form, so that would be a little bit difficult.” (P20)

H. General perceptions

AQLQ-S

Many participants mentioned that the AQLQ-S was quick and easy to complete, and that it was an unambiguous questionnaire.

“So it is short, and it is probably less tiring for the individual to fill out, but it gets all the bases covered.” (P10)

Interviewees shared the view that the AQLQ-S had a focus on the social, attitudinal and emotional rather than the medical aspects of asthma.

One participant thought that one needed to be very emotive about one's asthma to be able to relate to the AQLQ-S and that it was relevant to a section of people with extreme asthma only. Participants mentioned that questions were widespread and related to everyday life.

“OK so I found that good because it covers everything again, sort of your mental health, your physical health and your day-to-day activities. It has got everything I want.” (P10)

However, some interviewees felt that the brevity of the questionnaire meant that it lacked both breadth and depth of coverage. It was described as “simplistic” or “light”.

AQLQ-J

The AQLQ-J was perceived as an asthma-specific ‘medical’ questionnaire with environmental focus and focus on activities. These foci were perceived as narrow by some participants, but as pertinent by others.

“(...) this one just isn’t as thorough for some reason, umm, and it is more sort of, it is more sort of, I think this is more sort of you can tell it is more of a medical questionnaire rather than a ‘well-being’ questionnaire.” (P11)

“So it is very much about the symptomatic side and the environmental thing which is a good touch.” (P20)

Being able to choose five activities was perceived as positive in that it added an individualised component to the questionnaire and made people think about those areas that are important to themselves. However, other participants found it difficult to choose five particular activities or thought that people would not choose the activities truly important to them in order to create a good impression. The way the AQLQ-J read and the manner in which it needed to be completed (several pages) was irritating for some interviewees and yet one participant described it as a simple questionnaire. Redundancies were noted with respect to activity items.

LWAQ

There was a strong perception that the LWAQ was a ‘holistic’ and ‘non-medical’ questionnaire with a focus on social and emotional aspects of asthma. A number of participants said that the content coverage of the questionnaire was wide ranging and that it was a thorough, in-depth questionnaire.

“Yeah, and there are more questions in there I think about, umm - like emotional and you know, stress and anxiety. So - and also things like about getting embarrassed and things like that. That ... I don’t think people generally ask those questions, but it is quite - it is a very valid question. Because there are certain things that you don’t ... that people don’t want to talk about.” (P17)

There was also a perception that the LWAQ was irritating because it actually created problems by its emotional focus and even that it was an invasive questionnaire. It was also described as too long, partly because of the perceived redundancies. The instructions were mainly seen as excessively

long although one participant said that they were fairly clear. Completion was felt to be burdensome by some participants, in particular because of the phrasing of response options (untrue of me/slightly true of me/very true of me) and the use of positive and negative items. However, the latter was also spoken about in a positive way, and one participant emphasised that this made him think a lot harder. Overall the questionnaire was perceived as 'noisy' and to some interviewees felt like a "test" or "quiz". This was contextualised in relation to both its layout and again the use of positive and negative items.

"So the 'Living with Asthma' questionnaire I thought it was good, it was more like psychometric testing (...) Just in the way that it asks you positive and negative and asks you to switch backwards and forwards between the answers on those things." (P20)

Table 24: Codes and illustrative quotes relating to the theme “general perception” (UK sample)

Code	Illustrative Quotes
General AQLQ-S	
Non-medical focus	<p>“And the sort of social - can’t say economic - but the sort of social type things. The other two are more geared towards the medical” (P1)</p> <p>“And it is talking - this one is perhaps a bit more about your mood - if you felt sad or depressed, or if you felt frustrated - if you felt anxious or under tension - if you have felt that asthma is preventing you from achieving what you want from life.” (P14)</p> <p>“(…) it is speaks a lot about my attitude towards asthma” (P18)</p> <p>“And it is very about emotions. It is not about practicality or symptomatic or how it effects ... can it limit you? It is purely - ‘Am I worried? Do I feel generally restricted? Do I feel it is controlling my life?’” (P20)</p> <p>“So it cuts out, I think this concentrates on the extreme: people with extreme asthma, as those are the ones that would have an emotional response to it.” (P20)</p>
Simplistic/light	<p>“The Marks Statement is a little bit simplistic” (P2)</p> <p>“I think the ‘Marks’ asthma quality of life questionnaire was (<i>inaudible</i>) because it was quite light.” (P20)</p>
Quick and easy	<p>“Well what was nice about this one, was that is much quicker to fill in (...) very straight forward” (P3)</p> <p>“It was simple to complete” (P8)</p> <p>“But nonetheless it is short - short and sweet in a way” (P8)</p> <p>“So it is short, and it is probably less tiring for the individual to fill out, but it gets all the bases covered.” (P10)</p> <p>“I felt that I answered this one quite quickly, because the questions were easy to understand” (P13)</p> <p>“It is simple. It is really simple and there are boxes and there is a simple description at the top. You don’t ... bosh! Done!” (P14)</p> <p>“‘Marks’ - nice and easy, and you just tick it la-la-la-la-la and job done.” (P15)</p> <p>“(…) less ambiguity I think in the ‘Marks’ questionnaire. It is just simple short statements” (P21)</p>

<i>Related to everyday life</i>	"I thought the questions were more related to my everyday life as well" (P5)
<i>Wide ranging content</i>	"This one is very general questions, just to say how you are feeling and what you are doing: shortness of breath: and what ... how many ... the doctor ask you about how much you are breathless or what you are doing" (P9) "The questions again are very relevant for me, they are very wide-spread. It is your general life style" (P10) "OK so I found that good because it covers everything again, sort of your mental health, your physical health and your day-to-day activities. It has got everything I want." (P10) "But it does cover everything that is covered in the other questionnaires, but perhaps it is in slightly less detail." (P14)
<i>Lack of coverage</i>	"Yeah, there ... yeah there are a lot of things not covered I guess." (P16) "I think these are all quite good questions, but what I would say is that it is too brief a questionnaire." (P22)
<i>Lack of depth</i>	"But I felt ... I felt that it was very, very brief and umm ... it didn't really allow me to go into any depth." (P22)
General AQLQ-J	
<i>Medical focus</i>	"I think that really the Juniper is much more medical about - 'coughing' 'clearing throat' ..." (P1) "do I feel I have to avoid situations' - and it wasn't too emotional - going into emotions" (P5) "I mean, I think that this one ... deals more with the physical side I think." (P7) "(...) this one just isn't as thorough for some reason, umm, and it is more sort of, it is more sort of, I think this is more sort of you can tell it is more of a medical questionnaire rather than a 'well-being' questionnaire." (P11)
<i>Environmental focus</i>	"So it is very much about the symptomatic side and the environmental thing which is a good touch" (P20)
<i>Asthma-specific</i>	"(...) went into the asthma specifics: like heavy breathing, clearing your throat, chest heaviness" (P5) "The Juniper. It is not looking at real life, it is more specific questions about specific things" (P10) "This one was a bit more specific. About cigarette smoke, the environment, dust, heavy breathing, perfume." (P14)

Narrow	<p>“I thought it was a little bit sort of narrow, in some respects” (P2)</p> <p>“There’s ... it covers bases but it is not really what day-to-day life consists of. So it is quite - well it doesn’t cover what it needs to I don’t think (...) Yes, I mean in this - the Juniper - it was, like I said, it was not tailored to me at all. It was questions that were, as far as I am concerned, irrelevant” (P10)</p> <p>“Yes this one focussed - I found that this, the ‘Juniper’ one focussed quite a lot on maybe things that were reactive for your asthma. So you know, smoke, dust and things like that, which they are a problem for some people with asthma, but then other people don’t have the same triggers. So by limiting that there, I think you probably wouldn’t get as broad spectrum of answers.” (P17)</p>
Pertinent	<p>“Mmm ... with Juniper I don’t think so, because it did actually capture the whole of my experience” (P8)</p> <p>“I said it looks like they knows how I feel at home, when I am living with the heavy asthma” (P9)</p>
Focus on activities	<p>“(...) is more what I would say - it asks you to focus on activities rather than general quality of your life”</p>
Choice of activities positive	<p>“it was good being able to choose activities” (P5)</p> <p>“I liked the different approach. It enabled me to pick the areas that I wanted to discuss, albeit only one set of questions fall into that (...)The variety is what makes it interesting, right at the beginning” (P8)</p> <p>“What I liked about this one is that it was - you had to think about the important activities for you, and I liked that. Because it actually made me think about, you know, how asthma does affect different things.” (P15)</p> <p>“I liked the fact that it was individualised and you could pick those out first of all.” (P21)</p>
Difficult to choose activities	<p>“There is a lot more that affects my life rather than activities that I can’t do” (P4)</p> <p>“So it was a struggle to find 5, to be honest” (P8)</p> <p>“I found this a bit too vague, especially where it says: ‘pick five from the last two weeks’” (P13)</p> <p>“The only one that really struck me, like I said, was the ‘Juniper’ and I felt that people may not necessarily choose the activities that are important to them because they want to give a different perception, to maybe the honest truth. Which we all do, don’t we? Everybody wants to give a good impression, so you wouldn’t necessarily write the truth.” (P15)</p> <p>“And err ... and just ... yes I just found ... I just found it a very (<i>chuckles</i>) eclectic and very weird mix.” (P22)</p>

<i>Irritating</i>	<p>“And err ... it is a bit ... off putting for some vague reason, and I don't know why (...)Perhaps because it doesn't read like a sentence - it is reading - it just reads a bit strangely” (P2)</p> <p>“Oh yes! Every one of them! The Juniper one is irritating by the way you have to fill it in. (...) Yes, yes I did. I found physically filling the questionnaire in difficult, because they wanted me to move from one page to another.” (P3)</p>
<i>Simple</i>	<p>“I thought the questions were quite ... you know ...the questions that were here on this one were quite good, and you know ... quite simple, which was good” (P11)</p>
<i>Redundancies</i>	<p>“Well what I am trying to say is you could probably cut that down to maybe half, if you married them up. Because, err ... sort of vacuuming and mopping or scrubbing the floor, and I can't really see a lot of difference between that, you know. And err ... 'doing maintenance' and then you have got 'woodwork' or 'carpentry' ... err ... to my mind they are virtually the same aren't they, you know?” (P19)</p> <p>“It does repeat itself a little bit.” (P20)</p>
General LWAQ	
<i>Non-medical focus</i>	<p>“That is much more about the emotional ... umm, impact of having a chronic disease” (P1)</p> <p>“And the sort of social - can't say economic - but the sort of social type things. The other two are more geared towards the medical” (P1)</p> <p>“And not that you ... there is an assumption, particularly in that questionnaire, that - yes particularly in that questionnaire - that, umm, your asthma is all about emotion (...) It is very emotive: it assumes you are absolutely loopy” (P3)</p> <p>“I feel like it is asking more holistic questions.” (P12)</p> <p>“I don't know, there is a lot more in this questionnaire about feelings.” (P12)</p> <p>“It feels more coherent and it seems to have context.” (P12)</p> <p>“Yeah, and there are more questions in there I think about, umm - like emotional and you know, stress and anxiety. So - and also things like about getting embarrassed and things like that. That ... I don't think people generally ask those questions, but it is quite - it is a very valid question. Because there are certain things that you don't ... that</p>

	people don't want to talk about." (P17)
Wide content coverage	<p>"That was very limited I think, yes. So ... the Juniper was a bit more, umm, err, (<i>pause</i>) but not particularly wide-ranging. So ... in effect perhaps the Highlands has more, umm, of a range of questions I think" (P2)</p> <p>"They vary - I just feel this one here captured everything. Although there is 66 questions" (P7)</p> <p>"But the number of questions meant that it addressed a wider range of umm, of aspects (...) So I felt it was more thorough" (P8)</p> <p>"So it was an in-depth one" (P10)</p> <p>"So it wasn't sort of just focussing on your mental state or your physical state, it was everything combined" (P10)</p> <p>"That was really thorough, umm and asked both about your physicality and your mentality" (P11)</p> <p>"And it went into quite a lot of detail, which is good." (P14)</p> <p>"You know, yeah, and it was very comprehensive, there were a lot of questions, umm, a lot of questions." (P15)</p> <p>"The questions on it ... they were a little bit ... they were ... there was a lot more variation in the questions so they spoke about sleep, they spoke about sport, general living and your medication which I think was probably the most important thing personally." (P18)</p> <p>"It covers more ground and I just think it is more thorough." (P20)</p>
Use of positive and negative items	<p>"Saying things like - 'I find it easy to carry shopping' - and then next page it is all - 'I don't...' and 'I feel tired so I never ...' - so it is asking positive statements and then negative statements which (...) which messes a bit with your mind (...) So it is the flipping between the negative and the positive questions that is definitely a little bit confusing (...) The flipping from negative to positive statements." (P2)</p> <p>"'I never worry that going on hospital (<i>holiday</i>) can make my asthma worse' - I would rather it have a -'I worry that going on holiday can make my asthma worse' - it is the negative. It made me think a lot harder about that one" (P5)</p> <p>"But because some of them are double negative questions, you have to re-read them to make sure that you have got it right." (P8)</p> <p>"I think they are almost worded in two different ways. It is like - 'I feel fed up with asthma' - 'I get emotional when puffy' - so it is 'I don't' and then 'I do' so I think that is what I mean. I struggled sometimes, and I had to read it again to make sure I had answered it correctly. But I like the statements but maybe they should almost have it in</p>

	<p>the same tense.” (P13)</p> <p>“And some of the questions here were a bit - because of the negative. Let me find an example (<i>pause</i>) I found some of them a little bit weird. When it is a negative - ‘I never feel fed up with my asthma’” (P14)</p> <p>“You wonder (<i>pause</i>) there must be a reason for them asking those questions, that are slightly different but the same way round. So I don’t think it is repeating it, but I did notice that you are asked a similar thing on a few occasions.” (P14)</p> <p>“Like they have got like double negative; negative things in the questions, and you could quite easily make a mistake and say true instead of false or vice versa.” (P16)</p>
<i>Irritating</i>	<p>“Umm ... I ... yes, so if you want to take them individually, this one I found very emotive, very irritating” (P3)</p> <p>“But it’s making ...it is making something out of ... it seems to me it is trying to make problems (...) Create issues that actually for most people are simply not there. You just crack on. You know.” (P3)</p> <p>“All ties in with those very invasive questions, that I felt weren’t really necessary. That was in the ‘Living with Asthma’ one.” (P22)</p>
<i>Too long</i>	<p>“It is too long. Umm, most of it is not ... it is just ... not relevant.” (P3)</p> <p>“The Hyland - it was possibly a tad too long.” (P10)</p> <p>“(..)the ‘Living with Asthma’ is quite long-winded (...) Because you know, as soon as you limit your answers to three, either extremes or whatever it is, it is like, you know, you are limiting yourself then. I think that is why the questions were may be a bit woolly, and you know, went on a bit I think, and that is because they give you a limited amount of answers.” (P11)</p> <p>“I wouldn’t ... I wouldn’t like to say that I would agree that this length of questionnaire is right for everybody. I don’t think it was right for me really.” (P19)</p> <p>“I thought the ‘Living with Asthma’ questionnaire probably a little long, with I don’t know, sixty-eight questions. I think anyone looking at sixty-eight questions would probably balk at the idea. Because people just don’t like filling in forms.” (P20)</p>

Burdensome	<p>“The Highland Questionnaire, I did find quite a burden: to have to complete something and keep having to read the responses: untrue of me/slightly true of me - to remind me what I am answering.” (P1)</p> <p>“And I just think an older person who someone who is really ill or not super-super literate or dyslexic, would really struggle to fill that out.” (P22)</p>
Redundancies	<p>“Because the reason the others are longer is that they are asking the same thing in many different ways (...) repeat-repeating.” (P1)</p> <p>“It does repeat itself a little bit.” (P20)</p>
Instruction	<p>“long explanation of how to tick boxes at the beginning was really confusing” (P5)</p> <p>“But I think that amount of explanation is a bit over-the-top.” (P12)</p> <p>“And the instructions were fairly clear.” (P21)</p>
Noisy	<p>“But presented like that, it looks very different; it is all a bit noisy and cramped; way too much instruction too” (P12)</p>
Like a test/quiz	<p>“I thought they were ... erring, almost like ... a couple of them were almost there to catch you out in a way.” (P11)</p> <p>“The only think I didn't like about it was, like it felt like it was a school exam, where they ... because they are obviously going to put it through a computer and scan it, and actually sometimes when you are doing these you just want to tick a box” (P15)</p> <p>“Although I personally (as I said before) some of the questions are backwards, so it is umm (<i>chuckle</i>) sort of like it trying to be an intelligence test or something.” (P16)</p> <p>“Well because this is quite confusing, it is much better to have a situation where you have a box where you can, you know, I would find this ... umm ... a bit like a puzzle ... a Sudoku or something like that, where you know, you're sort of worrying more about what the answers are up here than the answer there and then making sure that you do it in the right box.” (P19)</p> <p>“So the 'Living with Asthma' questionnaire I thought it was good, it was more like psychometric testing (...) Just in the way that it asks you positive and negative and asks you to switch backwards and forwards between the answers on those things.” (P20)</p>

I. Comparative aspects

Interviewees made a number of statements comparing the different questionnaires. The AQLQ-S was situated between the AQLQ-J and LWAQ because it was partly a “social” and partly a “medical” questionnaire. It was emphasised that the LWAQ dealt worse with symptomatology but also that it was the questionnaire which was most reflective of the impact of asthma on quality of life. The AQLQ-S was considered to be concise and “short and sweet”. In comparison to the AQLQ-S and the LWAQ being able to choose activity items was again seen as an advantage of the AQLQ-J.

Table 25: Illustrative quotes relating to theme “Comparative aspects” (UK sample)

AQLQ-S	AQLQ-J	LWAQ
“The Marks is sort of a medium [between AQLQ-J and LWAQ]. Because it is asking about ‘wheezing attacks’ ‘shortness of breath’ - but it is also addressing the prevention of achieving or being able to do what you want to do (...) So that sort of part social/part medical ” (P1)		“Umm, I think the Hyland is probably the least ... favourite of my questionnaires. It is much ... the questions ... there are many more questions” (P2)
“I think that the Juniper and the Marks deal better with symptomatology than ... umm... than this here, the Hyland” (P1)	“I think that the Juniper and the Marks deal better with symptomatology than ... umm... than this here, the Hyland” (P1)	“So I think some of those questions are very apt. Umm, whereas some of the ... the Marks one is very simplistic I think.” (P2)
“I think ... this one is better than - what is this one? [AQLQ-S] (...)more easy to kind of relate to, than all of these kind of ... ‘all of the time’ ‘some of the	“Whereas the ‘Juniper’ starts off with you whittling down five activities so it makes it very relevant to you.” (P21)	“This one [was more difficult to complete], only because of the way they were asking for answers” (P9)

time' 'a little of the time' [AQLQ-J]" (P4)		
"That [AQLQ-S] was more accurate than the 'Living with Asthma' questionnaire (...) There are not so many of the emotional questions." (P5)		"So, it kind of seemed to be a bit more accessible to my experience." (P12)
"It - this one compared to the first one [LWAQ], is more concise. But then again it feels exactly what it needs to ask." (P10)		"But in a sense I also quite like the fact that it doesn't have this narrow time-frame and it is a bit more embracing." (P12)
"I think, like I said, Marks was my favourite because it was short and sweet almost." (P13)		"Maybe, or maybe if you are older or with worse eyesight, never mind your asthma, you might find that this one is a bit more difficult to complete. Or, if you are not feeling very well, so people are doing a study and they are not very well, they might prefer to fill in something a bit quicker." (P14)
"I would say the 'Marks' questionnaire was obviously the easiest ... the easiest to fill out." (P18)		"then the 'Living with Asthma' questionnaire could possibly be of a lot more use to a consultant, because it would give them a more general idea about your lifestyle and where you ... yeah" (P15)
		"And if it is living with asthma and it is a quality of life living with asthma, then probably that was the most reflective of your quality of life and the impact of asthma on it." (P15)

4.5 Discussion

The qualitative interview study presented here is novel in two respects. First, a study using an in-depth approach involving patients to provide views on asthma-specific questionnaires in terms of format and content has not yet been conducted. Second, the study is unique in that several questionnaires are used together, adding a comparative component.

4.5.1 Summary of findings

Summary of findings from the German sample

In Germany, ten adult patients with asthma from the Rhine-Neckar region were included and demonstrated a range of diverse views with respect to format and content of three commonly used asthma-specific QoL questionnaires. The majority of participants expressed a preference for three or five response options, and considered limited recall periods as inappropriate for acute or fluctuating asthma. Patients mentioned that a more specific definition of the response option labelling (such as “some of the time”) would be desirable. Colds, environmental triggers factors (such as allergies or climate) and the restrictions arising from the ongoing dependence on medication were mentioned as missing areas of concern in the questionnaires. At the same time, items pertaining to sexual frustration and depression were perceived as irrelevant, being short of breath was perceived as self-evident. Redundancies were described with respect to items enquiring about asthma symptoms because of a certain exposure (dust, smoke)/items asking about the necessity to avoid certain situations because of that exposure in the AQLQ-J and the use of positive and negative items for the same content in the FLA. Despite the diversity of views expressed, participants mostly agreed on the ranking of the questionnaires and – overall – favoured the AQLQ-S.

Summary of findings from the UK sample

The study conducted in the UK included 22 adult participants with asthma from the Brighton and Hove area on the south coast of England. Participants likewise expressed a wide variety of views in relation to format and content of the three questionnaires. The entire thematic framework that had emerged from the German sample was relevant and could be applied to the UK sample. However, data was richer and more themes emerged from the analysis, probably due to the larger sample and a refined interviewing technique. The thematic framework that had emerged from the German interviews was thus both expanded and enriched. New themes identified were “confusing content” and “irritating content”. Chest tightness, feeling emotionally upset when puffy or feeling angry with one’s body caused confusion in the participants’ perception. The emotional focus of the LWAQ as well as the use of positive and negative items were perceived as irritating by some participants. Whilst it was felt to be burdensome to complete and described as a “test” or “quiz”, a recurrent theme was that the LWAQ was a wide-ranging, embracing and holistic questionnaire.

In contrast, the AQLQ-J was perceived as a ‘narrow’ ‘medical’ questionnaire with a focus on symptoms, environment and activities. The choice of activities was perceived to be positive by some and difficult by others. The AQLQ-S was described as a simple, quick and easy questionnaire, but there was also a perception that it lacked depth at the same time. Overall, the AQLQ-S was situated ‘between’ the AQLQ-J as a ‘medical’ questionnaire and the LWAQ as an ‘emotional’ questionnaire.

4.5.2 Differences and similarities between the two parts of the study

Some differences between the two parts of the study need to be mentioned. First, the German equivalent to the LWAQ is not a linguistically equivalent questionnaire of the original but a revised and shorter version. The original AQLQ-J was used in the UK while the standardised AQLQ-J was used in Germany. Hence participants shared views on the possibility to pick activities

in the UK only. Caution was taken in the German interviews to administer the questionnaires in different orders in the interviews, in order to account for potentially differing perceptions according to which questionnaire was first completed (“ordering effect”). However, because this approach stems from the quantitative research paradigm and the in-depth approach was used to make sure issues were explored in relation to all three questionnaires, administering the questionnaires in differing orders was abandoned for the UK interviews. Participants were explicitly asked to rank the questionnaires in Germany, so means could be calculated for each questionnaire (table 14). However, this was also not felt entirely appropriate in a qualitative framework and could be potentially seen as forcing patients to make a choice when in fact they might wish to share a more balanced view. Therefore, patients were not asked to explicitly rank the questionnaires in the UK part of the study. The thematic framework that emerged from the German part of the study was applied to the data from the UK and expanded. Important new themes which emerged from the UK sample were “confusing/difficult content” as well as “irritating content”.

Response format

Participants were ambiguous with respect to having an “n/a” option in both Germany and the UK. Although there was a perception that more response options were better and allowed respondents to capture the continuum of ‘very little’ to ‘extreme impairment’ more effectively, the common theme was that seven options were too many in both locations. Unease was expressed with respect to both the meaning of the response option labelling and narrow time frames in both countries. However, a preference for the use of either four weeks or using no time frame emerged more clearly in the UK. Participants spoke about their preference for ticking a box rather than filling a circle in the UK only. The German revision of the LWAQ, the FLA, uses boxes, not circles.

Missing content

The missing contents that emerged from the German sample did also emerge in the UK data but the UK data allowed for a more detailed analysis of what was missing in the particular questionnaires. Whereas the German interviewees talked about the restrictions arising from the ongoing dependence on medication the theme extended to asthma management in a more general sense in the UK sample, including asthma control by medication and self-monitoring (by peak flow measurement for instance), as well as the necessity to see a doctor or go to hospital. While the latter imposes a burden in terms of time and effort for the individual patient, the former has several aspects. The dependence on medication represents quality of life impairment in itself as it is a constant reminder of suffering from a chronic illness. Taking the medication and doing peak-flow measurements takes time and may not always be compatible with work and/or social life. Thirdly, and importantly, a quality of life profile may look entirely different if the asthma is well as opposed to poorly controlled.

Redundant or similar content

Participants alluded to redundant or similar content in relation to all three questionnaires in both localities. A recurrent theme in both samples was that the questions about asthma symptoms from certain exposures (such as dust or cigarette smoke) and having to avoid situations because of these exposures were perceived as redundant in the AQLQ-J/AQLQ-J-s. The perception of the use of positive and negative items as creating redundancies in the LWAQ/FLA was another common theme.

Irrelevant content

Items pertaining to feeling depressed or sexual intercourse were mentioned by participants in both samples. Overall, a greater number of items perceived to be irrelevant emerged from the UK sample. One important difference was

that the items relating to cigarette smoke were recurrently mentioned by participants in the UK, but not in Germany. This certainly reflects the differing regulations with regard to smoking. While a comprehensive ban on smoking came into force in England in 2007, there is no comparable comprehensive smoking ban in Germany but regulations differ between federal states. The state of Baden-Württemberg in which the participants of the German sample are living allows people to smoke in restaurants or bars if there is a separate room.

Layout

In both samples, the layout of the AQLQ-S was perceived in a positive way and contrasted with the layout of the AQLQ-J/AQLQ-J-s and LWAQ/FLA. For instance, while the AQLQ-S was perceived to be presented in a clear way, participants in both samples mentioned that they did not like the parallel use of small and capital letters in the AQLQ-J/AQLQ-J-s.

4.5.3 Ideas for improving the questionnaires

The findings from this qualitative interview study suggest potential avenues for improving the questionnaires. This pertains for instance to the recall period which was often judged to be inadequate. Other important findings pertain to the number of response options and the question format. Three or five response options compared to seven seemed to be preferred by patients in both studies. Seven options were often perceived as too many as they require a very fine graded patient response. Also, participants preferred ticking boxes rather than colouring circles and they expressed a desire for clarity both in layout and labelling of the response option.

In general, there is a lack of evidence with respect to the functioning of different rating scales in the literature. A study looked at the functioning of a wide range of rating scales found in 17 different PROMs which were

developed to measure the impact of cataract and/or outcomes of cataract surgery (158). Results showed that items with a simple question format, a uniform question format, four or five categories and labelled categories were more likely to be functional. They often showed hierarchical ordering, even utilisation of categories and a good coverage of the latent trait under measurement. Other studies have found that PROMs with a larger number of categories and complicated question formats are more likely to have a dysfunctional rating scale (159-161). One of these studies for instance found that five-point scales outperformed 10-point scales in a randomised comparison of item scaling for the Patient Experiences Questionnaire (159).

This evidence resonates with the findings presented above: the question format should be clear and uniform and the number of response options should be limited to a maximum of five.

Items perceived as redundant could potentially be merged into one, for instance the questions in the AQLQ-S which ask about being limited in housework or being limited with respect to hobbies because of asthma/shortness of breath. Another example where items might potentially be merged into one are the items on having symptoms as a result of a particular exposure and avoiding situations because of that exposure in the AQLQ-J. However, it is important to bear in mind that the content of the items is indeed different. Being limited in housework is different from being limited in one's hobbies and being limited in light housework is also different from being limited in hard housework. The same is true for experiencing symptoms as a result of dust exposure and the need to avoid a situation because of dust exposure.

The redundancies identified around the use of positive and negative items in the LWAQ/FLA should be viewed in a different way. A study examined the performance of negatively and positively phrased items in questionnaires measuring perceptions of children and parents pertaining to oral HrQoL in children(162). It found that the positively worded items elicited substantially more "Don't know" responses or missing values compared to the negatively worded items and also did not discriminate between groups. In addition, the

two item sets (one consisting of the positively worded items and one consisting of the negatively worded items) loaded onto different factors when factor analysis was applied. It was concluded from this study that the use of positively worded items was not satisfactory and that their use to reduce acquiescence bias needed to be questioned. This evidence in connection with the patients' views in the qualitative study presented here, would justify omitting and/or changing the positively worded items in the LWAQ/FLA.

4.5.4 Lost items

When patients spoke about missing items, accounts were mostly centred around factors which trigger asthma such as cough, allergies or odours. Patients also felt that the impairment arising from asthma control was missing. With regard to the latter, one may argue that asthma control is a different construct measured by different patient-reported outcome measures such as the Asthma Control Questionnaire (ACQ) (163), the Asthma Therapy Assessment Questionnaire (ATAQ) (164) or the Asthma Control Test (ACT) (144). These measures assess the degree to which asthma is controlled. The patients' views, however, suggest that items assessing restrictions experienced in connection with having to use regular medication should be part of an asthma-specific quality of life measure. This notion is different from an asthma control measure.

The initial process in questionnaire development normally involves patients (usually through interviews or focus groups) generating an item pool, i.e. a large number of areas of concern or bother. The size and heterogeneity of the item pool is a result of the different subjective experiences of individuals with the same disease.

Item reduction techniques (such as factor analysis or reduction by importance scores) are then used to produce questionnaires with an acceptable number of items that can be administered and are easy to use. Hence, items are necessarily lost, and it is therefore not surprising that

patients talk about missing content when asked to reflect on existing HrQoL questionnaires.

The findings from this study reflect the tension between objective measurement and subjective experience. A questionnaire development process will always yield a questionnaire with items that are judged as most important by patients or which contain items that form an internally consistent dimensional structure.

In the original development of the AQLQ-J-s, the importance method was used. The original item pool was later reanalysed using factor analysis, and it emerged that the two methods of analysis lead to differential selection of items when applied to the same list of potentially troublesome items (127). The emotional and environmental items with the highest impact were actually discarded when factor analysis was used. In summary, however, both methods discard items from a pool of potentially relevant items.

4.5.5 Strengths and weaknesses of this research

Patients are usually involved in the development of a questionnaire, but in-depth patient involvement ceases as the questionnaire development process progresses. In a “rush to measurement” (165) detailed in-depth research often seems to be sacrificed. The use of focus groups and interviews in the development of PROMs has been given relatively little attention in the PROM literature compared to the many quantitative articles on psychometric properties (166). The studies presented here have generated evidence for the much needed guidance with respect to choice of instrument. This evidence can also be considered a starting point for the potential de novo development of an asthma-specific QoL questionnaire with greater content validity compared to the existing ones.

In the structured literature review presented in chapter two (148) sources used for item generation for the questionnaires were reviewed among which qualitative methods are mentioned (patient interviews for the AQLQ-J, focus

groups for the AQLQ-S and the LWAQ). It needs to be acknowledged that the development of all the questionnaires involved qualitative work with patients. However, the question "Which questionnaire is most valid from the patients' perspective?" can only be answered by eliciting patients' views on the final questionnaires. Taking this stance represents the novelty of the qualitative studies presented here. It was their aim to elicit patients' views on the end-product-questionnaires to understand issues patients might have with design and content of commonly used asthma-specific questionnaires.

Although the number of patients in the German sample was limited, patients with a range of socio-demographic and clinical characteristics were included using four different recruitment channels. In the UK, likewise, patients with a wide age range and variability in disease duration were interviewed as evidenced by their demographic characteristics (chapter 4.4). However, it must be acknowledged there was a female preponderance and that the sample is of White British origin with only one female reporting an ethnic minority background.

The interviewer in the German study was a female master-level student in Public Health and presented herself as such, the interviewer in the UK study was a male PhD student and presented himself as such. Both interviewers were close in age to some of the interviewees which may have helped to reduce the power differential and increase rapport. The interviewer in the UK study had asthma and hay fever as a child and adolescent, and still suffers from hay fever and various allergies to aero-allergens. He shared his experience with some of the interviewees which may have helped in increasing rapport, but perhaps he had stronger assumptions about the questionnaires compared to someone without the experience of asthma and allergies. This was especially the case in relation to the lack of content pertaining to allergies and asthma control. Having experienced varying impact of symptoms in different periods of the year but also in relation to varying expectations over time, the interviewer in the UK held the view that symptoms per se should not be part of an asthma-specific QoL questionnaire. An effort was made to minimise any impact of such a priori assumptions on the interviews.

Open discussion may have been impeded had the interviewers been medical doctors or nurses. The research team included an epidemiologist, respiratory consultants, a psychologist and an academic GP with long-standing experience in health services research. Therefore, a diversity of perspectives was brought to data interpretation.

Interviews and not focus groups were chosen for this study because interviews are more suitable for sensitive issues and because it would have been very difficult to find a time slot to bring participants together. However, it cannot be excluded that different or additional themes may have emerged in focus groups as group interaction may have enriched the information generated by helping people to explore and clarify their views (167-169).

Another interesting technique which seems to be suitable for this kind of research is “think aloud” (170, 171). “Think aloud” is a form of cognitive interviewing in which participants are asked to verbalise all thoughts that would normally be silent when completing a questionnaire. Participants are asked to talk about what they are currently thinking about and not asked to explain or comment on their thinking. Unlike traditional qualitative interviewing, this method involves less dialogue between interviewer and respondent and may lead to the elicitation of purer thoughts. However, respondents may also mention less areas of concern to them when not probed as in qualitative interviews. In this context, a further study using the “think aloud” technique would be interesting, allowing a comparison of findings with the findings from the interviews presented in this thesis.

Caution needs to be exercised when generalising findings from this study. Generalisability as conceptualised in empirical quantitative research is not usually sought in qualitative research which seeks theoretical but not empirical generalisability (157). However, it was very interesting to see that most of the themes emerged from both sets of data. One reason for this is certainly the fact that the thematic framework at least partly reflects the interview topic guide. The thematic framework created from the UK data represents an extension of the thematic framework created from the German data set. It includes themes such as ‘irritating content’ which were not

included in the topic guide initially. It remains speculative to what degree the inclusion of more men would have changed the thematic framework. Albeit common themes were identified in Germany and in the UK, particular caution needs to be exercised with regard to cultural settings very different to European culture, such as Asian or African settings.

4.5.6 Similarity to other published work

In a qualitative assessment of the most widely used health status questionnaire, the Short-Form (SF) – 36 Health Status Questionnaire, some important problems were revealed (172). The study explored how older people with chronic health problems interpret the questions used in the SF-36. Like in the study presented here, participants considered some of the questions as vague, for instance “Can you walk half a mile?” or “How about lifting or carrying groceries?” It was unclear to the participants how far half a mile would actually be, and the question about groceries doesn’t make clear how heavy these are (by for instance saying “a bag of groceries”). In the German sample, for instance, questions about activities such as swimming or decorating were likewise described as vague. In the UK sample, a large number of items caused confusion in participants, such as ‘having been restricted in walking up hills’ in the AQLQ-S, ‘chest tightness’ in the AQLQ-J or ‘getting emotionally upset when puffy’ in the LWAQ. It is very important that questions are phrased in an unambiguous and clear way.

A study was performed to assess the Oxford hip score (OHS) from the patient’s perspective using unprompted annotations which were written on the OHS by patients (173). The OHS is a widely used, joint specific measure to assess disability in patients who undergo total hip replacement (THR). The study found that patients experienced five main areas of difficulty: lacking question clarity (in particular pertaining to the use of aids), difficulty in reporting pain, restrictive and irrelevant questions, the influence of co-morbidities and double-barrelled questions (i.e. questions containing two

questions in one, such as “have you had any trouble getting in and out of a car or using public transport because of your hip?” in the OHS).

There is a resonance between the findings from the OHS study and the findings from the presented asthma study in four areas of difficulty. In the OHS study patients were unsure whether they should report their actual disability level or the disability level taking the use of aids or specialised devices into consideration, i.e. whether they should report actual or relative disability. In the study presented here patients were unclear about asthma control, i.e. whether they are asked about impairments due to asthma or impairments when asthma is controlled. The second resemblance is that patients in the OHS study found it difficult to report an average level of pain as pain is a dynamic rather than a static entity. In the asthma study patients likewise reiterated the dynamic nature of asthma by alluding to its fluctuating nature. As reported a number of items were perceived as irrelevant and allergies, coughs and infections were mentioned as co-morbidities influencing responses.

The OHS study could be critiqued because annotations were only made by 17 % of patients. However, earlier qualitative work also raised concerns about the clarity, coverage, and content validity of the score (174).

Items not being relevant or important to all individuals and performing certain activities being non-stable are phenomena which occur with many validated patient-centred outcome measures (173). It does indeed reflect the tension between the subjectivity of the PROMs and the nomothetic claim to “measure”. The authors suggest to weight items according to their importance which would allow to generate a more individualised outcome measure.

4.5.7 Implications

The findings from the qualitative study presented highlight the need to involve patients iteratively in questionnaire development and to listen to them

until the very end of that process. However, the patient's view needs to be balanced with a research perspective. For instance, clinical trials often have limited timeframes and are expected to demonstrate effects over the period of the trial. Hence, the choice of recall period often depends on the purpose of the research, even though participants in this study perceived short recall periods as inadequate. One participant thought that asking about being depressed or sad was irrelevant but depression has been found to affect both asthma control and quality of life (175). This means that while single patient perceptions provide valuable insights their views may not represent what is known from epidemiological studies.

Based on the findings from the interviews, the AQLQ-S seems to be the questionnaire with the best rating from the patients' perspective and seems most appealing in terms of format and response options at the same time. Interestingly, the aforementioned structured review (chapter 2) including a quantitative assessment of the questionnaires also suggested the AQLQ-S to be the most promising questionnaire (176) which should hence be recommended for clinical practice and research. However, there may be reasons for using the AQLQ-J/AQLQ-J-s in multinational studies as it exists in many different languages. The LWAQ/FLA might be considered if there is a particular interest in the psychological aspects of suffering from asthma. Future research will need to explore patient responses in other cultural or language settings and will benefit from involving a larger and more diverse sample.

5 Discussion of thesis

The starting point of this thesis was the fact that at least six adult asthma-specific measures of health-related quality of life exist, and that it is unclear which of these measures is most valid in capturing the impact asthma has on the quality of life of those affected. Three different approaches were chosen in this thesis to investigate the validity of asthma-specific quality of life questionnaires: a structured literature review, a psychometric analysis and a qualitative study.

The main finding from the structured literature review presented in chapter 2 (148) was that the questionnaires show important differences when standard criteria (conceptual and measurement model, reliability, validity, interpretability, burden, administration format and translations) are used to review them. It can therefore not be assumed that they measure the same thing. Of particular concern is the lack of conceptual frameworks for the measures.

In order to be able to better assist in guiding the choice of instrument for a given purpose it is of importance to gain a more comprehensive understanding of the content validity of the questionnaires. One way of doing this is to compare the contents using an established reference such as the ICF (45). The ICF is based on a conceptual framework (biopsychosocial model of functioning, disability and health) and also provides a detailed classification system allowing to explore the contents of a given instrument in a comprehensive, standardized and transparent way. Such a comparison has been done for instance using stroke-related quality of life measures (177). Two hundred different ICF categories were used to map 979 concepts identified in six generic and seven stroke-specific HRQoL measures. It was found that none of the ICF categories was contained in all of the instruments. "Emotional functions" was the most frequently used category overall. "Mental functions" were more often addressed by stroke-specific measures while the generic instruments more often included "Environmental Factors". Closer to our research is a content comparison of HrQoL instruments for COPD which

also used the ICF as a reference (178). The eleven instruments which were compared varied strongly with respect to the number of concepts they contained and also the number of ICF categories that were used to map the concepts. The only single category which was covered by all instruments was “dyspnoea”.

A similar comparison against the ICF would be useful to map the concepts contained in the asthma-specific measures. Both the psychometric analysis (chapter 3) and the findings from the qualitative study (chapter 4) indicate that the AQLQ-J has a greater focus on symptoms, activity limitations and environmental factors compared to the AQLQ-S and the LWAQ. A concept mapping exercise would allow to further investigate the relative importance of different concepts in the different measures.

Since the structured literature review presented in chapter 2 (148) was published two other attempts have been made to review PRO instruments for asthma, one in the UK and one in the USA.

The Patient-reported Outcome Measurement Group (POMG) in England has completed a comprehensive structured review of patient-reported outcome measures for people with asthma which was reported to the Department of Health (152). The difference to the review reported here is that it does not only encompass asthma-specific quality of life measures, but also measures of health status, asthma control, utilities and symptoms. Twenty-two asthma-specific measures were evaluated. Based on the volume of evaluations and good measurement and operational characteristics the AQLQ-J (57), the AQLQ-J-s (67) and the mini AQLQ-J (66) as well as the AQLQ-S (59) were presented to a multidisciplinary panel for discussion. The mini AQLQ was recommended as an asthma-specific instrument. Its ease of use and patient acceptability as well as the good concordance between postal and supervised administration was considered to be an important characteristic for measuring outcomes in NHS clinical care.

Despite the fact that its reduced responsiveness meant that its use would be limited in a research context the instrument was considered to be acceptable for use in clinical practice.

The POMG report is neglectful of the conceptual differences and overlaps between the measures under consideration. It does not seem to compare like with like which may be related to the aim of choosing a measure suitable in determining the quality of services in the NHS. It is coherent with this aim to compromise between measurement properties and ease of use which led to recommending the mini AQLQ. If validity is considered a 'unitary' concept as proposed by the *Standards for Educational and Psychological Testing* (124) then the requirements should however not be different for measures used for monitoring or clinical practice as compared to research.

The second important review comes from the United States. In the light of a lack of adequate outcomes standardisation several National Institutes of Health (NIH) institutes supporting asthma research as well as the Agency for Healthcare Research and Quality in the US have agreed to make an effort towards outcomes standardisation. As part of this effort, the published documentation relating to asthma-specific quality of life (QoL) measures was reviewed (135). In this review, the existing instruments were classified as follows:

- *Core outcomes*: "selective set of asthma outcomes to be considered by participating NIH institutes and other federal agencies as requirements for institute/agency-initiated funding of clinical trials and large observational studies in asthma"(135)
- *Supplemental outcomes*: "asthma outcomes for which standard definitions can or have been developed, methods for measurement can be specified, and validity has been proved but whose inclusion in funded clinical asthma research will be optional"(135)
- *Emerging outcomes*: "asthma outcomes that have the potential to (1) expand and/or improve current aspects of disease monitoring and (2) improve translation of basic and animal model-based asthma research into clinical research. Emerging outcomes may be new or may have been previously used in asthma clinical research, but they are not yet standardised and require further development and validation"(135)

The US review is more comprehensive than the review presented in this thesis (148) in that it identifies eleven instruments for adults and six instruments for children. The instruments reviewed that are used for adult study populations were the ABP (99), the Asthma Impact Survey (133), the AQLQ-J-s (67), the mini AQLQ-J (66), the LWAQ (69), the modified AQLQ-S (179), the Asthma Short Form (134), the SGRQ (62, 63) and the AQ-20 (179).

None of these fell into the core outcome category because they mainly measured asthma control (symptoms and/or functional status), failed to yield a distinct and reliable score which measures all dimensions central to the intended construct, and/or they lacked adequate evidence of psychometric properties. The authors strongly recommended to develop and evaluate measures that provide a distinct and reliable measure of the patient's perception of the impact of asthma on all of the dimensions central to QoL.

In line with the stance taken in this thesis, the US review conceptualises QoL as the perceived impact that asthma has on the patient's QoL and distinguishes it from asthma control, signs and symptoms of asthma or health status all of which are partly or fully incorporated in the asthma-specific measures available. Because there is no instrument available that truly assesses QoL, the questionnaires reviewed entirely fall into the categories "emerging" or "supplemental".

Comparing our review to the US review we did miss the ABP, the Asthma Impact Survey and the Asthma Short Form. The mini AQLQ-J, the modified AQLQ-S and the AQ-20 which were included in the US review were not included in our review as we had excluded any derivatives of original QoL questionnaires. The US review, in contrast, does not include the Rhinasthma and the QOL-RIQ which is obvious as these were not developed in English language. Like our review, the US review does not report a systematic search algorithm. Furthermore, it does not provide any guidance as to how to further choose between those measures classified as either "supplemental" or "emerging". For the time being choosing from existing questionnaires

requires a compromise based on the rigour of the development process and the target patient group (176).

In order to choose a questionnaire amongst those existing I propose a two-step algorithm and advise to (1) classify the measure and (2) assess its adequacy and robustness. A model-based classification system for health outcome measures has been introduced in chapter one. Within this framework a measure is classified along the axes “construct”, “population” and “measurement” (43). Robustness of a measure is assessed in terms of its measurement properties (validity, reliability and responsiveness to change). Adequacy can be assessed by looking at the degree of patient involvement in item generation, time needed to completion and whether there is guidance on interpretability (e.g. minimal important difference (87)).

Applying this algorithm, in the short term I recommend the use of measures which are solely designed for asthma such as the Sydney Asthma QoL Questionnaire (60) or the Living With Asthma Questionnaire (57). However, for use in multinational studies it may be convenient or practical to use questionnaires that have been linguistically validated in many languages such as the (standardised) Juniper Asthma Quality of Life Questionnaire (57, 67) or the St George’s Respiratory Questionnaire (63).

Evidence for the construct validity of all the measures considered in the structured review of chapter 2 has been published, mainly by reporting estimates of reliability (test-retest, internal consistency) and performing correlational analyses with similar or different constructs or studying known-groups validity. This evidence has been summarised in tables 2 and 3. Validation, however, is an ongoing process and evidence for the validity of a measure needs to accumulate over time (124). In particular, it is not clear that a measure which proves valid for one population (e.g. people with asthma in Canada) is also valid in another population (e.g. people with asthma in the UK). This led to the study presented in chapter 3 which adds to the evidence base supporting the validity of the mini version of the AQLQ-J and the AQLQ-S. Weak or absent correlations of the two measures with lung function parameters suggest that these questionnaires measure a construct

distinct from a physiological, objective outcome like lung function. Discriminant validity of the two measures was evidenced by their ability to discriminate between levels of asthma severity and health care usage. However, the strong correlations with asthma symptoms and asthma control raise questions about overlap of the constructs of quality of life as operationalised in the mini AQLQ-J and the AQLQ-S with the construct “symptoms” and the construct “asthma control”, supporting the notion that current existing questionnaires focus more on symptoms, functional status and asthma control rather than perceived impact of asthma. Any findings however, from this psychometric study, are limited. Although 99% of patients with asthma in the UK are managed in primary care the findings from the study are not generalisable to the whole population of people with asthma because the sample excluded patients older than 45 years of age and patients with very severe or difficult-to-treat asthma. Secondly, the RCT was not designed as a validation study so the power calculations were made without consideration for reliability or validity analyses.

While the structured review gives a summary of the properties of the existing questionnaires and helps orientate the user, the psychometric analysis generated some new evidence for the construct validity of two particular QoL measures and shows which constructs these measures are close to. Ultimately, however, it is only consumers who can tell to what degree existing measures adequately capture the lived experience of having asthma. It was therefore decided to conduct a qualitative study which involved participants in Germany and the UK. The findings of this qualitative study (n=32) can further help to guide the choice of instrument as, despite the diversity of views expressed, the AQLQ-S was perceived to be the most advantageous questionnaire and was situated between the AQLQ-J as a ‘medical’ questionnaire and the LWAQ as an ‘emotional’ questionnaire. This resonates with the finding from the quantitative quality assessment in the literature review and the recommendation given in this discussion section. The findings from the qualitative study also demonstrate avenues for improvement of the questionnaires, in particular with respect to layout, number and clarity of response options and confusing and/or irritating

content. However, perhaps the most important finding was that interviewees likewise spoke about missing and irrelevant content in the questionnaires. So just as the content covered was irrelevant to some respondents but not others, some participants spoke of content that was missing from the questionnaires but others did not. Any findings from the qualitative study must be set against the fact that the thematic framework which was generated mirrors the analytical framework as reflected in the interview topic guide. This is certainly the case for any interview study which uses semi-structured interviews. A study using open interviews may have generated different and/or more themes. However, the analytical framework of the topic guide was expanded, particularly when the data collected in the UK were analysed. "Irritating content", for instance, was a category that had newly emerged and was not represented in the topic guide. Also, the codes subsumed under each broad theme reveal the richness of the data and had not been previously expected. In general, we know little about the impact of different analytical qualitative techniques on the conclusions reached.

The finding that items on a given scale are unimportant, or irrelevant, to some respondents, has been noted in other areas such as osteoarthritis (173, 180). The tension between missing and irrelevant content may be interpreted as a feature of PROMs. It has been noted in the area of hip replacement that no single activity is important to all individuals nor is the importance of being able to perform that activity stable over time (181).

The varying weights and values which respondents attach to the contents covered by quality of life questionnaires have led several groups to develop instruments that reflect individuals' priorities (182). One such instrument is the *patient generated index* (PGI) of quality of life (183), originally validated in people with low back pain (184). Its conceptual basis is not a narrow definition of impairment and disability but Calman's definition of quality of life as "the extent to which our hopes and ambitions are matched by experience" (185). The PGI is completed in three stages. First, patients are asked to specify the five most important areas of life affected by their condition. In stage two, patients are asked to rate how affected they are in each of these areas on a scale from 0 to 100 with 0 representing the worst they can

imagine for themselves and 100 representing a state in which they would like to be. In a sixth box patients rate all other areas of their life (either areas of their life which are affected by their medical condition but not important enough to be included in the five boxes in stage one as well as areas of their life which might be unrelated to their condition or even their health). Finally, patients are given “points” to “spend” across one or more areas that they would most like to improve. Patients are asked to imagine that areas receiving no points remain unimproved. The index is generated by multiplying the ratings for each area by the fraction of points given to that area. The score then represents the extent to which reality matches expectations (=quality of life), exactly in those areas of life in which patients most value an improvement.

However, difficulties in understanding and completing the PGI have been observed and a low response rate has been reported when the index is given to patients as a questionnaire for self-completion (183). It seems that interview administration is necessary at least at the initial stage of assessment (186), which may limit its use in routine health service settings as well as postal surveys. Concerns have also been addressed about the use of the PGI in clinical trials on grounds of poor practicality (187). It must be noted that the paper in which the AQLQ-J-s is described states that in large clinical trials “the ease and convenience of standardized questions may outweigh the benefits of individualized questions” (67). It is also argued that for cross-sectional surveys in which burden of illness is compared between groups of patients standardised questions are preferable.

In conclusion, although the PGI (and similar approaches like the schedule for the evaluation of individual quality of life, abbreviated to SEIQoL (181)) offers an interesting approach to overcome the failure of standard quality of life measures to address the diversity of concerns patients have and that they might adapt, there are limitations in terms of applicability.

Where do we go from here?

Based on our literature review (148), the review done by the expert group convened by the National Institutes of Health (NIH) institutes and other federal agencies in the US and in the light of the patients' voices, research is necessary to develop and validate a new asthma-specific quality of life measure. The need to move forward and develop new quality of life measures has been noted for measures in other areas such as the Dermatology Life Quality Index (DLQI) (188), the most widely used measure of HrQoL in skin disease (189).

The ideal stages in developing a measure as proposed by the FDA guidance draft document have been described in chapter 2.4. It is not sufficient to just follow the proposed steps. A prerequisite, and important difference in comparison to the development of the existing measures, is that meticulously documented qualitative and advanced quantitative methods need to be used in order to ensure content validity. This is advocated by leading PRO measurement experts in the Patient Reported Outcomes Measurement Information System (PROMIS) initiative (190). While the FDA guidance document (32) emphasises the patient's perspective in PRO development, a PROMIS paper states that in practice often a combination of patient and expert input is used. What is important is that the process is well documented, so that the sources from which the items were derived are being made explicit. In particular, often very little information is given with respect to the qualitative research that leads to deriving initial items for QoL measures. In the light of this an overarching phenomenological theoretical framework with grounded theory data collection and analysis methods has been proposed to yield PRO items and scales that have content validity (166). Thorough qualitative work may lead to conceptual models which are different from those implicit in many measures of HrQoL. For instance, the analysis of transcripts from patient interviews conducted during the development of the Quality of Life in Depression Scale yielded a needs-based model of QoL (191).

McKenna argues that a needs-based approach to QoL assessment has advantages for the measurement of impact of disease and treatment (192). Within a needs-based concept, items are developed which do not enquire about function directly, but enquire about the needs satisfied by a particular function. McKenna refers to the example of items enquiring about sexual performance which are often judged as irrelevant or unacceptable, a finding which is corroborated by the findings from the qualitative study in this thesis. The needs-based approach would enquire about needs related to sexual activity, such as love or intimacy, instead. It also deals better than existing measures with the fact that patients with chronic illnesses often adapt to their illness and whilst being restricted in certain activities may still maintain good QoL, for example by using aids or replacing activities they can no longer do with other activities that might equally fulfil their needs. The tension between missing and irrelevant content that emerged from the qualitative study (chapter 4) may be resolved by re-conceptualising the content of the examined asthma-specific questionnaires within a needs-based model in a new measure.

Another thorough approach of interest, that has been taken in the development of a conceptual and measurement model to understand the burden of low back pain, was to hold concept mapping workshops with patients, professionals and international experts in which a nominal group process was used to maximise the richness and depth of the data obtained (193). The concept mapping processes went to great length in order to be as exhaustive as possible and reach saturation.

Besides using rigorous qualitative research as the foundation for PRO development (166), psychometric analysis needs to go beyond classical test theory for PRO validation (188). Item response theory (IRT) is now considered the gold standard (194, 195). The use of IRT as measurement theory allows modelling that provides detailed information about dimensionality, response categories and differential item functioning (DIF). When the above mentioned DLQI was subjected to Rasch analysis, an IRT model, it became evident that it suffered from item bias, i.e. significant DIF (196-198). This means that item responses are affected by external factors

such as age, gender, disease or nationality: item responses of men cannot be compared to those of women, young cannot be compared with old, responses of patients with psoriasis cannot be compared to those of patients with atopic dermatitis and responses of patients from Italy cannot be compared with responses of patients from the UK. Using IRT to investigate dimensionality and DIF in asthma-specific measures of HrQoL is overdue. It is likely that these measures suffer from item bias similar to the DLQI as they were developed around the same time and can be considered first-generation instruments.

In conclusion, the absence of explicit conceptual frameworks underpinning the existing measures, their differing foci and the findings from qualitative work with patients call for the development of a second-generation asthma-specific quality of life measure. A combination of using rigorous grounded approaches for construct definition and rigorous modern psychometric analysis for construct validation will be required to achieve this. Only then will it be possible to obtain a measure that measures content which is important to patients with asthma and shows robust psychometric properties at the same time.

References

1. U.S. Department of Health and Human Services, National Institutes of Health & National Heart, Lung, and Blood Institute. Guidelines for the Diagnosis and Management of Asthma - Summary Report 2007 (National Asthma Education and Prevention Program Expert Panel Report 3, NIH Publication Number 08-5846). Available from: <http://www.nhlbi.nih.gov/guidelines/asthma/asthsumm.htm>.
2. British Thoracic Society & Scottish Intercollegiate Guidelines Network. British Guideline on the Management of Asthma. A national clinical guideline. May 2008, revised May 2011. Available from: <http://www.sign.ac.uk/guidelines/fulltext/101/index.html>.
3. International Union Against Tuberculosis and Lung Disease & ISSAC (The International Study of Asthma and Allergies in Childhood). The Global Asthma Report 2011. Available from: <http://www.globalasthmareport.org/>.
4. Eder W, Ege MJ, von Mutius E. The asthma epidemic. *N Engl J Med*. 2006 Nov 23;355(21):2226-35.
5. Toelle BG, Ng K, Belousova E, Salome CM, Peat JK, Marks GB. Prevalence of asthma and allergy in schoolchildren in Belmont, Australia: three cross sectional surveys over 20 years. *BMJ*. 2004 Feb 14;328(7436):386-7.
6. von Mutius E, Weiland SK, Fritzsche C, Duhme H, Keil U. Increasing prevalence of hay fever and atopy among children in Leipzig, East Germany. *Lancet*. 1998 Mar 21;351(9106):862-6.
7. Barraclough R, Devereux G, Hendrick DJ, Stenton SC. Apparent but not real increase in asthma prevalence during the 1990s. *Eur Respir J*. 2002 Oct;20(4):826-33.
8. Burr ML, Butland BK, King S, Vaughan-Williams E. Changes in asthma prevalence: two surveys 15 years apart. *Arch Dis Child*. 1989 Oct;64(10):1452-6.
9. Lai CK, Beasley R, Crane J, Foliaki S, Shah J, Weiland S. Global variation in the prevalence and severity of asthma symptoms: phase three of the International Study of Asthma and Allergies in Childhood (ISAAC). *Thorax*. 2009 Jun;64(6):476-83.
10. Schlaud M, Atzpodien K, Thierfelder W. [Allergic diseases. Results from the German Health Interview and Examination Survey for Children and Adolescents (KiGGS)]. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz*. 2007 May-Jun;50(5-6):701-10.
11. Pearce N, Ait-Khaled N, Beasley R, Mallo J, Keil U, Mitchell E, et al. Worldwide trends in the prevalence of asthma symptoms: phase III of the International Study of Asthma and Allergies in Childhood (ISAAC). *Thorax*. 2007 Sep;62(9):758-66.
12. Sembajwe G, Cifuentes M, Tak SW, Kriebel D, Gore R, Punnett L. National income, self-reported wheezing and asthma diagnosis from the World Health Survey. *Eur Respir J*. 2010 Feb;35(2):279-86.
13. Masoli M, Fabian D, Holt S, Beasley R. The global burden of asthma: executive summary of the GINA Dissemination Committee report. *Allergy*. 2004 May;59(5):469-78.
14. Anandan C, Nurmatov U, van Schayck OC, Sheikh A. Is the prevalence of asthma declining? Systematic review of epidemiological studies. *Allergy*. 2010 Feb;65(2):152-67.
15. Strachan DP, Butland BK, Anderson HR. Incidence and prognosis of asthma and wheezing illness from early childhood to age 33 in a national British cohort. *BMJ*. 1996 May 11;312(7040):1195-9.
16. Genuneit J, Weinmayr G, Radon K, Dressel H, Windstetter D, Rzehak P, et al. Smoking and the incidence of asthma during adolescence: results of a large cohort study in Germany. *Thorax*. 2006 Jul;61(7):572-8.
17. Anderson HR, Ruggles R, Pandey KD, Kapetanakis V, Brunekreef B, Lai CK, et al. Ambient particulate pollution and the world-wide prevalence of asthma, rhinoconjunctivitis

and eczema in children: Phase One of the International Study of Asthma and Allergies in Childhood (ISAAC). *Occup Environ Med*. 2010 May;67(5):293-300.

18. Andersen ZJ, Bonnelykke K, Hvidberg M, Jensen SS, Ketznel M, Loft S, et al. Long-term exposure to air pollution and asthma hospitalisations in older adults: a cohort study. *Thorax*. 2012 Jan;67(1):6-11.

19. Lau S, Illi S, Sommerfeld C, Niggemann B, Bergmann R, von Mutius E, et al. Early exposure to house-dust mite and cat allergens and development of childhood asthma: a cohort study. Multicentre Allergy Study Group. *Lancet*. 2000 Oct 21;356(9239):1392-7.

20. Illi S, von Mutius E, Lau S, Niggemann B, Gruber C, Wahn U. Perennial allergen sensitisation early in life and chronic asthma in children: a birth cohort study. *Lancet*. 2006 Aug 26;368(9537):763-70.

21. Beuther DA, Sutherland ER. Overweight, obesity, and incident asthma: a meta-analysis of prospective epidemiologic studies. *Am J Respir Crit Care Med*. 2007 Apr 1;175(7):661-6.

22. Loerbroks A, Apfelbacher CJ, Amelang M, Sturmer T. Obesity and adult asthma: potential effect modification by gender, but not by hay fever. *Ann Epidemiol*. 2008 Apr;18(4):283-9.

23. Ellwood P, Asher MI, Bjorksten B, Burr M, Pearce N, Robertson CF. Diet and asthma, allergic rhinoconjunctivitis and atopic eczema symptom prevalence: an ecological analysis of the International Study of Asthma and Allergies in Childhood (ISAAC) data. ISAAC Phase One Study Group. *Eur Respir J*. 2001 Mar;17(3):436-43.

24. McKeever TM, Britton J. Diet and asthma. *Am J Respir Crit Care Med*. 2004 Oct 1;170(7):725-9.

25. Loss G, Apprigh S, Waser M, Kneifel W, Genuneit J, Buchele G, et al. The protective effect of farm milk consumption on childhood asthma and atopy: the GABRIELA study. *J Allergy Clin Immunol*. 2011 Oct;128(4):766-73 e4.

26. Brew BK, Allen CW, Toelle BG, Marks GB. Systematic review and meta-analysis investigating breast feeding and childhood wheezing illness. *Paediatr Perinat Epidemiol*. 2011 Nov;25(6):507-18.

27. Bjorksten B, Ait-Khaled N, Innes Asher M, Clayton TO, Robertson C. Global analysis of breast feeding and risk of symptoms of asthma, rhinoconjunctivitis and eczema in 6-7 year old children: ISAAC Phase Three. *Allergol Immunopathol (Madr)*. 2011 Nov;39(6):318-25.

28. Braun-Fahrlander C, Lauener R. Farming and protective agents against allergy and asthma. *Clin Exp Allergy*. 2003 Apr;33(4):409-11.

29. Lampi J, Canoy D, Jarvis D, Hartikainen AL, Keski-Nisula L, Jarvelin MR, et al. Farming environment and prevalence of atopy at age 31: prospective birth cohort study in Finland. *Clin Exp Allergy*. 2011 Jul;41(7):987-93.

30. Garratt A, Schmidt L, Mackintosh A, Fitzpatrick R. Quality of life measurement: bibliographic study of patient assessed health outcome measures. *Bmj*. 2002 Jun 15;324(7351):1417.

31. Guyatt GH, Kirshner B, Jaeschke R. A methodologic framework for health status measures: clarity or oversimplification? *J Clin Epidemiol*. 1992 Dec;45(12):1353-5.

32. U.S. Department of Health and Human Services Food and Drug Administration. 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.

33. U.S. Department of Health and Human Services Food and Drug Administration: Food and Drug Administration guidance for industry on patient-reported outcome measures: use in medical product development to support labeling claims. 2009. Available from:

<http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm071324.pdf>.

34. Tully MP, Cantrill JA. Subjective outcome measurement--a primer. *Pharm World Sci*. 1999 Jun;21(3):101-9.
35. Emery MP, Perrier LL, Acquadro C. Patient-reported outcome and quality of life instruments database (PROQOLID): frequently asked questions. *Health Qual Life Outcomes*. 2005;3:12.
36. Osoba D. A taxonomy of the uses of health-related quality-of-life instruments in cancer care and the clinical meaningfulness of the results. *Med Care*. 2002 Jun;40(6 Suppl):III31-8.
37. Kirshner B, Guyatt G. A methodological framework for assessing health indices. *J Chronic Dis*. 1985;38(1):27-36.
38. Guyatt GH, Veldhuyzen Van Zanten SJ, Feeny DH, Patrick DL. Measuring quality of life in clinical trials: a taxonomy and review. *CMAJ*. 1989 Jun 15;140(12):1441-8.
39. Guyatt GH, Feeny DH, Patrick DL. Measuring health-related quality of life. *Ann Intern Med*. 1993 Apr 15;118(8):622-9.
40. Patrick DL, Chiang YP. Measurement of health outcomes in treatment effectiveness evaluations: conceptual and methodological challenges. *Med Care*. 2000 Sep;38(9 Suppl):II14-25.
41. Cella D, Yount S, Rothrock N, Gershon R, Cook K, Reeve B, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS): progress of an NIH Roadmap cooperative group during its first two years. *Med Care*. 2007 May;45(5 Suppl 1):S3-S11.
42. Bowling A. *Measuring health: a review of quality of life measurement scales*. 3rd ed. Maidenhead: Open University Press; 2005.
43. Valderas JM, Alonso J. Patient reported outcome measures: a model-based classification system for research and clinical practice. *Qual Life Res*. 2008 Nov;17(9):1125-35.
44. Wilson IB, Cleary PD. Linking clinical variables with health-related quality of life. A conceptual model of patient outcomes. *JAMA*. 1995 Jan 4;273(1):59-65.
45. Ustun TB, Chatterji S, Bickenbach J, Kostanjsek N, Schneider M. The International Classification of Functioning, Disability and Health: a new tool for understanding disability and health. *Disabil Rehabil*. 2003 Jun 3-17;25(11-12):565-71.
46. Lenderking W. Task Force report of the Patient-Reported Outcomes Harmonization Group: too much harmony, not enough melody? *Value Health*. 2003 Sep-Oct;6(5):503-4.
47. Acquadro C, Berzon R, Dubois D, Leidy NK, Marquis P, Revicki D, et al. Incorporating the patient's perspective into drug development and communication: an ad hoc task force report of the Patient-Reported Outcomes (PRO) Harmonization Group meeting at the Food and Drug Administration, February 16, 2001. *Value Health*. 2003 Sep-Oct;6(5):522-31.
48. The World Health Organization Quality of Life assessment (WHOQOL): position paper from the World Health Organization. *Soc Sci Med*. 1995 Nov;41(10):1403-9.
49. The World Health Organization Quality of Life Assessment (WHOQOL): development and general psychometric properties. *Soc Sci Med*. 1998 Jun;46(12):1569-85.
50. Taillefer MC, Dupuis G, Roberge MA, Le May S. Health-related quality of life models: Systematic review of the literature. *Soc Indic Res*. 2003 Nov;64(2):293-323.
51. Tennant A. Quality of life--a measure too far? *Ann Rheum Dis*. 1995 Jun;54(6):439-40.
52. Ware JE, Jr., Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. *Med Care*. 1992 Jun;30(6):473-83.
53. Hunt SM, McEwen J, McKenna SP. *Measuring Health Status*. London: Croom Helm; 1986.

54. EuroQol--a new facility for the measurement of health-related quality of life. The EuroQol Group. *Health Policy*. 1990 Dec;16(3):199-208.
55. Mokkink LB, Terwee CB, Patrick DL, Alonso J, Stratford PW, Knol DL, et al. The COSMIN study reached international consensus on taxonomy, terminology, and definitions of measurement properties for health-related patient-reported outcomes. *J Clin Epidemiol*. 2010 Jul;63(7):737-45.
56. Streiner DL, Norman GR. *Health Measurement Scales: A practical guide to their development and use*. Fourth Edition ed. Oxford: Oxford University Press; 2008.
57. 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 Feb;47(2):76-83.
58. Juniper EF, Guyatt GH, Ferrie PJ, Griffith LE. Measuring quality of life in asthma. *Am Rev Respir Dis*. 1993 Apr;147(4):832-8.
59. Marks GB, Dunn SM, Woolcock AJ. A scale for the measurement of quality of life in adults with asthma. *J Clin Epidemiol*. 1992 May;45(5):461-72.
60. 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 Oct;46(10):1103-11.
61. Hyland ME, Finnis S, Irvine SH. A scale for assessing quality of life in adult asthma sufferers. *J Psychosom Res*. 1991;35(1):99-110.
62. Jones PW, Quirk FH, Baveystock CM. The St George's Respiratory Questionnaire. *Respir Med*. 1991 Sep;85 Suppl B:25-31; discussion 3-7.
63. 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 Jun;145(6):1321-7.
64. Maille AR, Koning CJ, Zwinderman 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 May;91(5):297-309.
65. 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 Apr;58(4):289-94.
66. 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 Jul;14(1):32-8.
67. Juniper EF, Buist AS, Cox FM, Ferrie PJ, King DR. Validation of a standardized version of the Asthma Quality of Life Questionnaire. *Chest*. 1999 May;115(5):1265-70.
68. Muhlig S, Bergmann KC, Emmermann E, Petermann F. ["Questionnaire on Quality of Life in Asthma"--studies of the dimensionality and references for evaluation]. *Pneumologie*. 1998 Jan;52(1):35-40.
69. Hyland ME. The Living with Asthma Questionnaire. *Respir Med*. 1991 Sep;85 Suppl B:13-6; discussion 33-7.
70. van Wijk RG. Quality of life, should we bother? *Allergy*. 2003 April;58(4):284-6.
71. Juniper EF, Guyatt GH, Feeny DH, Ferrie PJ, Griffith LE, Townsend M. Measuring quality of life in children with asthma. *Qual Life Res*. 1996 Feb;5(1):35-46.
72. 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.
73. 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 Sep;8(6):491-9.

74. Muldoon MF, Barger SD, Flory JD, Manuck SB. What are quality of life measurements measuring? *Bmj*. 1998 Feb 14;316(7130):542-5.
75. Garratt AM, Schmidt L, Fitzpatrick R. Patient-assessed health outcome measures for diabetes: a structured review. *Diabet Med*. 2002 Jan;19(1):1-11.
76. Assessing health status and quality-of-life instruments: attributes and review criteria. *Qual Life Res*. 2002 May;11(3):193-205.
77. 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 Dec;62(12):1359-71.
78. Hays RD, Hadorn D. Responsiveness to change: an aspect of validity, not a separate dimension. *Qual Life Res*. 1992 Feb;1(1):73-5.
79. Cronbach LJ. Coefficient Alpha and the Internal Structure of Tests. *Psychometrika*. 1951;16:297-334.
80. 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 Oct;42(10):773-8.
81. 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 Dec;57(11):2161-72.
82. Stewart AL, Hays RD, Ware JE, Jr. The MOS short-form general health survey. Reliability and validity in a patient population. *Med Care*. 1988 Jul;26(7):724-35.
83. Bergner M, Bobbitt RA, Carter WB, Gilson BS. The Sickness Impact Profile: development and final revision of a health status measure. *Med Care*. 1981 Aug;19(8):787-805.
84. Rowe BH, Oxman AD. Performance of an asthma quality of life questionnaire in an outpatient setting. *Am Rev Respir Dis*. 1993 Sep;148(3):675-81.
85. Rowe BH, Oxman AD. An assessment of the sensibility of a quality-of-life instrument. *Am J Emerg Med*. 1993 Jul;11(4):374-80.
86. Jaeschke R, Singer J, Guyatt GH. Measurement of health status. Ascertaining the minimal clinically important difference. *Control Clin Trials*. 1989 Dec;10(4):407-15.
87. 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 Jan;47(1):81-7.
88. 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 Jun;91(6):1121-7.
89. 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 May;31(5):219-26.
90. 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 Feb;54(2):182-9.
91. Leidy NK, Coughlin C. Psychometric performance of the Asthma Quality of Life Questionnaire in a US sample. *Qual Life Res*. 1998 Feb;7(2):127-34.
92. 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 Apr;45(2):188-94.
93. Ware JE, Jr. Standards for validating health measures: definition and content. *J Chronic Dis*. 1987;40(6):473-80.
94. Gupchup GV, Wolfgang AP, Thomas J, 3rd. 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 Sep-Oct;19(5):1116-25.

95. 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(6):513-21.
96. 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 Feb 4;136(5-6):89-95.
97. 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 Nov;32 (Pt 4):505-11.
98. Hyland ME, Crocker GR. Validation of an asthma quality of life diary in a clinical trial. *Thorax*. 1995 Jul;50(7):724-30.
99. Haave E, Hyland ME. Norwegian versions of the Living with Asthma Questionnaire (LWAQ) and Asthma Bother Profile (ABP), validation and comparison of two asthma groups. *Scand J Psychol*. 2004 Apr;45(2):163-7.
100. 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 Jul;79(1):17-21.
101. 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 Dec;140(6):1538-43.
102. Jones PW, Spencer S, Adie S. *The St George's Respiratory Questionnaire Manual*. Version 2.1. 2003.
103. 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 Feb;4(2):167-71.
104. Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand*. 1983 Jun;67(6):361-70.
105. 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 Jun;9(6):1160-6.
106. 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 Jan;11(1):61-6.
107. 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 Sep;22(9):1121-45.
108. 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(11-12):497-503.
109. 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 Jul;100(7):455-60.
110. Maille AR, Kaptein AA, Koning CJ, Zwinderman AH. Developing a quality-of-life questionnaire for patients with respiratory illness. *Monaldi Arch Chest Dis*. 1994 Feb;49(1):76-8.
111. Spilker B. Introduction. In: B. S, editor. *Quality of Life Assessments in Clinical Trials*. New York: Raven Press; 1990.
112. Guyatt GH, Bombardier C, Tugwell PX. Measuring disease-specific quality of life in clinical trials. *Cmaj*. 1986 Apr 15;134(8):889-95.

113. 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 Mar;12(2):133-45.
114. 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 Sep 22-29;282(12):1157-62.
115. Passalacqua G, Ciprandi G, Canonica GW. United airways disease: therapeutic aspects. *Thorax.* 2000 Oct;55 Suppl 2:S26-7.
116. Passalacqua G, Ciprandi G, Canonica GW. The nose-lung interaction in allergic rhinitis and asthma: united airways disease. *Curr Opin Allergy Clin Immunol.* 2001 Feb;1(1):7-13.
117. 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 May;55(5):357-64.
118. 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(4-5):417-21.
119. Kinsman RA, Luparello T, O'Banion K, Spector S. Multidimensional analysis of the subjective symptomatology of asthma. *Psychosom Med.* 1973 May-Jun;35(3):250-67.
120. Brooks CM, Richards JM, Jr., Bailey WC, Martin B, Windsor RA, Soong SJ. Subjective symptomatology of asthma in an outpatient population. *Psychosom Med.* 1989 Jan-Feb;51(1):102-8.
121. 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.
122. Gimeno-Santos E, Frei A, Dobbels F, Rudell K, Puhan MA, Garcia-Aymerich J. Validity of instruments to measure physical activity may be questionable due to a lack of conceptual frameworks: a systematic review. *Health Qual Life Outcomes.* 2011;9:86.
123. O'Brien KK, Bayoumi AM, Strike C, Young NL, Davis AM. Exploring disability from the perspective of adults living with HIV/AIDS: development of a conceptual framework. *Health Qual Life Outcomes.* 2008;6:76.
124. American Psychological Association (APA), National Council on Measurement in Education (NCME), American Educational Research Association (AERA): Standards for educational and psychological testing. Washington, D.C.1999.
125. 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 Apr;5(2):287-301.
126. 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 Oct 22;309(6961):1065-8.
127. Juniper EF, Guyatt GH, Streiner DL, King DR. Clinical impact versus factor analysis for quality of life questionnaire construction. *J Clin Epidemiol.* 1997 Mar;50(3):233-8.
128. Hyland ME. Quality-of-life assessment in respiratory disease: an examination of the content and validity of four questionnaires. *Pharmacoeconomics.* 1992 Jul;2(1):43-53.
129. 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 Dec;11(8):729-38.
130. 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 Oct;122(4):1228-33.

131. 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 Jun;8(6):888-98.
132. 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 Jul;12(1):30-4.
133. Schatz M, Mosen D, Kosinski M, Vollmer WM, O'Connor E, Cook EF, et al. Validation of the asthma impact survey, a brief asthma-specific quality of life tool. *Qual Life Res.* 2007 Mar;16(2):345-55.
134. Bayliss MS, Espindle DM, Buchner D, Blaiss MS, Ware JE. A new tool for monitoring asthma outcomes: the ITG Asthma Short Form. *Qual Life Res.* 2000;9(4):451-66.
135. Wilson SR, Rand CS, Cabana MD, Foggs MB, Halterman JS, Olson L, et al. Asthma outcomes: quality of life. *J Allergy Clin Immunol.* [Review]. 2012 Mar;129(3 Suppl):S88-123.
136. Nunnally JC, Bernstein IH. *Psychometric theory.* 3rd ed: McGraw-Hill; 1994.
137. van der Molen T, Postma DS, Schreurs AJ, Bosveld HE, Sears MR, Meyboom de Jong B. Discriminative aspects of two generic and two asthma-specific instruments: relation with symptoms, bronchodilator use and lung function in patients with mild asthma. *Qual Life Res.* 1997 May;6(4):353-61.
138. Barley EA, Jones PW. A comparison of global questions versus health status questionnaires as measures of the severity and impact of asthma. *Eur Respir J.* 1999 Sep;14(3):591-6.
139. Brooks R, Rabin R, Charro F, editors. *The measurement and valuation of health status using EQ-5D: A European Perspective.* Dordrecht: Kluwer Academic Publishers; 2003.
140. Quanjer PH, Tammeling GJ, Cotes JE, Pedersen OF, Peslin R, Yernault JC. Lung volumes and forced ventilatory flows. Report Working Party Standardization of Lung Function Tests, European Community for Steel and Coal. Official Statement of the European Respiratory Society. *Eur Respir J Suppl.* 1993 Mar;16:5-40.
141. Roca J, Burgos F, Sunyer J, Saez M, Chinn S, Anto JM, et al. Reference values for forced spirometry. Group of the European Community Respiratory Health Survey. *Eur Respir J.* 1998 Jun;11(6):1354-62.
142. Wasserfallen JB, Gold K, Schulman KA, Baraniuk JN. Development and validation of a rhinoconjunctivitis and asthma symptom score for use as an outcome measure in clinical trials. *J Allergy Clin Immunol.* 1997 Jul;100(1):16-22.
143. Wasserfallen JB, Gold K, Schulman KA, Baraniuk JN. Item responsiveness of a rhinitis and asthma symptom score during a pollen season. *J Asthma.* 1999 Aug;36(5):459-65.
144. Nathan RA, Sorkness CA, Kosinski M, Schatz M, Li JT, Marcus P, et al. Development of the asthma control test: a survey for assessing asthma control. *J Allergy Clin Immunol.* 2004 Jan;113(1):59-65.
145. Schatz M, Sorkness CA, Li JT, Marcus P, Murray JJ, Nathan RA, et al. Asthma Control Test: reliability, validity, and responsiveness in patients not previously followed by asthma specialists. *J Allergy Clin Immunol.* 2006 Mar;117(3):549-56.
146. Hyland ME, Ley A, Fisher DW, Woodward V. Measurement of psychological distress in asthma and asthma management programmes. *Br J Clin Psychol.* 1995 Nov;34 (Pt 4):601-11.
147. Pickard AS, Yang Y, Lee TA. Comparison of health-related quality of life measures in chronic obstructive pulmonary disease. *Health Qual Life Outcomes.* 2011;9:26.
148. Apfelbacher CJ, Hankins M, Stenner P, Frew AJ, Smith HE. Measuring asthma-specific quality of life: structured review. *Allergy.* 2011 Apr;66(4):439-57.

149. Chhabra SK, Chhabra P. Gender differences in perception of dyspnea, assessment of control, and quality of life in asthma. *J Asthma*. 2011 Aug;48(6):609-15.
150. Pope C, Mays N. Reaching the parts other methods cannot reach: an introduction to qualitative methods in health and health services research. *BMJ*. 1995 Jul 1;311(6996):42-5.
151. Ritchie J, Lewis J, editors. *Qualitative Research Practice. A Guide for Social Science Students and Researchers*. Los Angeles, London, New Delhi, Singapore, Washington DC: SAGE; 2003.
152. Gibbons E, Fitzpatrick R. A structured review of patient-reported outcome measures for people with asthma: an update 2009, 2009. Available from: <http://phi.uhce.ox.ac.uk/>.
153. Bundesärztekammer (BÄK), Kassenärztliche Bundesvereinigung (KBV), (AWMF) AdWMF. Nationale VersorgungsLeitlinie Asthma – Langfassung, 2. Auflage. Version 1.2, 2010. Available from: www.versorgungsleitlinien.de/themen/asthma.
154. Burnard P. A method of analysing interview transcripts in qualitative research. *Nurse Educ Today*. 1991 Dec;11(6):461-6.
155. atlas.ti. Version 6.2.17. Berlin: ATLAS.ti GmbH, Parts copyright by Cincom Systems, Inc.
156. Friese S. *Qualitative Data Analysis with ATLAS.ti*. Los Angeles, London, New Delhi, Singapore, Washington DC: SAGE; 2012.
157. Graneheim UH, Lundman B. Qualitative content analysis in nursing research: concepts, procedures and measures to achieve trustworthiness. *Nurse Educ Today*. 2004 Feb;24(2):105-12.
158. Khadka J, Gothwal VK, McAlinden C, Lamoureux EL, Pesudovs K. The importance of rating scales in measuring patient-reported outcomes. *Health Qual Life Outcomes*. 2012 Jul 13;10(1):80.
159. Garratt AM, Helgeland J, Gulbrandsen P. Five-point scales outperform 10-point scales in a randomized comparison of item scaling for the Patient Experiences Questionnaire. *J Clin Epidemiol*. [Randomized Controlled Trial]. 2011 Feb;64(2):200-7.
160. Preston CC, Colman AM. Optimal number of response categories in rating scales: reliability, validity, discriminating power, and respondent preferences. *Acta psychologica*. [Research Support, Non-U.S. Gov't]. 2000 Mar;104(1):1-15.
161. Hjermstad MJ, Fayers PM, Haugen DF, Caraceni A, Hanks GW, Loge JH, et al. Studies comparing Numerical Rating Scales, Verbal Rating Scales, and Visual Analogue Scales for assessment of pain intensity in adults: a systematic literature review. *Journal of pain and symptom management*. 2011 Jun;41(6):1073-93.
162. Locker D, Jokovic A, Allison P. Direction of wording and responses to items in oral health-related quality of life questionnaires for children and their parents. *Community Dent Oral Epidemiol*. 2007 Aug;35(4):255-62.
163. Juniper EF, O'Byrne PM, Guyatt GH, Ferrie PJ, King DR. Development and validation of a questionnaire to measure asthma control. *Eur Respir J*. 1999 Oct;14(4):902-7.
164. Skinner EA, Diette GB, Algatt-Bergstrom PJ, Nguyen TT, Clark RD, Markson LE, et al. The Asthma Therapy Assessment Questionnaire (ATAQ) for children and adolescents. *Dis Manag*. 2004 Winter;7(4):305-13.
165. Hunt SM. The problem of quality of life. *Qual Life Res*. 1997 Apr;6(3):205-12.
166. Lasch KE, Marquis P, Vigneux M, Abetz L, Arnould B, Bayliss M, et al. PRO development: rigorous qualitative research as the crucial foundation. *Qual Life Res*. 2010 Oct;19(8):1087-96.
167. Sim J. Collecting and analysing qualitative data: issues raised by the focus group. *J Adv Nurs*. 1998 Aug;28(2):345-52.

168. Kitzinger J. Qualitative research. Introducing focus groups. *BMJ*. 1995 Jul 29;311(7000):299-302.
169. Coenen M, Stamm TA, Stucki G, Cieza A. Individual interviews and focus groups in patients with rheumatoid arthritis: a comparison of two qualitative methods. *Qual Life Res*. 2012 Mar;21(2):359-70.
170. Ericsson KA, Simon HA. Protocol analysis: Verbal reports as data. revised edn. ed. Cambridge, MA: MIT Press; 1993.
171. Green C, Gilhooly K. Protocol analysis: Practical implementation. In: Richardson JTE, editor. *Handbook of qualitative research methods for psychology and the social sciences*. Leicester: BPS Books; 1996. p. 55-74.
172. Mallinson S. Listening to respondents: a qualitative assessment of the Short-Form 36 Health Status Questionnaire. *Soc Sci Med*. 2002 Jan;54(1):11-21.
173. Wylde V, Learmonth ID, Cavendish VJ. The Oxford hip score: the patient's perspective. *Health Qual Life Outcomes*. 2005;3:66.
174. McMurray R, Heaton J, Sloper P, Nettleton S. Measurement of patient perceptions of pain and disability in relation to total hip replacement: the place of the Oxford hip score in mixed methods. *Qual Health Care*. 1999 Dec;8(4):228-33.
175. Urrutia I, Aguirre U, Pascual S, Esteban C, Ballaz A, Arrizubieta I, et al. Impact of anxiety and depression on disease control and quality of life in asthma patients. *J Asthma*. 2012 Mar;49(2):201-8.
176. Apfelbacher CJ, Hankins M, Stenner P, Frew AJ, Smith HE. Measuring asthma-specific quality of life: structured review. *Allergy*. 2010 Nov 8.
177. Geyh S, Cieza A, Kollerits B, Grimby G, Stucki G. Content comparison of health-related quality of life measures used in stroke based on the international classification of functioning, disability and health (ICF): a systematic review. *Qual Life Res*. 2007 Jun;16(5):833-51.
178. Stucki A, Stucki G, Cieza A, Schuurmans MM, Kostanjsek N, Ruof J. Content comparison of health-related quality of life instruments for COPD. *Respir Med*. 2007 Jun;101(6):1113-22.
179. Adams RJ, Ruffin RE, Smith BJ. Validity of a modified version of the Marks Asthma Quality of Life Questionnaire. *J Asthma*. 2000 Apr;37(2):131-43.
180. Nilsson AK, Lohmander LS, Klassbo M, Roos EM. Hip disability and osteoarthritis outcome score (HOOS)--validity and responsiveness in total hip replacement. *BMC Musculoskelet Disord*. 2003 May 30;4:10.
181. O'Boyle CA, McGee H, Hickey A, O'Malley K, Joyce CR. Individual quality of life in patients undergoing hip replacement. *Lancet*. 1992 May 2;339(8801):1088-91.
182. Fitzpatrick R. Assessment of quality of life as an outcome: finding measurements that reflect individuals' priorities. *Qual Health Care*. 1999 Mar;8(1):1-2.
183. Ruta DA, Garratt AM, Russell IT. Patient centred assessment of quality of life for patients with four common conditions. *Qual Health Care*. 1999 Mar;8(1):22-9.
184. Ruta DA, Garratt AM, Leng M, Russell IT, MacDonald LM. A new approach to the measurement of quality of life. The Patient-Generated Index. *Med Care*. 1994 Nov;32(11):1109-26.
185. Calman KC. Quality of life in cancer patients--an hypothesis. *J Med Ethics*. 1984 Sep;10(3):124-7.
186. Herd RM, Tidman MJ, Ruta DA, Hunter JA. Measurement of quality of life in atopic dermatitis: correlation and validation of two different methods. *Br J Dermatol*. 1997 Apr;136(4):502-7.
187. Patel KK, Veenstra DL, Patrick DL. A review of selected patient-generated outcome measures and their application in clinical trials. *Value Health*. 2003 Sep-Oct;6(5):595-603.

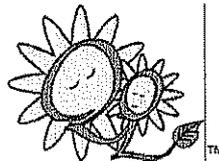
188. Nijsten T. Dermatology life quality index: time to move forward. *J Invest Dermatol*. 2012 Jan;132(1):11-3.
189. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI)--a simple practical measure for routine clinical use. *Clin Exp Dermatol*. 1994 May;19(3):210-6.
190. Magasi S, Ryan G, Revicki D, Lenderking W, Hays RD, Brod M, et al. Content validity of patient-reported outcome measures: perspectives from a PROMIS meeting. *Qual Life Res*. 2012 Jun;21(5):739-46.
191. Hunt SM, McKenna SP. The QLDS: a scale for the measurement of quality of life in depression. *Health Policy*. 1992 Oct;22(3):307-19.
192. McKenna SP. Measuring patient-reported outcomes: moving beyond misplaced common sense to hard science. *BMC Med*. 2011;9:86.
193. Buchbinder R, Batterham R, Elsworth G, Dionne CE, Irvin E, Osborne RH. A validity-driven approach to the understanding of the personal and societal burden of low back pain: development of a conceptual and measurement model. *Arthritis research & therapy*. [Research Support, Non-U.S. Gov't]. 2011;13(5):R152.
194. McHorney CA. Generic health measurement: past accomplishments and a measurement paradigm for the 21st century. *Ann Intern Med*. 1997 Oct 15;127(8 Pt 2):743-50.
195. Tennant A, McKenna SP, Hagell P. Application of Rasch analysis in the development and application of quality of life instruments. *Value Health*. 2004 Sep-Oct;7 Suppl 1:S22-6.
196. Nijsten T, Meads DM, McKenna SP. Dimensionality of the dermatology life quality index (DLQI): a commentary. *Acta Derm Venereol*. 2006;86(3):284-5; author reply 5-6.
197. Nijsten T, Meads DM, de Korte J, Sampogna F, Gelfand JM, Ongenaes K, et al. Cross-cultural inequivalence of dermatology-specific health-related quality of life instruments in psoriasis patients. *J Invest Dermatol*. 2007 Oct;127(10):2315-22.
198. Twiss J, Meads DM, Preston EP, Crawford SR, McKenna SP. Can we rely on the Dermatology Life Quality Index as a measure of the impact of psoriasis or atopic dermatitis? *J Invest Dermatol*. 2012 Jan;132(1):76-84.

APPENDIX

FRAGEBOGEN ZUR LEBENSQUALITÄT VON ASTHMAPATIENTEN - VERSION MIT STANDARDISIERTEN TÄTIGKEITEN (AQLQ(S))

PATIENTENFRAGEBOGEN (SELF-ADMINISTERED) GERMAN VERSION

© 1999
QOL TECHNOLOGIES LTD.



Weitere Informationen:

Elizabeth Juniper, MCSP, MSc
Professor
20 Marcuse Fields
Bosham
West Sussex
PO18 8NA. UK
Telephone: + 44 (0) 1243 572124
Fax: + 44 (0) 1243 573680
E-mail: juniper@qoltech.co.uk
WWW: <http://www.qoltech.co.uk>

This translation has been made possible through
a grant from SMITHKLINE BEECHAM.
Translated by MAPI RESEARCH INSTITUTE
Senior translator: Thomas Finger M.A.

© Der AQLQ(S) ist urheberrechtlich geschützt. Der Fragebogen darf nicht ohne schriftliche Zustimmung von Elizabeth Juniper geändert, verkauft, übersetzt oder auf ein anderes Medium übertragen werden.

JANUAR 1999

FRAGEBOGEN ZUR LEBENSQUALITÄT
 VON ASTHMAPATIENTEN (S)
 (GERMAN VERSION)
 PATIENTENFRAGEBOGEN

PATIENTENKENNUMMER: _____

DATUM: _____

Bitte beantworten Sie **alle** Fragen, indem Sie die Zahl zu der Antwort ankreuzen, die am besten beschreibt, wie es Ihnen in den **letzten 2 Wochen wegen Ihres Asthmas ging**.

WIE SEHR WAREN SIE IN DEN **LETZTEN 2 WOCHEN DURCH IHR ASTHMA BEEINTRÄCHTIGT WENN SIE DIESE TÄTIGKEITEN AUSGEÜBT HABEN?**

	Völlig beeinträchtigt	Äußerst beeinträchtigt	Sehr beeinträchtigt	Mäßig beeinträchtigt	Etwas beeinträchtigt	Sehr wenig beeinträchtigt	Überhaupt nicht beeinträchtigt
1. ANSTRENGENDE TÄTIGKEITEN (z.B. sich beeilen, Fitnessstraining, Treppen hochlaufen, Sport treiben)	1	2	3	4	5	6	7
2. MITTELSCHWERE TÄTIGKEITEN (z.B. Spazieren gehen, Haushalt, Gartenarbeit, Einkaufen, Treppen steigen)	1	2	3	4	5	6	7
3. TÄTIGKEITEN MIT ANDEREN MENSCHEN (z.B. reden, mit Haustieren/Kindern spielen, Freunde/ Verwandte besuchen)	1	2	3	4	5	6	7
4. TÄTIGKEITEN BEI DER ARBEIT (Aufgaben, die Sie bei der Arbeit erledigen müssen*)	1	2	3	4	5	6	7
* Wenn Sie nicht berufstätig sind sollten dies Tätigkeiten sein, die Sie beinahe jeden Tag ausüben müssen.							
5. SCHLAFEN	1	2	3	4	5	6	7

WIE SEHR HABEN IHNEN IN DEN LETZTEN 2 WOCHEN DIE FOLGENDEN BESCHWERDEN KÖRPERLICH ODER PSYCHISCH ZU SCHAFFEN GEMACHT?

	Sehr stark	Stark	Ziemlich stark	Mäßig	Etwas	Sehr wenig	Gar nicht
6. Wie sehr hat Ihnen in den letzten 2 Wochen ein ENGEGEFÜHL IN DER BRUST körperlich oder psychisch zu schaffen gemacht?	1	2	3	4	5	6	7

ALLES IN ALLEM, WIE OFT IN DEN LETZTEN 2 WOCHEN:

	Immer	Meistens	Oft	Manchmal	Selten	Fast nie	Nie
7. Haben Sie sich SORGEN WEGEN IHRES ASTHMAS gemacht?	1	2	3	4	5	6	7
8. Waren Sie wegen Ihres Asthmas KURZATMIG?	1	2	3	4	5	6	7
9. Haben Sie Asthmabeschwerden bekommen, WEIL SIE ZIGARETTENRAUCH AUSGESETZT WAREN?	1	2	3	4	5	6	7
10. Haben Sie ein PFEIFEN in Ihrer Brust bemerkt?	1	2	3	4	5	6	7
11. Hatten Sie das Gefühl, Sie müßten EINE SITUATION ODER UMGEBUNG WEGEN ZIGARETTENRAUCHS MEIDEN?	1	2	3	4	5	6	7

WIE SEHR HABEN IHNEN IN DEN LETZTEN 2 WOCHEN DIE FOLGENDEN BESCHWERDEN KÖRPERLICH ODER PSYCHISCH ZU SCHAFFEN GEMACHT?

	Sehr stark	Stark	Ziemlich stark	Mäßig	Etwas	Sehr wenig	Gar nicht
12. Wie sehr hat Ihnen in den letzten 2 Wochen HUSTEN körperlich oder psychisch zu schaffen gemacht?	1	2	3	4	5	6	7

FRAGEBOGEN ZUR LEBENSQUALITÄT
 VON ASTHMAPATIENTEN (S)
 (GERMAN VERSION)
 PATIENTENFRAGEBOGEN

PATIENTENKENNNUMMER: _____

DATUM: _____

ALLES IN ALLEM, WIE OFT IN DEN LETZTEN 2 WOCHEN:

	Immer	Meistens	Oft	Manchmal	Selten	Fast nie	Nie
13. Waren Sie FRUSTRIERT wegen Ihres Asthmas?	1	2	3	4	5	6	7
14. Haben Sie einen DRUCK AUF DER BRUST verspürt?	1	2	3	4	5	6	7
15. Haben Sie sich SORGEN GEMACHT, WEIL SIE WEGEN IHRES ASTHMAS MEDIKAMENTE EINNEHMEN MÜSSEN?	1	2	3	4	5	6	7
16. Hatten Sie das Gefühl, SICH RÄUSPERN ZU MÜSSEN?	1	2	3	4	5	6	7
17. Haben Sie Asthmabeschwerden bekommen, WEIL SIE STAUB AUSGESETZT WAREN?	1	2	3	4	5	6	7
18. Hatten Sie SCHWIERIGKEITEN AUSZUATMEN wegen Ihres Asthmas?	1	2	3	4	5	6	7
19. Hatten Sie das Gefühl, Sie müssten EINE SITUATION ODER UMGEBUNG WEGEN STAUBES MEIDEN?	1	2	3	4	5	6	7
20. SIND SIE MORGENS MIT ASTHMABESCHWERDEN AUFGEWACHT?	1	2	3	4	5	6	7
21. Hatten SIE ANGST, IHRE ASTHMAMEDIKAMENTE NICHT ZUR VERFÜGUNG ZU HABEN?	1	2	3	4	5	6	7

FRAGEBOGEN ZUR LEBENSQUALITÄT
 VON ASTHMAPATIENTEN (S)
 (GERMAN VERSION)
 PATIENTENFRAGEBOGEN

PATIENTENKENNUMMER: _____

DATUM: _____

ALLES IN ALLEM, WIE OFT IN DEN LETZTEN 2 WOCHEN:

	Immer	Meistens	Oft	Manchmal	Selten	Fast nie	Nie
22. Hat es Ihnen zu schaffen gemacht, daß das ATMEN SCHWER war?	1	2	3	4	5	6	7
23. Haben Sie Asthmabeschwerden WEGEN DES WETTERS ODER DER LUFTVERSCHMUTZUNG bekommen?	1	2	3	4	5	6	7
24. Sind Sie NACHTS durch ihr Asthma GEWECKT WORDEN?	1	2	3	4	5	6	7
25. MUSSTEN SIE WEGEN DES WETTERS ODER DER LUFTVERSCHMUTZUNG DEN AUFENTHALT IM FREIEN EINSCHRÄNKEN ODER VERMEIDEN?	1	2	3	4	5	6	7
26. Haben Sie Asthmabeschwerden bekommen, WEIL SIE STARKEN GERÜCHEN ODER PARFÜM AUSGESETZT WAREN?	1	2	3	4	5	6	7
27. Hatten Sie ANGST, DASS SIE KEINE LUFT MEHR BEKOMMEN?	1	2	3	4	5	6	7
28. Hatten Sie das Gefühl, Sie müssten EINE SITUATION ODER UMGEBUNG WEGEN STARKER GERÜCHE ODER PARFÜMS MEIDEN?	1	2	3	4	5	6	7
29. Haben Sie wegen Ihres Asthmas NACHTS NICHT GUT GESCHLAFEN?	1	2	3	4	5	6	7
30. Hatten Sie das Gefühl, NACH LUFT RINGEN ZU MÜSSEN?	1	2	3	4	5	6	7

FRAGEBOGEN ZUR LEBENSQUALITÄT
 VON ASTHMAPATIENTEN (S)
 (GERMAN VERSION)
 PATIENTENFRAGEBOGEN

PATIENTENKENNUMMER: _____

DATUM: _____

WIE SEHR WAREN SIE IN DEN LETZTEN 2 WOCHEN IN IHREN TÄTIGKEITEN EINGESCHRÄNKT?

	Sehr stark ein- geschränkt [die meisten Tätigkeiten nicht ausgeübt]	Stark ein- geschränkt	Mäßig ein- geschränkt [mehrere Tätigkeiten nicht ausgeübt]	Wenig ein- geschränkt	Sehr wenig eingeschränkt [nur sehr wenige Tätigkeiten nicht ausgeübt]	Fast gar nicht ein- geschränkt	Überhaupt nicht eingeschränkt [alle Tätigkeiten ausgeübt, die ich ausüben wollte]
31. Denken Sie an ALLE TÄTIGKEITEN, zu denen Sie in den letzten 2 Wochen Lust gehabt hätten. Wie sehr hat Ihr Asthma die ANZAHL DER TÄTIGKEITEN, die für Sie möglich waren, eingeschränkt?	1	2	3	4	5	6	7

	Völlig be- einträchtigt	Äußerst be- einträchtigt	Sehr be- einträchtigt	Mäßig be- einträchtigt	Etwas be- einträchtigt	Sehr wenig beeinträchtigt	Überhaupt nicht be- einträchtigt
32. Wenn Sie an ALLE TÄTIGKEITEN denken, die Sie in den letzten 2 Wochen tatsächlich ausgeübt haben, wie sehr sind Sie durch Ihr Asthma beeinträchtigt gewesen?	1	2	3	4	5	6	7

BEREICHSCODES:

Symptome: 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 29, 30
 Beeinträchtigung bei Tätigkeiten: 1, 2, 3, 4, 5, 11, 19, 25, 28, 31, 32
 Gefühlsleben: 7, 13, 15, 21, 27
 Umweltreize: 9, 17, 23, 26

FRAGEBOGEN ZUR LEBENSQUALITÄT VON ASTHMAPATIENTEN

– Marks AQLA –

Wir danken Ihnen, dass Sie sich mit diesem Fragebogen befassen. Er ist Bestandteil eines Forschungsprojektes, bei dem man herausfinden möchte, wie Asthma das Leben der betroffenen Personen beeinträchtigt. Alle Ihre Antworten werden vertraulich behandelt. Es folgt eine Reihe von Aussagen, in denen beschrieben wird, wie Asthma selbst oder die Behandlung von Asthma in das Leben der betroffenen Personen eingreift. Wir bitten Sie, bei jeder der folgenden Aussage diejenige Antwort anzukreuzen, die für **die letzten 4 Wochen** am ehesten zutrifft.

	Nie	Selten	Manchmal	Häufig	Sehr häufig
1	<input type="radio"/>				
2	<input type="radio"/>				
3	<input type="radio"/>				
4	<input type="radio"/>				
5	<input type="radio"/>				
6	<input type="radio"/>				
7	<input type="radio"/>				
8	<input type="radio"/>				
9	<input type="radio"/>				

		Nie	Selten	Manchmal	Häufig	Sehr häufig
10	Ich fühle mich ängstlich, angespannt oder belastet	<input type="radio"/>				
11	Ich habe das Gefühl, Asthmabeschwerden oder Kurzatmigkeit hindern mich daran, das zu erreichen, was ich im Leben erwarte	<input type="radio"/>				
12	Asthmabeschwerden oder Kurzatmigkeit beeinträchtigen meinen Kontakt zu anderen Menschen	<input type="radio"/>				
13	Ich vermeide es, an bestimmte Orte zu gehen, weil sich dort mein Asthma verschlechtert	<input type="radio"/>				
14	Ich vermeide es, an bestimmte Orte zu gehen, weil ich fürchte, dass dort ein Asthmaanfall ausgelöst und mir nicht geholfen werden kann	<input type="radio"/>				
15	Beim Sporttreiben, bei meinen Hobbies oder bei anderen Freizeitbeschäftigungen werde ich durch Asthmabeschwerden oder Kurzatmigkeit eingeschränkt	<input type="radio"/>				

16	Ich fühle mich allgemein eingeschränkt	<input type="radio"/>				
		Nie	Selten	Manchmal	Häufig	Sehr häufig
17	Ich habe das Gefühl, dass das Asthma in meinem Leben die führende Rolle spielt	<input type="radio"/>				
18	Ich mache mir wegen des Asthmas Sorgen über meinen jetzigen oder zukünftigen Gesundheitszustand	<input type="radio"/>				
19	Ich mache mir Sorgen darüber, dass das Asthma meine Lebenserwartung verkürzen könnte	<input type="radio"/>				
20	Ich fühle mich abhängig von den Asthmamitteln, die ich inhaliere	<input type="radio"/>				

Code:

--	--	--	--	--	--	--	--	--	--

Fragebogen zur Lebensqualität bei Asthma (FLA)

Erläuterungen zum Fragebogen zur Lebensqualität bei Asthma

Sehr geehrte Patientin, sehr geehrter Patient,

mit Hilfe dieses Fragebogens wollen wir mehr darüber erfahren, wie Ihr Asthma Ihnen zu schaffen macht und wie es Ihr Leben eventuell beeinträchtigt.

Kreuzen Sie bitte zu jeder Aussage die Zahl an, die auf Sie am besten zutrifft.

	<i>stimmt genau</i>	<i>stimmt in etwa</i>	<i>stimmt nicht</i>	<i>nicht anwendbar</i>
1. Bei privaten Einladungen befürchte ich, daß irgendetwas in der dortigen Umgebung einen Atemnot- oder Hustenanfall auslösen könnte.	1	2	3	4
2. Aufgrund meines Asthmas sind meine Urlaubsmöglichkeiten beschränkt.	1	2	3	4
3. Ich habe einen gesunden Schlaf.	1	2	3	4
4. Es fällt mir leicht, meine Einkäufe zu tragen.	1	2	3	4
5. Ich denke fast nie an mein Asthma.	1	2	3	4
6. Manchmal muß ich Menschen enttäuschen, weil ich Versprechungen wegen meines Asthmas nicht immer einhalten kann.	1	2	3	4
7. Ich mache mir niemals Sorgen, daß ein geplanter Urlaub negative Auswirkungen auf mein Asthma haben könnte.	1	2	3	4
8. In den meisten Nächten wache ich auf und brauche mein Dosieraerosol oder Inhalationsgerät.	1	2	3	4
9. Arbeiten, die mich körperlich stark beanspruchen (z.B. Gartenarbeit), fallen mir schwer.	1	2	3	4
10. Ich nehme die ersten Anzeichen einer Erkältung eher wahr als andere Leute.	1	2	3	4
11. Von Zeit zu Zeit habe ich Schwierigkeiten, mich im Hause zu bewegen.	1	2	3	4
12. Ich glaube, daß mein Asthma keine Auswirkungen auf das Leben meiner Angehörigen hat.	1	2	3	4
13. Ich habe das Gefühl, etwas zu versäumen, da ich an einigen sportlichen Aktivitäten nicht teilnehmen kann.	1	2	3	4
14. Ich kann auf die gleiche Art und Weise wie jeder andere Urlaub machen.	1	2	3	4
15. Mir fällt die Hausarbeit leicht.	1	2	3	4
16. Ich habe das Gefühl, meinen Körper nicht unter Kontrolle zu haben.	1	2	3	4
17. Ich bin besorgt, weil ich nicht weiß, wann ich den nächsten Atemnot-/Hustenanfall haben werde.	1	2	3	4
18. Ich werde unruhig, wenn ich kurzatmig bin.	1	2	3	4
19. Aufgrund meines Asthmas schlafe ich schlecht.	1	2	3	4
20. Heimwerker-Aktivitäten wie z.B. Tapezieren fallen mir schwer.	1	2	3	4

	<i>stimmt genau</i>	<i>stimmt in etwa</i>	<i>stimmt nicht</i>	<i>nicht anwendbar</i>
21. Ich kann ohne Probleme in eine Gaststätte gehen.	1	2	3	4
22. Ich muß nachts häufig husten.	1	2	3	4
23. Aufgrund meines Asthmas kann ich einige Arbeiten, die ich gerne verrichten würde, nicht ausführen.	1	2	3	4
24. Ich neige dazu, Personen mit Erkältung zu meiden.	1	2	3	4
25. Ich kann eine Treppe hinaufgehen, ohne anzuhalten.	1	2	3	4
26. Ich versuche, Aufregungen zu vermeiden, weil sich dadurch mein Asthma verschlimmert.	1	2	3	4
27. Ich fühle mich so hilflos, weil ich Asthma habe.	1	2	3	4
28. Wenn ich ausgehe, muß ich wegen meines Asthmas manchmal früher nach Hause gehen als andere.	1	2	3	4
29. Der Ablauf meiner Arbeit ändert sich durch mein Asthma nicht.	1	2	3	4
30. Erkältungen dauern bei mir länger als bei anderen.	1	2	3	4
31. Ich kann eine Treppe nur dann hinaufgehen, wenn ich eine oder mehrere Pausen einlege.	1	2	3	4
32. Ich habe eine gute Zukunft vor mir.	1	2	3	4
33. Wenn mein Asthma sich verschlechtert, dann arbeite ich auch schlecht.	1	2	3	4
34. Es gibt Orte, wo ich gerne hinginge, es aber aufgrund meines Asthmas nicht kann.	1	2	3	4
35. Wegen meines Asthmas fühle ich mich manchmal sexuell frustriert.	1	2	3	4
36. Ich mache mir Sorgen darüber, wie mein Gesundheitszustand in 10 Jahren aussehen wird.	1	2	3	4
37. Ich bin oft deprimiert wegen meines Asthmas.	1	2	3	4
38. Ich kann mich gut entspannen.	1	2	3	4
39. Mein Asthma beeinträchtigt mich tatsächlich nur bei einem Anfall.	1	2	3	4
40. Ich vertraue auf meine Fähigkeit, mit einem Husten-/Atemnotanfall fertig zu werden.	1	2	3	4

Auswertungsanleitung

Vorläufige Auswertungshinweise für den FLA¹

1) Dateneingabe

Die Kategorie „stimmt genau“ wird mit „1“ kodiert, die Kategorie „stimmt in etwa“ mit „2“ und die Kategorie „stimmt nicht“ mit „3“. Die Kategorie „nicht anwendbar“ wird als fehlender Wert („Missing“) kodiert, ebenso Items, die nicht beantwortet wurden oder Antworten, die nicht auswertbar sind.

2) Werte außerhalb des Wertebereichs in fehlende Daten („Missings“) umwandeln

Nach erfolgter Dateneingabe sollte kontrolliert werden, ob bei der Eingabe Fehler gemacht wurden (Datenbereinigung). Dazu werden stichprobenartig einige der eingegebenen Fragebögen überprüft. Anschließend werden für jedes Item alle Angaben, die außerhalb des festgelegten Wertebereichs (1-3) liegen als „Missing“ kodiert bzw. manuell korrigiert. Dies läßt sich erreichen, indem man den Wertebereich definiert und andere Werte automatisch als „Missing“ kodieren läßt oder sich die Häufigkeitsverteilungen der einzelnen Items anzeigen läßt und entdeckte Fehler anhand der vorliegenden, ausgefüllten Fragebögen manuell korrigiert.

3) Umpolung der Werte bei 14 Items

Die positiv formulierten Items (Item-Nr.: 3, 4, 5, 7, 12, 14, 15, 21, 25, 29, 32, 38, 39, 40) werden umgepolt, d.h. die Kategorie „stimmt genau“ wird nun mit „3“ kodiert, die Kategorie „stimmt in etwa“ bleibt „2“ und die Kategorie „stimmt nicht“ wird zu „1“. Die Umkehrung der Itemwerte führt dazu, daß bei allen Items des FLA ein höherer Itemwert eine bessere Lebensqualität anzeigt.

4) Fälle mit zu vielen „Missings“ ausschließen

Alle Fälle, die im FLA mehr als fünf „Missings“ aufweisen, sollten von den weiteren Analysen ausgeschlossen werden.

5) Fehlende Werte durch Mittelwertsschätzungen ersetzen

Bei den übrigen Fragebögen werden fehlende Werte einer Person bei einzelnen Items durch den Mittelwert ersetzt, der aus den Antworten der Person auf die beantworteten Items gebildet wird.

6) Rohwert für den Gesamttest berechnen

Die Antworten auf die Items des FLA werden aufsummiert.

7) Rohwerte für die drei Dimensionen berechnen

Das gleiche Vorgehen wie unter Punkt 6 wird auf die einzelnen Dimensionen des FLA („Physische Merkmale“, „Psychische Belastung“, Funktionaler Status“) angewendet.

8) Rohwerte in 0-100-Skalenwerte transformieren

Im letzten Schritt werden die Rohwerte der drei Dimensionen sowie der Gesamtskala in eine 0 bis 100 Skala umgerechnet. Durch diese Lineartransformation des Summenwerts erhält man einen Index für Lebensqualität, der zwischen 0 und 100 variiert. Dabei bedeutet ein Wert von 0, daß alle Fragen im Sinne einer geringen Lebensqualität, ein Wert von 100 hingegen, daß alle Fragen im Sinne einer hohen Lebensqualität beantwortet wurden. Dies erleichtert die Interpretation der Ergebnisse, da ein Wert direkt den prozentualen Anteil am höchstmöglichen Wert darstellt. Die Transformation wird nach folgender Formel vollzogen:

$$\text{Transformierte Skala} = \frac{[(\text{tatsächlicher Rohwert} - \text{niedrigst möglicher Rohwert}) / \text{mögliche Spannweite der Rohwerte}] \times 100}$$

Tab. 1: Werte für die Berechnung der transformierten Lebensqualitätswerte.

¹ wird künftig weiter ausgearbeitet

Dimension/ Skala	Summe der Itemwerte	Niedrigster und höchst möglicher Rohwert	Mögliche Spannweite des Rohwertes
Gesamtskala	1+2+3+4+5+6+7+8+9+10+11+12+13+14 +15+16+17+18+19+20+21+22+23+24+2 5+26+27+28+29+30+31+32+33+34+35+ 36+37+38+39+40	40, 120	80
Physische Merkmale	3+8+9+10+11+19+22+24+25+30+31	11, 33	22
Psychische Belastung	1+5+7+13+16+17+18+26+27+32+35+36 +37+38+40	15, 45	30
Funktionaler Status	2+4+6+12+14+15+20+21+23+28+29+33 +34+39	14, 42	28

Tab. 2: Die Dimensionen des FLA mit genauem Itemwortlaut.

Dimension 1 (11 Items): Physische Merkmale (körperliche Empfindungen, Krankheitssymptome, Begleiterscheinungen)

3. Ich habe einen gesunden Schlaf.
8. In den meisten Nächten wache ich auf und brauche mein Dosieraerosol oder Inhalationsgerät.
9. Arbeiten, die mich körperlich stark beanspruchen (z.B. Gartenarbeit), fallen mir schwer.
10. Ich nehme die ersten Anzeichen einer Erkältung eher wahr als andere Menschen.
11. Von Zeit zu Zeit habe ich Schwierigkeiten, mich im Hause zu bewegen.
19. Aufgrund meines Asthmas schlafe ich schlecht.
22. Ich muß nachts häufig husten.
24. Ich neige dazu, Personen mit Erkältungen zu meiden.
25. Ich kann eine Treppe hinaufgehen, ohne anzuhalten.
30. Erkältungen dauern bei mir länger als bei anderen.
31. Ich kann eine Treppe nur dann hinaufgehen, wenn ich eine oder mehrere Pausen einlege.

Dimension 2 (15 Items): Psychische Belastung

1. Bei privaten Einladungen befürchte ich, daß irgendetwas in der dortigen Umgebung einen Atemnot- oder Hustenanfall auslösen könnte.
5. Ich denke fast nie an mein Asthma.
7. Ich mache mir niemals Sorgen, daß ein geplanter Urlaub negative Auswirkungen auf mein Asthma haben könnte.
13. Ich habe das Gefühl, etwas zu versäumen, da ich an einigen sportlichen Aktivitäten nicht teilnehmen kann
16. Ich habe das Gefühl, meinen Körper nicht unter Kontrolle zu haben.
17. Ich bin besorgt, weil ich nicht weiß, wann ich den nächsten Atemnot-/Hustenanfall haben werde.
18. Ich werde unruhig, wenn ich kurzatmig bin.
26. Ich versuche Aufregungen zu vermeiden, weil sich dadurch mein Asthma verschlimmert.
27. Ich fühle mich so hilflos, weil ich Asthma habe.
32. Ich habe eine gute Zukunft vor mir.
35. Wegen meines Asthmas fühle ich mich manchmal sexuell frustriert.
36. Ich mache mir Sorgen darüber, wie mein Gesundheitszustand in 10 Jahren aussehen wird.
37. Ich bin oft deprimiert wegen meines Asthmas.
38. Ich kann mich gut entspannen.
40. Ich vertraue auf meine Fähigkeit, mit einem Husten-/Atemnotanfall fertig zu werden.

Dimension 3 (14 Items): Funktionaler Status (Aktivitätsniveau im Alltag, berufliche Belastbarkeit)

2. Aufgrund meines Asthmas sind meine Urlaubsmöglichkeiten beschränkt.
4. Es fällt mir leicht, meine Einkäufe zu tragen.
6. Manchmal muß ich Menschen enttäuschen, weil ich Versprechungen wegen meines Asthmas nicht immer einhalten kann.
12. Ich glaube, daß mein Asthma keine Auswirkungen auf das Leben meiner Angehörigen hat.
14. Ich kann auf die gleiche Art und Weise wie jeder andere Urlaub machen.
15. Mir fällt die Hausarbeit leicht.
20. Heimwerker-Aktivitäten wie z.B. Tapezieren fallen mir schwer.
21. Ich kann ohne Probleme in eine Gaststätte gehen.
23. Aufgrund meines Asthmas kann ich einige Arbeiten, die ich gerne verrichten würde, nicht ausführen.
28. Wenn ich ausgehe, muß ich wegen meines Asthmas manchmal früher nach Hause gehen als andere.
29. Der Ablauf meiner Arbeit ändert sich durch mein Asthma nicht.
33. Wenn mein Asthma sich verschlechtert, dann arbeite ich auch schlecht.
34. Es gibt Orte, wo ich gerne hinginge, es aber aufgrund meines Asthmas nicht kann.
39. Mein Asthma beeinträchtigt mich tatsächlich nur bei einem Anfall.

ASTHMA QUALITY OF LIFE QUESTIONNAIRE WITH STANDARDISED ACTIVITIES (AQLQ(S))

SELF-ADMINISTERED UNITED KINGDOM VERSION

© 1998
QOL TECHNOLOGIES LTD.



For further information:

Elizabeth Juniper, MCSP, MSc
Professor
20 Marcuse Fields
Bosham
West Sussex
PO18 8NA. UK
Telephone: + 44 (0) 1243 572124
Fax: + 44 (0) 1243 573680
E-mail: juniper@qoltech.co.uk
WWW.qoltech.co.uk

Translated by MAPI RESEARCH INSTITUTE
Translator: Prof. Elizabeth Juniper

© The AQLQ(S) is copyrighted. It may not be altered, sold (paper or electronic), translated or adapted for another medium without the permission of Elizabeth Juniper.

ASTHMA QUALITY OF LIFE QUESTIONNAIRE (S)
 (UNITED KINGDOM)
 SELF-ADMINISTERED

PATIENT ID _____

DATE _____

Please complete **all** questions by circling the number that best describes how you have been during the **last 2 weeks as a result of your asthma**.

HOW LIMITED HAVE YOU BEEN DURING THE LAST 2 WEEKS IN THESE ACTIVITIES AS A RESULT OF YOUR ASTHMA?

	Totally Limited	Extremely Limited	Very Limited	Moderate Limitation	Some Limitation	A Little Limitation	Not at all Limited
1. STRENUOUS ACTIVITIES (such as hurrying, exercising, running up stairs, sports)	1	2	3	4	5	6	7
2. MODERATE ACTIVITIES (such as walking, housework, gardening, shopping, climbing stairs)	1	2	3	4	5	6	7
3. SOCIAL ACTIVITIES (such as talking, playing with pets/children, visiting friends/relatives)	1	2	3	4	5	6	7
4. WORK-RELATED ACTIVITIES* (tasks you have to do at work)	1	2	3	4	5	6	7

*If you are not employed or self-employed, these should be tasks you have to do most days.

5. SLEEPING	1	2	3	4	5	6	7
-------------	---	---	---	---	---	---	---

HOW MUCH DISCOMFORT OR DISTRESS HAVE YOU FELT DURING THE LAST 2 WEEKS?

	A Very Great Deal	A Great Deal	A Good Deal	Moderate Amount	Some	Very Little	None	
6. How much discomfort or distress have you felt over the last 2 weeks as a result of CHEST TIGHTNESS?		1	2	3	4	5	6	7

IN GENERAL, **HOW MUCH OF THE TIME DURING THE LAST 2 WEEKS** DID YOU:

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	Hardly Any of the Time	None of the Time
7. Feel CONCERNED ABOUT HAVING ASTHMA?	1	2	3	4	5	6	7
8. Feel SHORT OF BREATH as a result of your asthma?	1	2	3	4	5	6	7
9. Experience asthma symptoms as a RESULT OF BEING EXPOSED TO CIGARETTE SMOKE?	1	2	3	4	5	6	7
10. Experience a WHEEZE in your chest?	1	2	3	4	5	6	7
11. Feel you had to AVOID A SITUATION OR ENVIRONMENT BECAUSE OF CIGARETTE SMOKE?	1	2	3	4	5	6	7

HOW MUCH DISCOMFORT OR DISTRESS HAVE YOU FELT **DURING THE LAST 2 WEEKS?**

	A Very Great Deal	A Great Deal	A Good Deal	Moderate Amount	Some	Very Little	None
12. How much discomfort or distress have you felt over the last 2 weeks as a result of COUGHING?	1	2	3	4	5	6	7

IN GENERAL, **HOW MUCH OF THE TIME DURING THE LAST 2 WEEKS** DID YOU:

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	Hardly Any of the Time	None of the Time
13. Feel FRUSTRATED as a result of your asthma?	1	2	3	4	5	6	7
14. Experience a feeling of CHEST HEAVINESS?	1	2	3	4	5	6	7

IN GENERAL, **HOW MUCH OF THE TIME DURING THE LAST 2 WEEKS DID YOU:**

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	Hardly Any of the Time	None of the Time
15. Feel CONCERNED ABOUT THE NEED TO USE MEDICATION for your asthma?	1	2	3	4	5	6	7
16. Feel the need to CLEAR YOUR THROAT?	1	2	3	4	5	6	7
17. Experience asthma symptoms as a RESULT OF BEING EXPOSED TO DUST?	1	2	3	4	5	6	7
18. Experience DIFFICULTY BREATHING OUT as a result of your asthma?	1	2	3	4	5	6	7
19. Feel you had to AVOID A SITUATION OR ENVIRONMENT BECAUSE OF DUST?	1	2	3	4	5	6	7
20. WAKE UP IN THE MORNING WITH ASTHMA SYMPTOMS?	1	2	3	4	5	6	7
21. Feel AFRAID OF NOT HAVING YOUR ASTHMA MEDICATION AVAILABLE?	1	2	3	4	5	6	7
22. Feel bothered by HEAVY BREATHING?	1	2	3	4	5	6	7
23. Experience asthma symptoms as a RESULT OF THE WEATHER OR AIR POLLUTION OUTSIDE?	1	2	3	4	5	6	7
24. Were you WOKEN AT NIGHT by your asthma?	1	2	3	4	5	6	7
25. AVOID OR LIMIT GOING OUTSIDE BECAUSE OF THE WEATHER OR AIR POLLUTION?	1	2	3	4	5	6	7
26. Experience asthma symptoms as a RESULT OF BEING EXPOSED TO STRONG SMELLS OR PERFUME?	1	2	3	4	5	6	7

IN GENERAL, **HOW MUCH OF THE TIME DURING THE LAST 2 WEEKS DID YOU:**

	All of the Time	Most of the Time	A Good Bit of the Time	Some of the Time	A Little of the Time	Hardly Any of the Time	None of the Time
27. Feel AFRAID OF GETTING OUT OF BREATH?	1	2	3	4	5	6	7
28. Feel you had to AVOID A SITUATION OR ENVIRONMENT BECAUSE OF STRONG SMELLS OR PERFUME?	1	2	3	4	5	6	7
29. Has your asthma INTERFERED WITH GETTING A GOOD NIGHT'S SLEEP?	1	2	3	4	5	6	7
30. Have a feeling of FIGHTING FOR AIR?	1	2	3	4	5	6	7

HOW LIMITED HAVE YOU BEEN **DURING THE LAST 2 WEEKS?**

	Most Not Done	Several Not Done	Very Few Not Done	No Limitation			
31. Think of the OVERALL RANGE OF ACTIVITIES that you would have liked to have done during the last 2 weeks. How much has your range of activities been limited by your asthma?	1	2	3	4	5	6	7

HOW LIMITED HAVE YOU BEEN DURING THE LAST 2 WEEKS?

	Totally Limited	Extremely Limited	Very Limited	Moderate Limitation	Some Limitation	A Little Limitation	Not at all Limited
32. Overall, among ALL THE ACTIVITIES that you have done during the last 2 weeks, how limited have you been by your asthma?	1	2	3	4	5	6	7

DOMAIN CODE:

Symptoms: 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 29, 30

Activity Limitation: 1, 2, 3, 4, 5, 11, 19, 25, 28, 31, 32

Emotional Function: 7, 13, 15, 21, 27

Environmental Stimuli: 9, 17, 23, 26

Marks Asthma Quality of Life

What follows is a series of statements describing the way in which asthma (or its treatment) affects some people. You are asked to tick () the response to each statement which closely applies to you **over the past 4 weeks**.

	Not at all	Mildly	Moderately	Severely	Very severely
I have been troubled by episodes of shortness of breath	<input type="checkbox"/>				
I have been troubled by wheezing attacks	<input type="checkbox"/>				
I have been troubled by tightness in the chest	<input type="checkbox"/>				
I have been restricted in walking down the street on level ground or doing light housework because of asthma	<input type="checkbox"/>				
I have been restricted in walking up hills or doing heavy housework because of asthma	<input type="checkbox"/>				
I have felt tired or a general lack of energy	<input type="checkbox"/>				
I have been unable to sleep at night	<input type="checkbox"/>				
I have felt sad or depressed	<input type="checkbox"/>				
I have felt frustrated with myself	<input type="checkbox"/>				
I have felt anxious, under tension or stressed	<input type="checkbox"/>				
I have felt that asthma is preventing me from achieving what I want from life	<input type="checkbox"/>				

P.T.O.

	Not at all	Mildly	Moderately	Severely	Very severely
Asthma has interfered with my social life	<input type="checkbox"/>				
I have been limited in going to certain places because they are bad for my asthma	<input type="checkbox"/>				
I have been limited in going to certain places because I have been afraid of getting an asthma attack and not being able to get help	<input type="checkbox"/>				
I have been restricted in the sports, hobbies, or other recreations I can engage in because of my asthma	<input type="checkbox"/>				
I have felt generally restricted	<input type="checkbox"/>				
I have felt asthma is controlling my life	<input type="checkbox"/>				
I have been worried about my present or future health because of asthma	<input type="checkbox"/>				
I am worried about asthma shortening my life	<input type="checkbox"/>				
I have felt dependent on my asthma sprays	<input type="checkbox"/>				

HOW TO FILL IN THIS FORM . . .

Here is a list of sentences describing everyday experiences of asthma sufferers.

Please use a pencil to write on this form and completely fill in the circle which corresponds to your answer.

For each sentence, please fill in one circle to show whether that sentence is

- untrue of me
- slightly true of me
- or
- very true of me

For example if you think the sentence 'I can take part in any sport I want' is very true of you, fill in the circle labelled 'Very true of me'. Like this:

Very true of me

Slightly true of me

Untrue of me

Not applicable

Example

1. I can take part in any sport I want.

If the sentence is slightly true of you, fill in the circle labelled 'Slightly true of me'; and if the sentence is untrue of you because you cannot take part in any sport you want, then fill in the circle labelled 'Untrue of me'.

A very few of the sentences will not be applicable to you. For example, if you don't want to take part in sport then it makes no difference whether you are physically able to or not.

Where a sentence is not applicable, and only where it is not applicable, please fill in the circle labelled 'Not Applicable' as in the following example:

Very true of me

Slightly true of me

Untrue of me

Not applicable

Example

1. I can take part in any sport I want.

Now, please answer the following questions as truthfully as you can.

Don't spend too long over one sentence, just give your first reaction.

Please make sure you fill in one circle, and only one circle, for each sentence.

Your answers will be treated in the strictest confidence.

Begin here . . .

Sample Markings

Wrong

Right

Untrue of me

Slightly true of me

Very true of me

1. I can take part in any sport I want.	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	Not applicable <input type="radio"/>
2. When invited round to a friend's house, I worry that there may be something there which sets off an attack.	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	Not applicable <input type="radio"/>
3. Having asthma restricts the sort of holiday I can take.	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	Not applicable <input type="radio"/>
4. I am a sound sleeper.	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	Not applicable <input type="radio"/>
5. I take good care to avoid doing things which make my asthma worse.	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	Not applicable <input type="radio"/>
6. I find it easy to carry shopping.	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	Not applicable <input type="radio"/>
7. I think that those who live with me find it stressful because of my asthma.	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	Not applicable <input type="radio"/>
8. I check all the time that I have my inhaler with me.	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	Not applicable <input type="radio"/>
9. I feel angry with my body.	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	Not applicable <input type="radio"/>
10. I hardly ever think about my asthma.	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	Not applicable <input type="radio"/>
11. I sometimes let people down because my asthma prevents me from doing something I have previously agreed to do.	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	Not applicable <input type="radio"/>
12. I can run like other people.	<input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/> <input type="radio"/>	Not applicable <input type="radio"/>

Now please turn over . . .

Continue here . . .

Very true of me
Slightly true of me
Untrue of me

Very true of me
Slightly true of me
Untrue of me

<p>13. I never worry that going on holiday can make my asthma worse.</p> <p style="text-align: center;">Not applicable <input type="radio"/></p>	<p>25. I can go on the same kind of holiday as anyone else.</p> <p style="text-align: right;">Not applicable <input type="radio"/></p>
<p>14. Most nights I wake up needing to use my inhaler.</p> <p style="text-align: center;">Not applicable <input type="radio"/></p>	<p>26. I find housework easy.</p> <p style="text-align: right;">Not applicable <input type="radio"/></p>
<p>15. I have difficulty doing physically demanding tasks like gardening.</p> <p style="text-align: center;">Not applicable <input type="radio"/></p>	<p>27. Because of my asthma I feel drained after a cold.</p> <p style="text-align: right;">Not applicable <input type="radio"/></p>
<p>16. I tend to be more conscious than other people of the early symptoms of a cold.</p> <p style="text-align: center;">Not applicable <input type="radio"/></p>	<p>28. I need to take regular stops when I walk up a hill.</p> <p style="text-align: right;">Not applicable <input type="radio"/></p>
<p>17. There are times when I have difficulty getting around the house.</p> <p style="text-align: center;">Not applicable <input type="radio"/></p>	<p>29. I don't feel in control of my body.</p> <p style="text-align: right;">Not applicable <input type="radio"/></p>
<p>18. I think that my asthma does not affect the lives of my relatives.</p> <p style="text-align: center;">Not applicable <input type="radio"/></p>	<p>30. I feel anxious about not knowing when my next asthma attack is coming.</p> <p style="text-align: right;">Not applicable <input type="radio"/></p>
<p>19. If I forgot my inhaler it would probably make no difference.</p> <p style="text-align: center;">Not applicable <input type="radio"/></p>	<p>31. I sometimes go into a toilet just to take a puff of my inhaler.</p> <p style="text-align: right;">Not applicable <input type="radio"/></p>
<p>20. I never feel fed up because I have asthma.</p> <p style="text-align: center;">Not applicable <input type="radio"/></p>	<p>32. I get emotionally upset when puffy.</p> <p style="text-align: right;">Not applicable <input type="radio"/></p>
<p>21. I feel that there are many worse things than asthma.</p> <p style="text-align: center;">Not applicable <input type="radio"/></p>	<p>33. I don't have to make excuses to my friends because of my asthma.</p> <p style="text-align: right;">Not applicable <input type="radio"/></p>
<p>22. Eating out can be ruined if the restaurant is smokey.</p> <p style="text-align: center;">Not applicable <input type="radio"/></p>	<p>34. I sleep badly because of my asthma.</p> <p style="text-align: right;">Not applicable <input type="radio"/></p>
<p>23. I feel that I miss out because there are some sporting activities I can not join in with.</p> <p style="text-align: center;">Not applicable <input type="radio"/></p>	<p>35. I find it difficult to do some DIY activities like decorating.</p> <p style="text-align: right;">Not applicable <input type="radio"/></p>
<p>24. I feel frustrated at being unable to engage in sports.</p> <p style="text-align: center;">Not applicable <input type="radio"/></p>	<p>36. Colds don't bother me much.</p> <p style="text-align: right;">Not applicable <input type="radio"/></p>

Living With Asthma Questionnaire

Continue here . . .

Very true of me
 Slightly true of me
 Untrue of me

Very true of me
 Slightly true of me
 Untrue of me

37. I can walk up a hill as fast as anyone else of my age.	49. I feel inadequate because of my asthma.
<input type="radio"/>	<input type="radio"/>
Not applicable <input type="radio"/>	Not applicable <input type="radio"/>
38. I can visit a pub without any problems.	50. I have a good future ahead of me.
<input type="radio"/>	<input type="radio"/>
Not applicable <input type="radio"/>	Not applicable <input type="radio"/>
39. I tend to cough a lot at night.	51. I work badly when my asthma is bad.
<input type="radio"/>	<input type="radio"/>
Not applicable <input type="radio"/>	Not applicable <input type="radio"/>
40. I can't do some jobs I would like to do because of my asthma.	52. There are places I would like to go to but can't because of my asthma.
<input type="radio"/>	<input type="radio"/>
Not applicable <input type="radio"/>	Not applicable <input type="radio"/>
41. I tend to avoid other people who have colds.	53. I find it a real nuisance having to use my inhaler.
<input type="radio"/>	<input type="radio"/>
Not applicable <input type="radio"/>	Not applicable <input type="radio"/>
42. I can walk up a flight of stairs without stopping.	54. I find it a real nuisance having to take my tablets for my asthma.
<input type="radio"/>	<input type="radio"/>
Not applicable <input type="radio"/>	Not applicable <input type="radio"/>
43. I try to avoid getting emotionally upset because it makes my asthma worse.	55. I am in charge of my own life.
<input type="radio"/>	<input type="radio"/>
Not applicable <input type="radio"/>	Not applicable <input type="radio"/>
44. My asthma makes me feel so helpless.	56. I sometimes feel sexually frustrated because of my asthma.
<input type="radio"/>	<input type="radio"/>
Not applicable <input type="radio"/>	Not applicable <input type="radio"/>
45. Having asthma means I sometimes have to go home after a night out sooner than other people.	57. I worry about what my condition will be like in 10 years time.
<input type="radio"/>	<input type="radio"/>
Not applicable <input type="radio"/>	Not applicable <input type="radio"/>
46. Having asthma makes no difference to the way I work.	58. I have panicky feelings when I think about the future.
<input type="radio"/>	<input type="radio"/>
Not applicable <input type="radio"/>	Not applicable <input type="radio"/>
47. My colds last longer than other people's.	59. I am embarrassed by having asthma.
<input type="radio"/>	<input type="radio"/>
Not applicable <input type="radio"/>	Not applicable <input type="radio"/>
48. I can only walk up a flight of stairs if I have one or more stops on the way.	60. I often feel depressed because of my asthma.
<input type="radio"/>	<input type="radio"/>
Not applicable <input type="radio"/>	Not applicable <input type="radio"/>

003204

Continue here . . .

Very true of me
Slightly true of me
Untrue of me

61. I find it easy to relax.	Not applicable <input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
62. Except when I have an attack, I am never really affected by asthma.	Not applicable <input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
63. I don't bother much about my asthma.	Not applicable <input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
64. My asthma does not amount to a serious health problem.	Not applicable <input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
65. I have confidence in my ability to cope with an asthma attack.	Not applicable <input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
66. I worry about the long term effects of asthma drugs on my health.	Not applicable <input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
67. I find that stress brings on an asthma attack.	Not applicable <input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
68. Having an asthma attack makes me angry.	Not applicable <input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Please give the following information:

Sex Male Female (please fill in one circle)

Age _____ yrs. (please write your age)

--

Do not mark in this box

Patient Study No.	Study	Inv.	Age	Misc.
0 0 0 0 0 0	0 0 0	0 0 0	0 0	0 0 0 0 0 0 0
1 1 1 1 1 1	1 1 1	1 1 1	1 1	1 1 1 1 1 1 1
2 2 2 2 2 2	2 2 2	2 2 2	2 2	2 2 2 2 2 2 2
3 3 3 3 3 3	3 3 3	3 3 3	3 3	3 3 3 3 3 3 3
4 4 4 4 4 4	4 4 4	4 4 4	4 4	4 4 4 4 4 4 4
5 5 5 5 5 5	5 5 5	5 5 5	5 5	5 5 5 5 5 5 5
6 6 6 6 6 6	6 6 6	6 6 6	6 6	6 6 6 6 6 6 6
7 7 7 7 7 7	7 7 7	7 7 7	7 7	7 7 7 7 7 7 7
8 8 8 8 8 8	8 8 8	8 8 8	8 8	8 8 8 8 8 8 8
9 9 9 9 9 9	9 9 9	9 9 9	9 9	9 9 9 9 9 9 9

Thank you for your help.