PATIENT-REPORTED OUTCOME MEASUREMENT GROUP, OXFORD

A STRUCTURED REVIEW OF PATIENT-REPORTED OUTCOME MEASURES (PROMs) FOR ASTHMA

Report to the Department of Health, 2009

Patient-Reported

O U T C O M E

Measures

A STRUCTURED REVIEW OF PATIENT-REPORTED OUTCOME MEASURES FOR PEOPLE WITH ASTHMA: AN UPDATE 2009.

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http://phi.uhce.ox.ac.uk/

A STRUCTURED REVIEW OF PATIENT-REPORTED OUTCOME MEASURES FOR PEOPLE WITH ASTHMA: An update 2009

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EXECUTIVE SUMMARY

Aims of the report

The aims of this report are to review the evidence of patient-reported outcome measures (PROMs) for people with asthma and to provide recommendations to the Department of Health of PROMs for asthma that could potentially be used on a large scale population basis, combining good measurement properties with the likelihood of modest burden to respondents in order not to jeopardise response rates. A literature review of relevant PROMs resulted in the identification of a short-list of both generic and asthma-specific instruments which were then presented to a multidisciplinary panel for discussion. The literature review of the evidence-base and the discussions of the multi-disciplinary panel underpin final recommendations to the Department of Health.

The Patient-reported Outcome Measurement Group previously submitted a report to the Department of Health of evidence of Patient-reported Outcome Measures (PROMs) for chronic conditions (Fitzpatrick et al., 2006). The report included a review of evidence regarding PROMs for asthma with some recommendations.[1]

The methods of the review are described and the results of the search including sources and search terms used to identify specific published research. Details of this updated evidence are presented firstly for generic PROMs evaluated with people with asthma, followed by asthma-specific PROM results. A number of newly identified asthma-specific measures are also briefly discussed. The report concludes with discussion and recommendations.

Results and short-list of PROMs for people with asthma

The previous review (PROM group, 2006) reported evidence for the following PROMs: SF-36, SF-12, EQ-5D, Sickness Impact Profile (SIP), and the Health Utilities Index (HUI). This update identified further evidence of performance for the SF-36, SF-12, EQ-5D and the HUI. An additional generic PROM, the SF-6D was identified with reporting of some evidence of performance.

Nine asthma-specific instruments were previously identified (2006):

a) Asthma Quality of Life Questionnaire (AQLQ)
b) MiniAQLQ
c) AQLQ(S)
d) Acute AQLQ
e) Asthma Control Questionnaire (ACQ)
f) Asthma Control Diary (ACD)
g) Marks Asthma Quality of Life Questionnaire (MAQLQ)
h) Living With Asthma Questionnaire (LWAQ)
i) St. Georges Respiratory Questionnaire (SGRQ)

[1] A Structured review of PROMs for Asthma 2006, can be downloaded from http://phi.uhce.ox.ac.uk/

In carrying out the current update of evidence, a further thirteen asthma-specific instruments were identified.

j) Asthma Control Test (ACT)
k) Asthma Impact Survey (AIS-6)
l) Asthma Therapy Assessment Questionnaire
m) Perceived Control of Asthma Questionnaire (PCAQ)
n) Asthma Outcomes Monitoring System
o) Asthma Control Scoring System (ACSS)
p) Asthma Quality of Life Utility Index AQL-5D
q) Asthma Symptom Utility Index (ASUI)
r) Asthma Questionnaire 20
s) Royal College of Physicians 3 questions:
t) Lara Asthma Symptom Scale
u) Asthma Self-efficacy Scale (ASES)
v) Work Productivity and Activity Impairment: Asthma (WPAI:Asthma)

Recommendations

Based on volume of evaluations and good measurement and operational characteristics, the following PROMs were presented to the multidisciplinary panel for discussion:

1. AQLQ; AQLQ(S); miniAQLQ
2. MAQLQ
3. SF-36

On the basis of appraisal of evidence by the PROM Group, and taking account of ratings and comments from the panel, the SF-36 and EQ-5D are considered suitable as generic measures in asthma. Given its brevity and the fact that it yields UK-derived preferences, the **EQ-5D** is recommended for use in combination with a condition-specific PROM. . The **miniAQLQ** is recommended as an asthma- specific instrument. These two measures used together will provide complementary evidence of health status of people with asthma in the context of potential population-level applications in the NHS. In making the final selection of PROMs considered suitable for piloting in the NHS, the DH will consider salient factors in addition to the evidence and multidisciplinary panel comments.

1. PATENT-REPORTED OUTCOME MEASURES FOR PEOPLE WITH ASTHMA: AN UPDATE OF EVIDENCE

Background

Patient-reported outcome measures (PROMs) offer enormous potential to improve the quality and results of health services. They provide validated evidence of health from the point of view of the user or patient. They may be used to assess levels of health and need in populations, and in users of services, and over time they can provide evidence of the outcomes of services for the purposes of audit, quality assurance and comparative performance evaluation. They may also improve the quality of interactions between health professionals and individual service users.

Lord Darzi's Interim Report on the future of the NHS recommends that patient-reported outcome measures (PROMs) should have a greater role in the NHS (Darzi 2007). The new Standard NHS Contract for Acute Services, introduced in April 2008, includes a requirement to report from April 2009 on patient-reported outcome measures (PROMs) for patients undergoing Primary Unilateral Hip or Knee replacements, Groin Hernia surgery or Varicose Vein. Furthermore, Lord Darzi's report 'High Quality Care for All' (2008) outlines policy regarding payments to hospitals based on quality measures as well as volume. These measures include PROMs as a reflection of patients' experience and views. Guidance has now been issued regarding the routine collection of PROMs for the selected elective procedures (DH, 2009).

The Patient-reported Outcome Measurement Group previously submitted a report to the Department of Health of evidence of Patient-reported Outcome Measures (PROMs) for chronic conditions, carer impact and patient perceptions of quality (Fitzpatrick et al., 2006). The report included a review of evidence regarding PROMs for asthma with some recommendations.

The aim of this report is two-fold: to provide an update of more recently published evidence for PROMs in asthma and to provide as clear recommendations as possible to Department of Health of PROMs that could be used on a potentially large scale population basis to assess health status of people with asthma to provide evidence relevant to determining the quality of services in the NHS. Recommended instruments would need to combine good measurement properties with the likelihood of low burden to respondents in order not to jeopardise responses rates. An additional consideration would be the availability of a PROM which yielded preference values derived from a UK source. As widely recommended, a strategy of combining a generic measure with a condition-specific measure was considered the most appropriate way of assessing complementary aspects of health status.

This current update review and recommendations draws on the existing evidence for each PROM up to 2006 but only provides fuller descriptive details of measurement and operational evidence which has emerged since 2006.

The full body of evidence was presented to a multidisciplinary panel for discussion. Details of their discussion and views are reported in Appendix F. The PROMs review group considered the combination of the full review of evidence and the multidisciplinary panel's views before reaching its own conclusions and recommendations. In making the

final selection of PROMs considered suitable for piloting in the NHS, the DH will consider salient factors in addition to the evidence and multidisciplinary panel comments.

Structure of the report

The methods of the update review are described and the results of the search including sources and search terms used to identify specific published research. Details of this updated evidence are presented firstly for generic PROMs evaluated with people with asthma, followed by asthma-specific PROM results. A number of newly identified asthma-specific measures are also briefly discussed. The report concludes with discussion and recommendations for short-listed PROMs.

Methods for the update review

Methods adopted were as described in previous reviews performed by the PROM group, Oxford. Comprehensive searches were conducted; articles retrieved were assessed for relevance and checked by another reviewer; and evidence of measurement performance and operational characteristics abstracted for each PROM identified. Assessment and evaluation of the PROMs was performed independently by two reviewers adapting the London School of Hygiene appraisal criteria (Appendix B) outlined in their review (Smith et al., 2005). These criteria were modified for our reviews. The final short listing of promising PROMs to formulate recommendations was based on these assessments and discussion between reviewers. The most promising PROMs were then presented to a multidisciplinary panel for final agreement.

Search terms and results: identification of articles

The methods for searching were conducted using three main sources:

The primary source of evidence was the bibliography compiled by the PROM group[2]. At the time of the review update, the PROM database comprised 16,054 records (up to December 2005) downloaded from several electronic databases using a complex search strategy (Appendix A). These records had been assessed as eligible for inclusion in the bibliography and assigned keywords. These records were searched using keywords 'respiratory' and further searches conducted using title OR abstract using terms resp* OR asthma.

A further 14,296 records covering the period January 2006-July 2007 had been downloaded using a revised search strategy (Appendix B) but not assessed or assigned keywords. The terms 'resp*' OR 'asthma' from title OR abstract were performed.

Supplementary searches included scanning the reference lists of key articles, checking instrument websites, where found, and drawing on other bibliographic resources. Hand searching of titles of key journal was conducted from 2006 to 2009. The following journals were selected:

- Chest
- Health and Quality of Life Outcomes

[2] Available online at http://phi.uhce.ox.ac.uk

- Medical Care
- Quality of Life Research
- Respiratory Medicine
- Thorax
- Journal of Asthma

In addition, PubMed records for the past two years (i.e. September 2006-2009) were searched using the term 'asthma' and the names of the instruments identified in the previous review and this update.

All abstracts were reviewed. When assessed against the review inclusion criteria, articles were retrieved and reviewed in full. Of these, 67 articles were included in the update review.
Results are presented in Table 1

Table 1. Number of articles identified by the literature review-

Source	***Results of search***	***No. of articles considered eligible***	***Number of articles included in review***
PROM database: 30,350	1372	128	15
Supplementary search	-	-	52
2009 TOTAL	-	-	**67**
2006 review			**50**
TOTAL			**117**

The recommendations are based on an assessment of the evidence from both the previous review (2006) and update review(2009) combined.

2. Result: Generic PROMs evaluated with people with asthma

The previous review reported evidence for the following PROMs:

a) SF-36
b) SF-12
c) EQ-5D
d) Sickness Impact Profile (SIP)
e) Health Utilities Index (HUI)

This update identified further evidence of performance for the SF-36, SF-12, EQ-5D and the HUI. An additional generic PROM, the SF-6D was identified with reporting of some evidence of performance.

Full details of the development, domains and scoring methods are detailed in Appendices C and D.

a). SF-36

Twelve studies describe the evaluation of the SF-36 in the previous review with all measurement and operational criteria reported. Two studies were identified in this update, one from the UK (Ritz et al., 2006).

The SF-36 discriminated patients with asthma with significantly lower scores compared to population norms (Ritz et al., 2006; Wyrwich et al., 2006). The SF-36 was not sensitive enough to detect small changes which were important to patients (Wyrwich et al., 2006).

b). SF-12

The SF-12 was evaluated in three studies in the previous review providing some good evidence of validity, responsiveness and acceptability. Four further studies are included in this update.

Construct validity is supported with asthma patients reporting scores below the population norms (Adams et al., 2006; Archea et al., 2007). The SF-12 PCS scores were related to subsequent increased use of controller medications for asthma and emergency department or hospital utilisation (Schatz et al,. 2006). The MCS scores were predictive of increased use of controller medications alone. Discriminative properties are reported with the SF-12 distinguishing between current and past smokers with asthma (Eisner and Iribarren., 2007).

Some evidence of construct validity is found with moderate hypothesised correlations between SF-12 PCS and MAQLQ (0.55) (Archea et al., 2007).

c). EQ-5D

Four studies were included in the previous review with good evidence of validity, limited evidence of responsiveness. Missing responses were reported for both the utility score and the VAS. Three studies were identified from the update.

The EQ-5D utility and VAS discriminates between patients who suffer an exacerbation of their asthma which requires the use of steroids or hospitalisation with statistically significant lower scores (a utility change of -0.20).

Some evidence of construct validity is reported with strong correlation between EQ-5D and other utility measures (HUI; SF-6D). Moderate correlation is reported between EQ-5D and self-reported asthma questionnaires (McTaggart-Cowen et al., 2008; Chen et al., 2007).

Based on a hypothesised difference of 0.05 in mean utility score, the EQ-5D utility and VAS differentiated between different levels of agonist use by patients and the presence of chronic conditions but not patient-reported asthma severity or control (McTaggart-Cowen et al., 2008).

Potential skewed distribution effects have been reported with 50% of patients having reporting utility indices ≥ 0.9 (McTaggart-Cowen et al., 2008).

d). SIP

Evidence from the previous review was limited with the SIP used as a reference PROM for hypothesising correlations between asthma-specific PROMs and the SIP. No further evidence was found in this update.

e). HUI

Limited evidence was found for the HUI in the previous review with the HUI used as a reference PROM for hypothesising correlations between asthma-specific PROMs. One study was found for this update.

Some evidence is reported for construct validity. The HUI did not discriminate between different levels of asthma control measured by self-report ACQ and medication use but did between the presence of other chronic conditions (McTaggart-Cowen et al., 2008).

Weak correlation has been reported between the HUI and respiratory function, strong correlation with the EQ-5D and SF-6D (0.73, 0.69). Correlations were moderate for ACQ, AQLQ(S), AQL-5D, and EQ-5D VAS (0.32 to 0.58) (McTaggart-Cowen et al., 2008).

Based on a hypothesised difference of 0.05 in mean utility measures the HUI differentiated between different levels of agonist use by patients and the presence of chronic conditions but not patient-reported asthma severity or control (McTaggart-Cowen et al., 2008).

Potential skewed distribution effects have been reported with 55% of patients having reporting utility indices ≥ 0.9 (McTaggart-Cowen et al., 2008).

f). SF-6D

No evidence was identified in the previous review for the SF-6D.

One evaluative study was identified in this update with results suggesting that the SF-6D was not useful in identifying patients with different levels of asthma control measured by self-report (ACQ) and by medication use (McTaggart-Cowen et al., 2008).

Weak correlation has been reported for the SF-6D and respiratory function; strong correlation between EQ-5D and HUI (0.67, 0.69); and moderate for AQL-5D, EQ-5D VAS, AQLQ(S) and ACQ (McTaggart-Cowen et al., 2008).

Based on a hypothesised difference of 0.05 in mean utility measures the SF-6D did not differentiate between different levels of agonist use by patients nor patient-reported asthma severity or control but discriminated between the presence of chronic conditions (McTaggart-Cowen et al., 2008).

Potential skewed distribution effects have been reported with 12% of patients having reporting utility indices ≥ 0.9 (McTaggart-Cowen et al., 2008).

3. Results: Asthma-specific PROMs

This section firstly provides a summary of the more recent evidence found for the nine asthma-specific instruments previously identified:

a) Asthma Quality of Life Questionnaire (AQLQ)
b) MiniAQLQ
c) AQLQ(S)
d) Acute AQLQ
e) Asthma Control Questionnaire (ACQ)
f) Asthma Control Diary (ACD)
g) Marks Asthma Quality of Life Questionnaire (MAQLQ)
h) Living With Asthma Questionnaire (LWAQ)
i) St. Georges Respiratory Questionnaire (SGRQ)

In carrying out the current update of evidence, a further thirteen asthma-specific instruments were identified. These newly identified instruments and their evidence-base are each briefly described. The thirteen PROMs briefly reviewed here are:

j) Asthma Control Test (ACT)
k) Asthma Impact Survey (AIS-6)
l) Asthma Therapy Assessment Questionnaire
m) Perceived Control of Asthma Questionnaire (PCAQ)
n) Asthma Outcomes Monitoring System
o) Asthma Control Scoring System (ACSS)
p) Asthma Quality of Life Utility Index AQL-5D
q) Asthma Symptom Utility Index (ASUI)
r) Asthma Questionnaire 20
s) Royal College of Physicians 3 questions:
t) Lara Asthma Symptom Scale
u) Asthma Self-efficacy Scale (ASES)
v) Work Productivity and Activity Impairment: Asthma (WPAI: Asthma)

Full details of the development, domains and scoring methods of previously identified instruments and those identified in this update are detailed in Appendices C and D.

Update of evidence for previously identified asthma-specific PROMs

a). Asthma Quality of Life Questionnaire (Juniper)

Seventeen studies were identified which evaluated the AQLQ in the previous review (2006) reporting evidence of good measurement performance and operational characteristics. A further seventeen studies have been identified in this update, three which were conducted in the UK (Aburuz et al., 2007; Morjaria et al., 2008; Thomas et al., 2007).

High internal consistency has been reported with alphas ≥ 0.80 (Schaffer et al., 2004 USA; Aburuz et al., 2007, UK). Test-retest reliability was established (Aburuz et al., 2007, UK) with ICC over a retest period of four weeks ≥ 0.82.

Construct validity has been demonstrated with the AQLQ discriminating between smokers and non-smokers and asthma severity groups with the ADSS as gold standard

(Lazarus et al., 2007 USA) and environmental factors contributing to asthma (Shedd et al., 2007).

Strong correlation is reported between AQLQ and an asthma-specific PROM (ADSS) and moderate with the EQ-5D and VAS) (Aburuz et al., 2007).

Several studies report evidence of responsiveness. The AQLQ, powered as a primary outcome and as a secondary end-point to detect change has been increasingly used in trials.

Interventions to improve asthma control and reduce symptoms were evaluated in trials and the AQLQ was used as the primary outcome in several studies (Slader et al., (2006; Lafond et al., 2007 ;Morjaria et al., 2008; Chipps et al., 2006). The AQLQ was used in other trials as a secondary outcome (Cox et al., 2007; Fitzgerald et al., 2000, Busse et al,. 2001, Malmstrom et al., 1999; Meltzer., 2002).

Non-significant changes were reported for the AQLQ and other measures (ACQ and clinical indicators) in a trial (powered to detect a 0.5 change in the Symptom domain) evaluating the effectiveness of breathing techniques on asthma symptoms (Slader et al., 2006). Small, but significant changes were reported for AQLQ in an intervention for corticosteroid refractory asthma patients (Morjaria et al., 2008) and medication for mild to moderate asthma (Nathan et al., 2008). Other primary outcomes in this study did not detect change (ACQ and respiratory function). Statistically significant changes were found in other trials supporting high responsiveness relative to physiological measures (Lafond et al., 2007; Cox et al., 2007; Ammar et al., 2008); clinical variables (Slader et al., 2006; Thomas et al., 2007); and patient-reported measures (Thomas et al., 2007). An improvement of ≥ 0.5 in scores was used in post hoc analysis of trial data to detect change. This was achieved with improvement of scores reported for a significantly greater number of patients in the treatment group (Price et al., 2007 UK).

A change of five points in scores has further been supported as clinically meaningful in several studies (Wyrwich et al., 2006; Chipps et al., 2006; Nathan et al., 2008). Further support of previously reported cut-off points for assessing clinically important change has been reported applying Rasch analysis (Metz et al., 2006).

High completion rates have been reported (Price et al., 2007).

b). miniAQLQ (Juniper)

Four studies were identified in the previous review which evaluated the miniAQLQ with good evidence of reproducibility, validity, responsiveness and high acceptability. Ten further studies supporting construct validity and responsiveness are reported in this update of evidence.

The miniAQLQ scores were related to subsequent increased use of controller medications for asthma (Schatz et al., 2006) and emergency department or hospital utilisation (Schatz et al,. 2005, USA). Hypothesised correlations were reported for the miniAQLQ with other PROMs (ACT and ATAQ) with higher correlations for the Symptom and Activity domains (Schatz et al., 2007).

Predictive validity is reported with a mini-AQLQ score cut-point of 4.7 significantly associated with subsequent exacerbations in patients without a history of prior acute episodes and high sensitivity (90%) for those patients with either a mini-AQLQ score <4.7 or a history of prior acute episodes. These patients were nearly 6 times more likely to require emergency hospital care (Schatz et al., 2008).

The mini-AQLQ (all domains and total scores) discriminates between patients who suffer an exacerbation of their asthma which requires the use of steroids or hospitalisation compared to other patients (Lloyd et al., 2007, UK). Further discriminative properties are reported using ATAQ scores to determine levels of control.

Construct validity is reported with moderate correlations between mini-AQLQ, ATAQ and EQ-5D utility and VAS (Chen et al., 2007).

Trial evidence supports responsiveness of the miniAQLQ with statistically significant changes in scores in the intervention group (Cleland et al., 2007, UK). The miniAQLQ was used as a primary outcome in this study and the results of other outcomes in these trials supported effectiveness of the intervention and therefore confirmation of responsiveness of the measure (Clark et al., 2007). The miniAQLQ was also responsive to change based on a prior improvement of ≥0.5 in scores in a trial of medication for patients with severe, allergic asthma (Niven et al., 2008 UK) and improvement of scores 1.5 +/- 0.2 ($p < 0.001$) in a trial of medical food supplementation (Surette et al., 2008) MiniAQLQ and ACQ scores improved by and 1.0 +/- 0.1, respectively.

Clinically important change, specified as ≥ 1.5 improvement in scores has been established ((Niven et al., UK 2008).

High response rates are reported (Schatz et al., 2008).

c) Asthma Quality of Life Questionnaire (S) (Juniper)

Two studies were included in the previous review providing good evidence of reliability, validity and responsiveness. Less missing data gas been reported for the AQLQ(S) than the AQLQ which may be attributed to the standardised Activity domain in the AQLQ(S).

Three studies were identified in this update.

The AQLQ(S) discriminated between respondents who had or did not have other chronic conditions and different levels of asthma control indicated by medication use. Hypothesised correlations with the ACQ were also reported (McTaggart-Cowen et al., 2008). The AQLQ(S) differentiated between different levels of agonist use by patients, the presence or absence of chronic conditions and patient-reported asthma severity or control (McTaggart-Cowen et al., 2008).

Weak correlation has been reported between the AQLQ(S) and respiratory function but strong correlations with the AQL-5D (0.91) and ACQ (0.83). Moderate correlations were found with EQ-5D, HUI and SF-6D (McTaggart-Cowen et al., 2008),

Score changes for the AQLQ(S) were statistically significantly different between the intervention and control group in patients participating in a medication trial. These were

consistent with the pattern of changes on other instruments (Murphy et al., 2008; Pogson et al., 2008 UK).

Responsiveness is established from trial data which was in relation to statistically significant changes in other patient-reported symptoms, control and number of rescue medications (Murphy et al., 2008) and non-significant changes in respiratory physiological outcomes (Pogson et al., 2008 UK).

High response rates reported (Pogson et al., 2008 UK).

d) Acute AQLQ

One study was included in the previous study reporting some evidence of reliability, validity and responsiveness. No further studies were identified in this update.

e) Asthma Control Questionnaire (ACQ)

Two studies provided evidence of reliability, validity and responsiveness in the previous review. Eleven studies provide further evidence in this update, two conducted in the UK (Morjaria et al., 2008; Thomas et al., 2007).

Acceptable internal consistency (0.83) is reported in one study (Scaffer et al., 2004) but a lower alpha level (0.66) in a study by Wallenstein et al., (2007).

Construct validity has been evaluated and the ACQ discriminated between different levels of asthma control measured by self-report, medication use, physiological function and the presences of chronic conditions (McTaggart-Cowen et al., 2008); smokers and non-smokers (Boulet et al., 2006; Chaudhuri et al., 2008); and between patients with better performance based test results (Mancuso et al., 2007); patients defined as well-controlled by physicians and lung function (Schaffer et al., 2004). The ACQ differentiated between different levels of agonist use by patients, the presence of chronic conditions and patient-reported asthma severity or control (McTaggart-Cowen et al., 2008).

Strong correlation has been reported between the ACQ and respiratory function, AQLQ(S) and some patient-reported utility measures (AQL-5D, EQ-5D VAS). Moderate correlations were observed with the EQ-5D utility, HUI and SF-6D (McTaggart-Cowen et al., 2008).

Trial evidence supports the responsiveness of the ACQ with statistically significant change or improvement in ACQ scores consistent with other respiratory and patient-reported outcomes in studies of the effectiveness of treatments for patients with corticosteroid refractory asthma (Morjaria et al., 2008) and trials of different medications (Cox et al., 2007; Pavord et al.,2007 UK; Thomas et al., 2007).

Data from a clinical trial, suggests that using a cut-off point of 0.75 or less, there is an 85% chance of the patient's asthma is well controlled. Conversely, identifying those who are not well-controlled by a cut-off point of 1.5 or above, there is a 88% chance of this being true (Juniper et al., 2006). Surette et al., (2008) suggest improvement of 1.0 +/- 0.1 in scores as a clinical cut-off value.

Patient acceptability was reported favourably in one study (Schaffer et al., 2004)

f) Asthma Control Diary (ACD)
One study was included in the previous review providing limited evidence of construct validity. No further studies were identified in this update of evidence.

g). Mark's Asthma Quality of Life Questionnaire (M-AQLQ)
Five studies provided good evidence of measurement performance of the MAQLQ in the previous review. A further four studies were identified in this update, one from the UK (Shaheen et al., 2007).

Internal consistencies for domains and total score were greater than 0.85 (Lowery et al., 2007).

Construct validity is reported with moderate correlations between MAQLQ and SF-12 PCS (0.55) (Archea et al., 2007). The MAQLQ discriminated between patients with workplace exacerbation of asthma with worse quality of life as predicted (Lowery et al., 2007) and poorer scores associated with reporting negative life events (Archea et al., 2007).
Discriminative properties are reported with the MAQLQ distinguishing between current and past smokers with asthma (Eisner and Iribarren., 2007).

Responsiveness has been demonstrated from trial evidence with significant differences reported for MAQLQ scores which were consistent with scores changes from other patient-reported outcomes and respiratory end-points (Armour et al., 2007).

Data were not normally distributed despite transformation on one study (Lowery et al., 2007).

h) Living With Asthma Questionnaire (LWAQ)
Three studies were included in the previous review reporting limited evidence for reliability and validity. No further studies were found in this update.

i) . St Georges Respiratory Questionnaire (SGRQ)
One study reported limited evidence in the previous review. Two studies were identified in this update.

Test-retest reliability is reported with ICC 0.83. Some evidence of construct validity is suggested with strong correlations between SGRQ and asthma severity. Responsiveness is suggested from trial data of breathing techniques with statistically significant improvement on scores (trial powered to detect a 12 point difference in scores) following breathing techniques. This was consistent with differences in scores in other outcomes (HADS and respiratory parameters) (Holloway & West., 2008; Nathan et al., 2006 UK).

No missing data and normal distribution has also been found.

Newly identified asthma-specific PROMs

j). Asthma Control Test
This measure was not included in the previous review. It was developed with the involvement of clinicians and patients (Nathan et al., 2004). Five items evaluate symptoms, role activities and asthma control. Scores are obtained from five-point Likert

scale. Items are summed to yield a score ranging from 5 (poor control of asthma) to 25 (complete control). Optimal cut-off for well-controlled asthma has been reported as 20 or higher and poorly controlled as 15 or lower (Schatz et al., 2007b).

Five studies provide some evidence of performance.

Acceptable internal consistency is reported 0.84 (Nathan et al., 2004) 0.79 to 0.85 (Schatz et al., 2006, 2007b) and 0.89 (Wallenstein et al., 2007). Reproducibility is reported with ICC 0.77 (Schatz et al., 2006).

Construct validity is demonstrated by moderate hypothesised correlations between ACT and ACQ, ATAQ, mini-AQLQ and clinicians ratings (Nathan et al., 2004; Schatz et al., 2006, 2007b).

Support for the discriminative ability of the ACT is provided with lower scores for patients with poorer levels of asthma control (Schatz et al., 2006; 2007a); those defined as well-controlled by physicians and different levels of lung function (Schatz et al., 2007a).

Responsiveness was established in longitudinal validity with high correlation between changes for ACT and ACQ (Schatz et al., 2006).

k). Asthma Impact Survey (AIS-6)

Items for this instrument were generated from a bank of items developed for the purpose of computerised adaptive assessment. Six items were selected from a pool of 52 items administered in a survey regarding the impact of asthma. Response options for the AIS-6 are scored on a 5 point Likert scale.

High internal consistency (0.95) is reported. The AIS discriminated between patients who were smokers; those who had a hospitalisation in the past year; and systematic corticosteroid use. Significant correlations were found with AIS-6 and mini-AQLQ (0.84) compared to correlations with ATAQ and AOMS (Schatz et al., 2007), providing some evidence of construct validity.

l). Asthma Therapy Assessment Questionnaire

The ATAQ was referred to in the previous review and further evidence is reported in this update. The ATAQ was developed in 1999 by Vollmer and was identified in the previous review. Items were generated by clinicians and focus groups with patents with asthma. The ATAQ instrument domains include asthma Control, Communication, Behaviour/Attitude, Self-Efficacy, and the Knowledge. Scores are obtained using a 3 point Likert scale. Vollmer presented data for the control domain. The instrument is used to identify patients whose asthma management may be sub-optimal. Five levels of asthma control is suggested (0= no control problems to 4= four control problems).

Higher number of control problems is significantly associated with healthcare utilisation and levels of health status and quality of life scores obtained from SF-36, AQLQ(S) and SGRQ (Vollmer et al., 1999). The ATAQ scores were predictive of future healthcare utilisation (Schatz et al., 2005; Peters et al., 2006; Sullivan et al., 2007); severe asthma related events (Sullivan et al., 2007) and the use of controller medications (Schatz et al,. 2005).

The number of control problems was directly related to dissatisfaction with treatment in a study by Markson et al., (2001) ATAQ scores indicative of more problems with control of their asthma in patients with persistent airflow limitation (Lee et al., 2007).

Construct validity is suggested with correlations reported higher with the symptoms and activity domains than the environmental and emotional domains of the mini AQLQ (Schatz et al., 2007). Further moderate correlations have been reported between ATAQ and mini-AQLQ (0.49) and weaker correlations with the EQ-5D (0.30) (Chen et al., 2007).

m). Perceived Control of Asthma Questionnaire (PCAQ)
The PCAQ was referred to in the previous review with one evaluation report. This update has identified six further studies reporting evidence of performance. There are eleven items measuring asthma control with a five point Likert scale of responses and reports suggest it takes five minutes to complete.

Acceptable internal consistency has been reported with Cronbach's alpha 0.73 to 0.79 (Katz et al., 1997; 2002; Schaffer et al., 2004).

Construct validity has been supported with moderate correlations between PCAQ and SF-36 and MAQLQ . A six point decrement in PCAQ score was predictive of increased risk of hospitalisation and frequent activity restriction (Katz et al., 1997; 2002). Scores have been reported to be comparable to other studies of asthma patients (Ritz et al., 2006). PCAQ higher scores were associated with better quality of life measured with SF-12 and MAQLQ (Calfee et al., 2006).

Responsiveness is suggested with changes in PCAQ scores consistent with changes observed for other instruments (SF-36, AQLQ). Correlations with AQLQ were moderate (0.44 to 0.56) and weak to moderate for SF-36 (0.14 to 0.65 for General Health (Olajos-Clow et al., 2005).

Significant improvement in scores was reported in trial evidence of a pharmacy based intervention which corresponded with changes in other patient-reported outcomes and lung function (Armour et al., 2007).

Patient acceptability is supported (Schaffer et al., 2004 USA).

n). Asthma Outcomes Monitoring System
This PROM was not identified in the previous review. It was developed by Bayliss et al., 1998 and details are found in the manual published by QualityMetric, Inc. Factor analysis yielded three factors represented by activity limitation, symptoms and concern or bother (Schatz et al,. 2005). High morbidity status has been defined as those with the highest score of 4 (Schatz et al., 2005).

The AOMS scores were related to subsequent increased use of controller medications for asthma (Schatz et al., 2006) and emergency department or hospital utilisation (Schatz et al,. 2005, USA). Factor analysis yielded three factors represented by activity limitation, symptoms and concern or bother.

o). Asthma Control Scoring System (ACSS)
This was not identified in the previous review. It is a clinical rating system developed by Boulet et al., (2006) with three domains: Clinical (symptoms, activities, use of rescue medications); Physiological response and Inflammatory assessment. Only the clinical domain is self-reported. The ACSS provides a percentage score. Two studies were identified in this review.

Results are reported for the clinical, patient-reported domains only. Reproducibility has not been established (r=0.59) for the patient-reported clinical domain (LeBlanc et al., 2007). High internal consistency has been established (0.84) (LeBlanc et al., 2007). The clinical domain correlates with quality of life measures (MAQOL), (Boulet et al., 2006), mini-AQLQ overall, symptoms and activities and the ACQ (LeBlanc et al., 2007) supporting construct validity.

Responsiveness has been demonstrated with strong correlation of change with other self-reported measures (mini-AQLQ, ACQ) and responsiveness index of 1.8 for the clinical parameter (LeBlanc et al., 2007).

p). Asthma Quality of Life Utility Index AQL-5D
This was not included in the previous review. This is a new classification system which has been derived from the AQLQ, based on Rasch analysis and other psychometric evidence. AQL-5D contains 5 attributes, each with 5 levels.

Three studies provide some evidence of performance.

AQL-5D discriminated between different levels of asthma control measured by self-report (ACQ) and medication use, physiological function and the presence of chronic conditions. Moderate correlations was found between generic (HUI, EQ-5D, SF-6D) and asthma-specific PROMs (AQLQ(S) and ACQ (McTaggart-Cowen et al., 2008).

The ASUI discriminates between patients who suffer an exacerbation of their asthma which requires the use of steroids or hospitalisation with statistically significant lower scores (Lloyd et al., 2007 UK).

Correlations have been reported as weak with the AQL-5D and respiratory function, moderate with EQ-5D, HUI and SF-6D and strong with AQLQ(S) and ACQ (0.82, 0.91) (McTaggart-Cowen et al., 2008).

Based on a hypothesised difference of 0.05 in mean utility measures the AQL-5D differentiated between different levels of agonist use by patients, the presence of chronic conditions and patient-reported asthma severity or control (McTaggart-Cowen et al., 2008).

Potential skewed distribution effects have been reported with 36% of patients having reporting utility indices ≥ 0.9 (McTaggart-Cowen et al., 2008).

q). Asthma Symptom Utility Index (ASUI)
This was not included in the previous review. This preference-based outcome measure was developed for use in US clinical trials and cost effectiveness studies for asthma interventions. A single index score derives from patient preferences for four symptoms

(cough, wheeze, shortness of breath, awakening at night) and two dimensions (frequency and severity). Flood (2006) published results of analysis of differences in multi-symptom states between European (including UK) and American countries. Statistically significant differences were found and therefore the multi-attribute utility functions derived within countries were different. The authors recommend that despite these differences, as long as the same algorithm is used within an international clinical trial, the relative ordering of mean ASUI scores by disease severity is preserved.

One study reports limited evidence of validity.

The ASUI discriminates between patients who suffer an exacerbation of their asthma which requires the use of steroids or hospitalisation with statistically significant lower scores (Lloyd et al., 2007 UK).

r). Asthma Questionnaire 20
The AQ-20/30 has been referred to in the previous review. The total score (expressed as a percentage) for the twenty items are summation of domain scores (Symptoms, Activity and Impacts). High scores indicate a poor quality of life. Several evaluations have been conducted on foreign languages

Two studies provide some evidence.

Reproducibility has been established with correlations ≥ 0.70 (Win et al., 2008).
Construct validity is supported with correlations reported with respiratory function, SGRQ and AQLQ (Barley et al., 1998; Win et al., 2008)). The AQ-20 has discriminative validity identifying patients who had experienced an exacerbation of their asthma (Win et al., 2008).

No evidence is reported of ceiling and floor effects (Win et al., 2008).

s). Royal College of Physicians 3 questions:
These questions were developed with clinical experts in collaboration with the Royal College of Physicians (Pearson 1999).

The Three questions are as follows.

In the last week (or month): Have you had difficulty sleeping because of your asthma symptoms (including cough?) Have you had your usual asthma symptoms during the day (cough, wheeze, chest tightness or breathlessness)? Has your asthma interfered with your usual activities (eg housework, work/school etc)?

One study provides limited evidence.

Construct validity is demonstrated with high correlation between the 3 questions and AQLQ and ACQ (≥ 0.7) (Thomas et al., 2008)

t). Lara Asthma Symptom Scale
This was not identified in the previous review. This eight item questionnaire has been developed and evaluated with an English and Spanish paediatric population (Lara et al., 2000). Items assess Symptoms (cough, wheeze, shortness of breath, asthma attacks, chest pain, nocturnal symptoms, and overall perceived severity of asthma) with a five-point

Likert response scale with Total scores ranging from 8 to 40. A single factor structure has been empirically confirmed. Item wording has been modified for use with adults.

Three studies were identified in this update.

High internal consistency has been established (0.84) (Wood et al., 2007). Construct validity is supported with high correlation between patient-reported quality of life (AQLQ) and moderate with pulmonary lung function and discriminates between different levels of asthma severity and predictive of healthcare utilisation (Wood et al., 2007) and presence of environmental factors (Shedd et al., 2007. Responsiveness has been established with change scores for LASS correlated with change scores for other patient-reported measures and pulmonary function (Wood et al., 2007).

u). Asthma Self-efficacy Scale (ASES)
This was not included in the previous review. The ASES is based on self-efficacy and locus of control principles. Patients report levels of confidence in avoiding an asthma attack on a five point Likert scale (1= no confidence, 5=very confident.) for 80 different situations. Mean scores are calculated. This PROM was not identified in the previous review.
Three studies provide some evidence of performance.

The instrument is internally consistent (0.95) (Mancuso 2001). Discriminative properties are found with lower self-efficacy associated with increased cardiovascular effect of asthma (Campbell et al., 2006); increased confidence was associated with greater asthma control (ACQ) and improved quality of life (AQLQ) Lavoie et al., 2008).

v). Work Productivity and Activity Impairment: Asthma (WPAI:Asthma)
This was not included in the previous review, One study provides limited evidence.

This instrument is a modified version of the WPAI: allergy-specific questionnaire. Nine items representing three domains: Work impairment, School impairment, Activity impairment. Patients only complete either the Work or School domain. The impact of their asthma is scored for each domain and a percentage of impairment obtained for each domain.

Construct validity has been reported. A 10 percent overall Work impairment was predictive of hospitalisation and emergency visits. Levels of impairment are associated with number of control problems (ATAQ) and quality of life (Mini-AQLQ) (Chen et al., 2008).

4. Discussion and recommendations

2006 review

The 2006 review identified five generic and 10 asthma-specific instruments. For full details of this evidence for each PROM please refer to the previous review. Details of the content, domains and scoring are outlined in Appendix C and D.

From the previous review, the most comprehensively evaluated asthma-specific PROMs were the Juniper Asthma Quality of Life Questionnaires (AQLQ, AQLQ(S), miniAQLQ and AcAQLQ). The SF-36 was the most frequently evaluated generic PROM.

Based on this evidence, the previous review recommended the following PROMs for use with people with asthma: The AQLQ (Juniper collection); the MAQLQ and the SF-36 as a generic PROM for the broad evaluation of health.

Discussion: Updated review 2009

Generic PROMs
Table 2 assesses the psychometric criteria and operational characteristics of the generic PROMs based on the totality of evidence from the review reported in 2006 and the update of evidence using the Appraisal criteria found in Appendix B. The previous review reported evidence for the SF-36, SF-12, EQ-5D, SIP and HUI. It is clear from the appraisal of the evidence as detailed in Table 2 that the SF-36 remains the most frequent generic PROM used in several evaluations with people with asthma with measurement and operational performance reported.

Some further evidence of construct validity is reported for the SF-12 which may be considered as a more pragmatic approach to the measurement of general health status due to its brevity, but further evaluations are required.

Construct validity is supported for the EQ-5D with moderate correlation with asthma-specific PROMs, and discriminative validity has been reported. However, limited evidence of responsiveness is available. Problems with ceiling effects and missing values have been reported.

Whilst the HUI discriminates patients with different health conditions, it appears insensitive to asthma-specific factors. Some evidence is reported for construct validity. Ceiling effects have also been reported for the HUI and the developers recommend interview administration which limits its use for postal survey or self-completion.

The SF-6D was identified in this update with limited evidence of performance. Whilst the SF-6D is positively correlated with other utility measures (EQ-5D and HUI), there is evidence against it use to discriminate patients with different severity of asthma.

There is no reported evidence for the SIP.

Table 2: Appraisal of psychometric and operational performance of generic PROMs for people with asthma

PROM	Reproducibility	Internal consistency	Validity: Content	Construct	Responsiveness	Interpretability	Floor/ceiling/ precision	Acceptability	Feasibility
SF-36	+++	+++	+++	+++	+++	+++		+++	
SF-12	0	0	+	++	+	0	0	0	0
EQ-5D	0	n/a	++	++	+	0	0	0	0
SIP	0	0	0	+	0	0	0	0	0
HUI	0	0	0	+	0	0	0	0	0
SF-6D	0	0	0	— +	0	0	0	0	0

Psychometric and operational criteria

0 *not reported*

— *no evidence in favour*

\+ *some limited evidence in favour*

\++ *some good evidence in favour*

\+++ *good evidence in favour.*

Asthma-specific PROMs

Table 3 assesses the psychometric criteria and operational characteristics of the asthma-specific PROMs based on the totality of evidence from the review reported in 2006 and the update of evidence using the Appraisal criteria outlined in Appendix B. The previous review reported and recommended the AQLQ Juniper collection of asthma-specific PROMs and the MAQLQ based on the number of evaluations reporting good measurement and operational performance. This is further supported with the emerging evidence from this update review (Table 3).

Further evidence of internal structure, instrument stability and responsiveness is strengthened for the AQLQ in particular and additional evidence of construct validity for the AQLQ(S). The miniAQLQ has further evidence of discriminative and construct validity and is responsive to change. These PROMs are multi-dimensional in structure and include domains relating to Symptoms, Psychological well-being and Role activities.

There is also further evidence of good overall performance for the MAQLQ.

The AOMS, a multi-dimensional PROM (Activity limitation, Symptoms and Concern) has some degree of evidence of construct validity, but further evaluations are necessary.

There is increasing development of shorter PROMs focusing on asthma-control which have multi-dimensional approaches including Symptoms, Control and the relationship with medication use and satisfaction with treatment. The ACT, ACQ, PCAQ and ATAQ are the most promising.

The ACQ is a seven item PROM focusing on Symptoms and Control. Limited evidence was reported in the previous review but in the update, additional evidence is demonstrated of performance with acceptable internal consistency, discriminative properties and responsiveness. Cut-off points are reported for levels of asthma control. Patient acceptability is reported.

The ACT is a newly identified PROM in this review with five items evaluating Symptoms, Role activities and Asthma control. Evidence is established of acceptable internal consistency, reproducibility, construct validity and responsiveness.

The ATAQ instrument is used to identify patients whose asthma management may be sub-optimal. Five levels of asthma controls. Evidence of construct and discriminative validity is supported in several studies.

The PCAQ another PROM with a focus on asthma control is reported. There are eleven items examining control. This was referred to in previous review and further evidence identified in the update of internal structure, domain structure and responsiveness from several evaluations.

Another ‘asthma control’ PROM identified is the ACSS but limited evidence is available.

Two Asthma-specific utility measures, the Asthma Quality of Life Utility Index AQL-5D and Asthma Symptom Utility Index (ASUI) were identified, but limited evidence is reported and further evaluations required.

Limited evidence is available for the SGRQ.

No further evaluations were identified for the following PROMs which were reported in the previous review: AcAQLQ, LWAQ and ACD.

Discussion:
For this update, tables 2 and 3 provide ratings of the evidence of measurement and operational performance applying the appraisal criteria for PROMs described in Appendix B to all of the available evidence. . Based on this appraisal, the following instruments were recommended for consideration by a multidisciplinary panel (see Appendix F).

- SF-36 as a generic measure
- Asthma Quality of Life Questionnaire (AQLQ)
- Asthma Quality of Life Questionnaire S (AQLQ-S)
- MiniAsthma Quality of Life Questionnaire (MiniAQLQ)
- Mark's Asthma Quality of Life Questionnaire (MAQLQ)

Recommendations

The multi-disciplinary panel were favourable toward the **SF-36** as generic measure of health status and the **miniAQLQ** as an asthma-specific measure. They felt that neither instrument should be used in isolation if the full range of patient experience is to be captured. Unfortunately it had been decided that there was insufficient data on EQ-5D in relation to asthma and it was not presented to the panel. Several members suggest that for the measurement of asthma control, the ACQ is the most favourable option. Having in mind an overall strategy of a generic and condition-specific measure being used in combination to assess complementary aspects of health status, and also having in mind the need for an approach that reduces the volume of questions and likely burden of responding, the current review recommends the combination of EQ-5D and miniAQLQ for use in potentially large scale population studies. The simplicity and the brevity of the EQ-5D, make it likely that it will not adversely influence response rates. The fact that it yields UK-derived preference values, makes it an attractive generic measure providing complementary evidence on health status alongside the miniAQLQ. A separate review by the group of evidence of EQ-5D in relation to long term conditions is favourable to the role of EQ-5D when directly compared to other preference measures. It is clear that EQ-5D in combination with miniAQLQ provide will provide a broad range of evidence of health status in asthma for possible uses in population health.

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Table 3: Appraisal of psychometric and operational performance of asthma-specific PROMs

PROM	Reproducibility	Internal consistency	Validity: Content	Construct	Responsiveness	Interpretability	Floor/ceiling/ precision	Acceptability	Feasibility
AQLQ	+++	+++	+++	+++	+++	+++	++	+	+
MiniAQLQ	++	0	+++	+++	+++	0	0	++	0
AQLQ(S)	++	++	++	++	+	0	0	+	0
AcAQLQ	+	0	+	+	+	0	0	0	0
ACQ	++	++	++	+++	+	0	0	0	0
ACD	0	0	0	+	0	0	0	0	0
MAQLQ	+++	+++	+++	+++	+++	0	+	+	0
LWAQ	+	0	0	+	0	0	0	0	0
SGRQ	+	0	+	+	+	0	+	+	0
ACT	+	+	+	++	+	0	0	0	0
AIS-6	0	+	0	+	0	0	0	0	0
ATAQ	0	0	0	++	0	0	0	0	0
PCAQ	0	+	++	++	++	0	0	+	0
AOMS	0	0	0	+	0	0	0	0	0
ASCC	0	0	0	+	0	0	0	0	0
AQL-5D	0	0	0	+	0	+	—	0	0
ASUI	0	0	0	+	0	0	0	0	0
AQ 20	+	0	0	+	0	0	0	0	0
RCP	0	0	0	+	0	0	0	0	0
LASS	0	+	0	+	+	0	0	0	0
ASES	0	+	0	+	0	0	0	0	0
WPAI	0	0	0	+	0	0	0	0	0

0 not reported — no evidence in favour + some limited evidence in favour ++ some good evidence in favour ++ + good evidence in favour.

5. Asthma-specific PROMs for children

Involving children and adolescents in assessing the impact of asthma is important and proxy judgment by parents or carers may have limitations. The PROMs identified in this review have been developed primarily for use with adult patients. Very few evaluations have applied these in paediatric populations. The Juniper collection of adult asthma-specific PROMs, the Asthma Quality of Life Questionnaires is by far the strongest contenders for application in the NHS. It has though been reported that the AQLQ individual Activity question does pose completion errors and difficulty for patients and the developers produced a modified version, the AQLQ(S) with a standardised Activity domain. This has been further adapted for use with adolescents (AQLQ12+) (Juniper et al., 2005). Psychometric performance was comparable for adolescents aged 12 to 17 and patients 18 years and older. Furthermore, Juniper and colleagues have developed paediatric-specific PROMs. These include the following:

-Paediatric Asthma Quality of Life Questionnaire (PAQLQ)
-Standardised Paediatric Asthma Quality of Life Questionnaire (PAQLQ(S))
-Mini Paediatric Asthma Quality of Life Questionnaire (Mini PAQLQ)
-Paediatric Asthma Caregivers Quality of Life Questionnaire (PACQLQ)

Some evidence of good performance has been reported for the PAQLQ and evaluations are currently in progress for PAQLQ(S) and MiniPAQLQ.

Both the Health Utilities Index-Mark III and the EQ 5D have been evaluated with children and parent proxy rating. Specific details of the psychometric performance of these utility measures in paediatric populations are beyond the scope of this discussion.

Many paediatric-specific generic PROMs have been developed and measurement performance widely reported. Examples include: Child Health Questionnaire (CHQ), Child Health and Illness Profile (CHIP), KIDSCREEN, Pediatric Quality of Life Inventory (PedsQL), and TNO AZL Children's Quality of Life (TACQOL). The evidence-base of these measures with children with asthma is beyond the scope of this discussion.

There are no reports of evaluations with children for the other asthma-specific PROMs included in this review.

There has though been an exponential growth of research related to the development and evaluation of paediatric-specific PROMs. Thirty generic and 64 condition-specific PROMs were identified in a review by Solans et al., (2008), 10 were specific to asthma. Quittner et al., (2008) identified twelve asthma-specific paediatric PROMs and reported evidence of measurement performance. Of these twelve, 4 had parent and child forms. The PAQLQ was reported as the most comprehensively evaluated PROM with good internal consistency, reproducibility and responsiveness (Quittner et al., 2008). Other promising PROMs were presented which included the PedsQOL-Asthma module for

children younger than 7 years of age; the About My Asthma (AMA) and the Childhood Asthma Questionnaires (CAQ).

The remit of this narrative was to examine whether adult asthma-specific PROMs could be applied with children in the NHS. There is very little evidence to support recommending any PROM identified in this review for use with children. Moreover, the conceptual and methodological challenges of adopting adult PROMs with children strengthen such judgement.

APPENDIX Ai: sources for PROM bibliography

1. AMED: Allied and Complementary Medicine Database
2. Biological Abstracts (BioAbs)
3. BNI: British Nursing Index Database, incorporating the RCN (Royal College of Nursing) Journals Database
4. CINAHL: Cumulative Index to Nursing and Allied Health Literature
5. Econlit - produced by the American Economic Association
6. EMBASE - produced by the scientific publishers Elsevier
7. MEDLINE - produced by the US National Library of Medicine
8. PAIS: Public Affairs Information Service
9. PsycINFO (formerly PsychLit) - produced by the American Psychological Association
10. SIGLE: System for Information on Grey Literature in Europe
11. Sociofile: Cambridge Scientific Abstracts Sociological Abstracts Database
12. In addition, all records from the journal 'Quality of Life Research' are downloaded via Medline.

APPENDIX Aii: PROM Bibliography search strategy[3]

a. records to December 2005 (downloads 1-12)

((acceptability or appropriateness or (component$ analysis) or comprehensibility or (effect size$) or (factor analys$) or (factor loading$) or (focus group$) or (item selection) or interpretability or (item response theory) or (latent trait theory) or (measurement propert$) or methodol$ or (multi attribute) or multiattribute or precision or preference$ or proxy or psychometric$ or qualitative or (rasch analysis) or reliabilit$ or replicability or repeatability or reproducibility or responsiveness or scaling or sensitivity or (standard gamble) or (summary score$) or (time trade off) or usefulness$ or (utility estimate) or valid$ or valuation or weighting$)

and

((COOP or (functional status) or (health index) or (health profile) or (health status) or HRQL or HRQoL or QALY$ or QL or QoL or (qualit$ of life) or (quality adjusted life year$) or SF-12 or SF-20 or SF?36 or SF-6) or ((disability or function or subjective or utilit$ or (well?being)) adj2 (index or indices or instrument or instruments or measure or measures or questionnaire$ or profile$ or scale$ or score$ or status or survey$))))

or

((bibliograph$ or interview$ or overview or review) adj5 ((COOP or (functional status) or (health index) or (health profile) or (health status) or HRQL or HRQoL or QALY$ or QL or QoL or (qualit$ of life) or (quality adjusted life year$) or SF-12 or SF-20 or SF?36 or SF-6) or ((disability or function or subjective or utilit$ or (well?being)) adj2 (index or indices or instrument or instruments or measure or measures or questionnaire$ or profile$ or scale$ or score$ or status or survey$))))

b. records from January 2006 (download 13)

(((acceptability or appropriateness or component$ analysis or comprehensibility or effect size$ or factor analys$ or factor loading$ or feasibility or focus group$ or item selection or interpretability or item response theory or latent trait theory or measurement propert$ or methodol$ or multi attribute or multiattribute or precision or preference$ or proxy or psychometric$ or qualitative or rasch analysis or reliabilit$ or replicability or repeatability or reproducibility or responsiveness or scaling or sensitivity or valid$ or valuation or weighting$)

and

(HRQL or HRQoL or QL or QoL or qualit$ of life or quality adjusted life year$ or QALY$ or disability adjusted life year$ or DALY$ or COOP or SF-12 or SF-20 or SF-36 or SF-6 or standard gamble or summary score$ or time trade off or health index or health profile or health status or ((patient or self$) adj (rated or reported or based or assessed)) or ((disability or function$ or subjective or utilit$ or well?being) adj2 (index or indices or instrument or instruments or measure or measures or questionnaire$ or profile$ or scale$ or score$ or status or survey$))))

or

((bibliograph$ or interview$ or overview or review) adj5 (HRQL or HRQoL or QL or QoL or qualit$ of life or quality adjusted life year$ or QALY$ or disability adjusted life year$ or DALY$ or COOP or SF-12 or SF-20 or SF-36 or SF-6 or standard gamble or summary score$ or time trade off or health index or health profile or health status or ((patient or self$) adj (rated or reported or based or assessed)) or ((disability or function$ or subjective or utilit$ or well?being) adj2 (index or indices or instrument or instruments or measure or measures or questionnaire$ or profile$ or scale$ or score$ or status or survey$)))))

[3] Note: the bibliography includes approximately 1,650 handsearched additions.

APPENDIX B: Psychometric criteria

Appraisal of PROMs

The methods that will be used for assessing the performance of PROMs were developed and tested against multi-disciplinary consensus and peer review (8). They focus on explicit criteria to assess reliability, validity, responsiveness, precision, acceptability and feasibility. A pragmatic combination of the criteria developed and used in previous reports to DH by the Oxford and LSHTM groups will be used.

The appraisal framework focuses on psychometric criteria and PROMs must fulfil some or all to be considered as a short-listed instrument. Practical or operational characteristics are also assessed (acceptability and feasibility) (Appendix B: Appraisal framework).

Once evidence has been assessed for eligibility, records considered as inclusions will be assembled for each PROM identified. Measurement performance and operational characteristics will be appraised using the following rating scale independently by two reviewers and inter-rater reliability calculated.

Psychometric and operational criteria

0	*not reported*
—	*no evidence in favour*
+	*some limited evidence in favour*
++	*some good evidence in favour*
++ +	*good evidence in favour.*

Appraisal of psychometric and operational performance of PROMs for xxxxxxxxxxxxxxxxx

PROM	Reproducibility	Internal consistency	Validity: Content	Construct	Responsiveness	Interpretability	Floor/ceiling/ precision	Acceptability	Feasibility

Appraisal criteria (adapted from Smith et al., 2005 and Fitzpatrick et al., 1998; 2006)

Appraisal component	Definition/test	Criteria for acceptability
Reliability		
Test-retest reliability	The stability of a measuring instrument over time; assessed by administering the instrument to respondents on two different occasions and examining the correlation between test and re-test scores	Test re-test reliability correlations for summary scores 0.70 for group comparisons
Internal consistency	The extent to which items comprising a scale measure the same construct (e.g. homogeneity of items in a scale); assessed by Cronbach's alpha's and item-total correlations	Cronbach's alphas for summary scores ≥0.70 for group comparisons Item-total correlations ≥ 0.20
Validity		
Content validity	The extent to which the content of a scale is representative of the conceptual domain it is intended to cover; assessed qualitatively during the questionnaire development phase through pre-testing with patients. Expert opinion and literature review	Qualitative evidence from pre-testing with patients, expert opinion and literature review that items in the scale represent the construct being measured Patients involved in the development stage and item generation

Construct validity	Evidence that the scale is correlated with other measures of the same or similar constructs in the hypothesised direction; assessed on the basis of correlations between the measure and other similar measures	High correlations between the scale and relevant constructs preferably based on a priori hypothesis with predicted strength of correlation
	The ability of the scale to differentiate known-groups; assessed by comparing scores for sub-groups who are expected to differ on the construct being measured (e.g a clinical group and control group)	Statistically significant differences between known groups and/or a difference of expected magnitude
Responsiveness	The ability of a scale to detect significant change over time; assessed by comparing scores before and after an intervention of known efficacy (on the basis of various methods including t-tests, effect sizes (ES), standardised response means (SRM) or responsiveness statistics	Statistically significant changes on scores from pre to post-treatment and/or difference of expected magnitude
Floor/ceiling effects	The ability of an instrument to measure accurately across full spectrum of a construct	Floor/ceiling effects for summary scores <15%
Practical properties		
Acceptability	Acceptability of an instrument reflects' respondents' willingness to complete it and impacts on quality of data	Low levels of incomplete data or non-response
Feasibility/burden	The time, energy, financial resources, personnel or other resources required of respondents or those administering the instrument	Reasonable time and resources to collect, process and analyse the data.

APPENDIX C:
i. GENERIC INSTRUMENTS

This Appendix provides a brief description of the generic PROMs included in this review. Their origins, development and content are briefly summarized (Section i). Content and format are further summarized in Sections i and ii.

a) SF-36: Medical Outcomes Study 36-item Short Form Health Survey (Ware and Sherbourne, 1992; Ware et al., 1994; Ware, 1997)

The Medical Outcomes Study (MOS) Short Form 36-item Health Survey (SF-36) is derived from the work of the Rand Corporation during the 1970s (Ware and Sherbourne, 1992; Ware et al., 1994; Ware, 1997). It was published in 1990 after criticism that the SF-20 was too brief and insensitive. The SF-36 is intended for application in a wide range of conditions and with the general population. Ware et al., (1994; 1997) proposed that the instrument should capture both mental and physical aspects of health. International interest in this instrument is increasing, and it is by far the most widely evaluated measure of health status (Garratt et al., 2002a).

Items were derived from several sources, including extensive literature reviews and existing instruments (Ware and Sherbourne, 1992; Ware and Gandek, 1998; Jenkinson and McGee 1998). The original Rand MOS Questionnaire (245 items) was the primary source, and several items were retained from the SF-20. The 36 items assess health across eight domains (Ware, 1997), namely bodily pain (BP: two items), general health perceptions (GH: five items), mental health (MH: five items), physical functioning (PF: ten items), role limitations due to emotional health problems (RE : three items), role limitations due to physical health problems (RP: four items), social functioning (SF: two items), and vitality (V: four items), as shown in Table 3.1. An additional health transition item, not included in the final score, assesses change in health. All items use categorical response options (range: 2-6 options). Scoring uses a weighted scoring algorithm and a computer-based programme is recommended. Eight domain scores give a health profile; scores are transformed into a scale from 0 to 100 scale, where 100 denotes the best health. Scores can be calculated when up to half of the items are omitted. Two component summary scores for physical and mental health (MPS and MCS, respectively) can also be calculated. A version of the SF-36 plus three depression questions has been developed and is variously called the Health Status Questionnaire (HSQ) or SF-36-D.

The SF-36 can be self-, interview-, or telephone-administered.

b) SF-12: Medical Outcomes Study 12-item Short Form Health Survey (Ware et al., 1995)

In response to the need to produce a shorter instrument that could be completed more rapidly, the developers of the Medical Outcomes Study (MOS) 36-item Short Form

Health Survey (SF-36) produced the 12-item Short Form Health Survey (SF-12) (Ware et al., 1995).

Using regression analysis, 12 items were selected that reproduced 90% of the variance in the overall Physical and Mental Health components of the SF-36 (Table 3.1). The same eight domains as the SF-36 are assessed and categorical response scales are used. A computer-based scoring algorithm is used to calculate scores: Physical Component Summary (PCS) and Mental (MCS) Component Summary scales are generated using norm-based methods. Scores are transformed to have a mean value of 50, standard deviation (SD) 10, where scores above or below 50 are above or below average physical or mental well-being, respectively. Completion by UK city-dwellers reporting the absence of health problems yielded a mean PCS score of 50.0 (SD 7.6) and MCS of 55.5 (SD 6.1) (Pettit et al., 2001). Although not recommended by the developers, Schofield and Mishra (1998) report eight domain scores and two summary scores. The SF-12 may be self-, interview-, or telephone-administered.

Several authors have proposed simplification of the scoring process and revision of the SF-12 summary score structure, where norm-based weighting is replaced by item summation to facilitate score interpretation (Resnick and Nahm, 2001; Resnick and Parker, 2001).

c) EuroQol-EQ-5D (The EuroQol Group, 1990; revised 1993)

The European Quality of Life instrument (EuroQol) was developed by researchers in five European countries to provide an instrument with a core set of generic health status items (The EuroQol Group, 1990; Brazier et al., 1993). Although providing a limited and standardized reflection of HRQL, it was intended that use of the EuroQol would be supplemented by disease-specific instruments. The developers recommend the EuroQol for use in evaluative studies and policy research; given that health states incorporate preferences, it can also be used for economic evaluation. It can be self or interview-administered.

Existing instruments, including the Nottingham Health Profile, Quality of Well-Being Scale, Rosser Index, and Sickness Impact Profile were reviewed to inform item content (The EuroQol Group, 1990). There are two sections to the EuroQol: the EQ-5D and the EQ thermometer. The EQ-5D assesses health across five domains: anxiety/depression (AD), mobility (M), pain/discomfort (PD), self-care (SC), and usual activities (UA), as shown in Table 3.1. Each domain has one item and a three-point categorical response scale; health ‘today’ is assessed. Weights based upon societal valuations of health states are used to calculate an index score of –0.59 to 1.00, where –0.59 is a state worse than death and 1.00 is maximum well-being. A score profile can be reported. The EQ thermometer is a single 20 cm vertical visual analogue scale with a range of 0 to 100, where 0 is the worst and 100 the best imaginable health.

d) Sickness Impact Profile (Bergner et al., 1976; revised: Bergner et al., 1981)

The Sickness Impact Profile (SIP) was developed in the USA to provide a broad measure of self-assessed health-related behaviour (Bergner et al., 1976; Bergner et al., 1981). It was intended for a variety of applications, including programme-planning and assessment of patients, and to inform policy decision-making (Bergner et al., 1976; Bergner et al., 1981; McDowell and Newell, 1996).

Instrument content was informed by the concept of 'sickness', which was defined as reflecting the change in an individual's activities of daily life, emotional status, and attitude as a result of ill-health (McDowell and Newell, 1996). Item derivation was based on literature reviews and statements from health professionals, carers, patient groups, and healthy subjects describing change in behaviour as a result of illness. The SIP has 136 items across 12 domains: alertness behaviour (AB: ten items), ambulation (A: 12 items), body care and movement (BCM: 23 items), communication (C: nine items), eating (E: nine items), emotional behaviour (EB: nine items), home management (HM: ten items), mobility (M: ten items), recreation and pastimes (RP: eight items), sleep and rest (SR: seven items), social interaction (SI: 20 items) and work (W: nine items).

Each item is a statement. Statements that best describe a respondent's perceived health state on the day the instrument is completed are ticked. Items are weighted, with higher weights representing increased impairment. The SIP percentage score can be calculated for the total SIP (index) or for each domain, where 0 is better health and 100 is worse health. Two summary scores are calculated: Physical function (SIP-PhysF), a summation of A, BCM, and M, and psychosocial function (SIP-PsychF), a summation of AB, C, EB, and SI. The five remaining categories are scored independently. The instrument may be self or interview-administered.

The Functional Limitation Profile (FLP) is an Anglicized version of the SIP (Patrick and Peach, 1989; McDowell and Newell, 1996). Wording and some weightings have been altered, and summary scores are calculated using different dimensions to those used in the SIP (i.e. FLP Physical summary calculated by summing A, BCM, M and HM; FLP Psychosocial summary calculated by summing RP, EB, AB, SI and SR. Several abbreviated versions of the SIP have been developed, including a 68-item version (De Bruin et al., 1992; Post et al, 1996).

e) Health Utilities Index

The Health Utilities Index (HUI) was designed as a comprehensive measure of health status and health related quality of life. The Health Utilities Index (Mark 3) is a system composed of a health status classification which defines 972,000 discrete health states, and a preference, or utility, function which can be used to calculate the desirability for each health state. The HUI3 health status classification was developed by Feeny et al., (1995) to assess capacity on eight dimensions: vision, hearing, speech, ambulation, dexterity, emotion, cognition and pain/discomfort. The utility function reflects community preferences and scores each unique health state on a scale ranging from 0

(death) to 1 (perfect health). An excellent summary of the development of the HUI measures can be found in Feeny et al., (1996). The HUI3 is a development of the Health Utilities Index containing a sub-set of items which constituted the HUI2. This report summarises data for the most recent version of the HUI (i.e. the HUI3).

f) SF-6D

The SF-6D was designed to be used in health economic analyses. It is a classification for describing health derived from a selection of SF-36 items. It is composed of six multi-level dimensions. It is a preference based algorithm based on a sub-set of items from the SF36, developed by Brazier et al., (2002). The SF-6D comes with a set of preference weights obtained from a sample of the general population. Using the valuation technique of standard gamble, members of the general population were asked to value a selection of health states from which a model has been estimated to predict all the health states described by the SF-6D.

Appendix C

ii: Generic patient-reported outcome measures

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Instrument	*Domains (no. items)*	*Response options*	*Score*	*Completion (time in minutes)*
SF-36: MOS 36-item Short Form Health Survey (36)	Bodily pain (BP) (2), General health (GH) (5) Mental health (MH) (5), Physical functioning (PF) (10) Role limitation-emotional (RE) (3), Role limitation-physical (RP) (4), Social functioning (SF) (2), Vitality (V) (4)	Categorical: 2-6 options Recall: standard 4 weeks, acute 1 week	Algorithm Domain profile (0-100, 100 best health) Summary: Physical (PCS), Mental (MCS) (mean 50, sd 10)	Interview (mean values 14-15) Self (mean 12.6)
SF-12: MOS 12-item Short Form Health Survey (12)	Bodily pain (BP) (1), Energy/Vitality (V) (1), General health (GH) (1), Mental health (MH) (2), Physical functioning (PF) (2), Role limitation-emotional (RE) (2), Role limitation-physical (RP) (2), Social functioning (SF) (1)	Categorical: 2-6 options Recall: standard 4 weeks, acute 1 week	Algorithm Domain profile (0-100, 100 best health) Summary: Physical (PCS), Mental (MCS) (mean 50, sd 10)	Interview or self
European Quality of Life Questionnaire (EuroQol-EQ5D) (5+1)	EQ-5D Anxiety/depression (1), Mobility (1), Pain/discomfort (1), Self-care (1), Usual activities (1) EQ-thermometer Global health (1)	EQ-5D Categorical: 3 options *EQ-thermometer* VAS Current health	EQ-5D Summation: domain profile Utility index (–0.59 to 1.00) *Thermometer* VAS (0-100)	Interview or self
Sickness Impact Profile (136)	Alertness behaviour (AB) (10), Ambulation (A) (12) Body care and movement (BCM) (23), Communication (C) (9) Eating (E) (9), Emotional behaviour (EB) (9) Home management (HM) (10), Mobility (M) (10) Recreation and pastimes (RP) (8), Sleep and rest (SR) (7) Social interaction (SI) (20), Work (W) (9)	Check applicable statements. Items weighted: higher weights indicate increased impairment Recall current health	Algorithm Domain profile (0-100%, 100 worst health); Index (0-100%) Summary: Physical (A, BCM, M), Psychosocial function (AB, C, EB, SI)	Interview (range: 21-33) Telephone: PF only (11.5) Self (19.7)
Health Utility Index 3 (Feeny et al, 1995) (8)	Vision, Hearing, Speech, Ambulation, Dexterity, Emotion, Cognition, Pain	Four domains have five response options and five have six response options	Global Utility index and single attribute utility scores for the eight separate dimensions	Self report, face to face and telephone interview
SF-6D: MOS 6-item Short Form Health Survey (12)	Bodily pain (BP) (1), Energy/Vitality (V) (1), Mental health (MH) (1), Physical functioning (PF) (1), Role limitation (1), Social functioning (SF) (1)	Categorical: 3 options	Algorithm Domain profile (0-100, 100 best health)	Interview or self

Appendix C

iii: Summary of generic instruments: health status domains *(after Fitzpatrick et al., 1998)*

Instrument	*Instrument domains*							
	Physical function	**Symptoms**	**Global judgement**	**Psychol. well-being**	**Social well-being**	**Cognitive functioning**	**Role activities**	**Personal construct**
SF-36 (36)	x	x	x	x	x		x	
SF-12 (12)	x	x	x	x	x		x	
EQ-5D (5+1)	x	x	x	x	x		x	
SIP (136)	x	x		x	x	x	x	
HUI	x			x		x		
SF-6D	x	x		x	x		x	

Appendix D: Asthma-specific PROMS

This Appendix provides a brief description of the asthma-specific PROMs included in this review. Their origins, development and content are briefly summarized (Section i). Content and format are further summarized in Sections i and ii.

a) Asthma Quality of Life Questionnaire (AQLQ)

The Asthma Quality of Life Questionnaire (AQLQ) was developed in Canada for evaluating health-related impairment of quality of life in adults with asthma in clinical trials (Juniper et al., 1992). The instrument addresses symptoms, emotional function, activity limitations and environmental stimuli.

Instrument content was derived from existing generic instruments; literature review; experiences of patients with chronic airflow limitation; expert consensus; and unstructured interviews with six patients with asthma. From this, 152 items were considered important and an item reduction questionnaire was developed and interview administered to 150 patients (18-70 years) with asthma. Patients were asked which of the 152 items were they affected by in the past year and indicate the importance on a five point Likert scale from 'not very important' to 'extremely important'. The items chosen most frequently and labelled most important were included in the questionnaire. A total of 32 items were included within four domains of symptoms (12 items), emotional function (5 items), exposure to environmental stimuli (4 items) and activity limitations (11 items) were included. For the activity domain, there was a wide range of activities reported by patients during the item reduction phase and the final version thus included five individualised questions relating to activities which patients identified as being problematic (activities offered to aid recall) and a further 6 questions relating to non-specific activities. The time to recall was suggested as two weeks. A seven point Likert scale (1 indicating maximal impairment and 7 no impairment) was developed for responses and scoring is conducted using the mean score per item and domain and an aggregated overall quality of life score.

The instrument underwent further pre-testing to examine face and content validity and acceptability to patients. Thirty patients were interviewed and time to administer was recorded as well as patient feedback about wording and what they understood each question to be asking. The questionnaire was then modified for self-report and then administered to five other patients and no further modifications were considered necessary. Both the interview administered and self-report format took a maximum of 15 minutes to complete.

b) MiniAQLQ

A shorter version of the AQLQ was developed for greater efficiency (Juniper et al., 1999a). Item-total correlations were examined in previously collected data and correlations greater than 0.70 were considered evidence of similar items and combined resulting in 26 items from the original 32. Further analysis of the original AQLQ item reduction questionnaire (Juniper et al., 1992) resulted in exclusion of those items which had the lowest impact for frequency and importance. The final

questionnaire was reduced to 15 items, Symptoms (5 items), Emotions (3 items), Environment (3 items) and for Activities (4 items). Generic items were included for the Activity domain thus removing the individualized questions. Nine patients were involved in the pre-testing of the questionnaire and minor wording and modifications were made. The final version included the seven point Likert scale, 2 week recall and took 7-10 minutes to complete by self-report at baseline and 3-5 minutes at follow-up.

c) Standardised Asthma Quality of Life Questionnaire (AQLQ(S))

A standardised version of the original AQLQ was developed (Juniper et al., 1999b) in which five generic activities replaced the individualised approach used in the AQLQ. The items were selected based on the impact and frequency of reporting activities in the item reduction questionnaire (Juniper et al., 1992) and classified as 'strenuous', 'moderate', 'social', 'work related' and 'sleeping'. The wording of the revised, standardised instrument was pre-tested in ten patients with asthma. Scoring and recall period remained the same as the AQLQ.

The questionnaire was administered to forty patients and the classifications of 'activities' were examined in relation to patients self reported activities (as per original instrument). The classifications of activities were considered to represent the patient-specific activities chosen by the patients.

d) Acute Asthma Quality of Life Questionnaire (Acute AQLQ)

The Acute AQLQ is a modification of the AQLQ with the intention of being specific to patients experiencing an acute severe asthma attack (Juniper et al., 2004). The 32 items from the AQLQ were examined and those considered not relevant or unlikely to change to patients during an acute exacerbation were excluded. The final instrument contains two domains: Symptoms (6 items) and Emotions (5 items) and scoring the same as other AQLQ instruments using a seven point scale. The format was tested with ten patients.

e) Asthma Control Questionnaire (ACQ)

Item generation for this patient-reported symptom focused questionnaire was informed by treatment goals from clinical guidelines, reviewing other asthma questionnaires and a postal survey of asthma clinicians to rank symptoms presented for content. The final instrument includes seven items relating to awakening at night by symptoms; waking in the morning with symptoms; limitations in activities; dyspnoea; wheeze and β_2-agonist use. One item, FEV_1 is clinician assessed (Juniper 1999c). Patient's responses are on a 7 point Likert scale and evaluation for the last 7 days. Scoring of the ACQ is computed as the mean of the 7 items with 0= well controlled and 6= poorly controlled.

f) Asthma Control Diary (ACD)

The Asthma Control Diary is modified form the Asthma Control Questionnaire for daily completion using PEF instead of FEV_1.

g) Asthma Quality of Life Questionnaire (Marks) (MAQLQ)

The initial items for the instrument were derived from analysis of results from a focus group with eight patients with a wide range of asthma severity; from patients participating in an asthma education programme and clinical experience of the developers (Marks et al., 1992). Initial testing was with 283 patients using principal components analysis. Further evaluation of measurement properties was conducted with seventy-seven patients with stable asthma and another sample of patients with unstable asthma (n=42).

The instrument measures the effect of the disease with negative statements (not at all; mildly; moderately; severely; very severely). Conceptually, the AQLQ is underpinned by a limitation and negative approach of the impact of asthma on the individual.

Content validity was examined empirically using principle components analysis. Items were excluded is they had highly skewed distribution; missing values; or low loadings. Principal components analysis gave a six component solution and items most strongly correlated with each component were labelled Breathlessness, Concerns, Mood, Social, Cough and Control. Item-total correlation ranged from 0.13 to 0.72 with correlations less than 0.5 for Cough and Control. These items were deleted based on weak correlation and being considered unrelated to quality of life. The final instrument contained four domains (Breathlessness, Concerns, Mood and Social) and a total of 20 items. Each item contributes to the total scale and domain scores are calculable.

g.i) Modified Marks Asthma Quality of Life Questionnaire

In the original instrument developed by Marks there were two items related to activities which were combined to a single item. Adams et al., (2000) extended the number of items to 22 in the instrument to allow for different responses for this ‘activity’ question. In addition, a seven point Likert scale was used with the intention of increasing reliability.

h) Living With Asthma Questionnaire (LWAQ)

The Living With Asthma Questionnaire was developed by Hyland (1991, UK) using a comprehensive methodology. Six focus groups were conducted, four with patients and two with the general population (under-graduates). Eleven themes (classified as domains) were identified from content analysis and further items and domains were developed following analysis. The questionnaire was further tested and refined in three phases with a total of 656 patients from primary care. Psychometric testing and item reduction included principal factor analysis, item variability analysis and patient comment. The final questionnaire contained eleven domains and 68 items with a 3 point response format to statements: ‘untrue of me’, ‘slightly true of me’, ‘very true of me’ with an additional option of ‘not applicable’. Hyland (1991) attempted to compensate for acquiescence bias by ensuring there were both negative and positive statements. Both negative and positive statements were included in the questionnaire with a third of statements negative. Factor analysis indicated a unifactorial solution.

The final instrument has five constructs: Avoidance, Distress, Preoccupation, Colds and Activities with eleven domains and 68 items. Mean scale scores are obtained with 2 indicating poor quality of life and 0 best.

h.i) ms-LWAQ

Modifications were made to the LWAQ by Reid et al., (1999) for use with Americans. The instrument has twenty-seven items and five subscales: Consequences (10 items); Affect (6 items); Leisure (4 items); Seriousness (5 items) and Drugs (2 items). Scoring is the same as the LWAQ but with different wording of responses.

i) St. George's Respiratory Questionnaire (SGRQ)

The SGRQ was developed in the UK to measure the impact of asthma and chronic obstructive pulmonary disease (COPD) from a patient perspective. There are two parts of the instrument. Part 1 is concerned with symptoms focusing on the severity, frequency and effect of respiratory symptoms over the last year and responses are obtained with a 5 point Likert scale. Part 2 includes two domains: Activity limitations and social and psychological impact and focuses on the patient's current state with True or False responses. Three components scores are calculated and a total score. All items have empirically derived weights and normative data are available. Scoring algorithms and calculators are available from the developers. Scores are expressed as the percentage of overall impairment with 100 equaling to worst possible health and zero the best.

Items were initially derived from studies with adult patients with asthma examining distress ratings relating to symptoms and the impacts of asthma (Quirk and Jones 1990) and the influence of demographic and disease factors with the degree of distress (Quirk et al., 1991). Empirical weights were obtained from one hundred and forty patients with asthma (Quirk 1991). Further analysis of previously derived weights were compared with patients with COPD with thirty-six patients (mean age 66) (Jones et al., 1991) and no significant differences between the item weights from the asthma patients (Quirk et al., 1991) and COPD patients.

j) Asthma Control Test (ACT)

This measure was not included in the previous review. It was developed with the involvement of clinicians and patients (Nathan et al., 2004). Five items evaluate symptoms, role activities and asthma control. Scores are obtained from Five-point Likert scale. Items are summed to yield a score ranging from 5 (poor control of asthma) to 25 (complete control). Optimal cut-off for well-controlled asthma has been reported as 20 or higher and poorly controlled as 15 or lower (Schatz et al., 2007b).

k) Asthma Impact Survey (AIS-6)

Items for this instrument were generated from a bank of items developed for the purpose of computerised adaptive assessment (Quality-Metric). Six items were selected based on percentage of responses from general population survey from which 52 deemed to be relevant to assess the impact of asthma. Response options for the AIS-6 are scored on a 5 point Likert scale.

l) Asthma Therapy Assessment Questionnaire

The ATAQ was referred to in the previous review and further evidence is reported in this update. The ATAQ was developed in 1999 by Vollmer and was identified in the previous review. Items were generated by clinicians and focus groups with patents with asthma. The ATAQ instrument domains include asthma Control, Communication, Behaviour/Attitude, Self-Efficacy, and the Knowledge. Scores are obtained using a 3 point Likert scale. Vollmer presented data for the control domain. The instrument is used to identify patients whose asthma management may be sub-optimal. Five levels of asthma control is suggested (0= no control problems to 4= four control problems).

m) Perceived Control of Asthma Questionnaire (PCAQ)

The PCAQ was referred to in the previous review with one evaluation report. This update has identified six further studies reporting evidence of performance. There are eleven items measuring asthma control with a five point Likert scale of responses and reports suggest it takes five minutes to complete.

n) Asthma Outcomes Monitoring System

This was developed by Bayliss et al., 1998 and details are found in the manual published by QualityMetric, Inc. Factor analysis yielded three factors represented by activity limitation, symptoms and concern or bother (Schatz et al,. 2005). High morbidity status has been defined as those with the highest score of 4 (Schatz et al., 2005).

o) Asthma Control Scoring System (ACSS)

This is clinical rating system developed by Boulet et al., (2002) with three domains: Clinical (symptoms, activities, use of rescue medications); Physiological response and Inflammatory assessment. Only the clinical domain is self-reported. The ACSS provides a percentage score.

p) Asthma Quality of Life Utility Index AQL-5D

This is a new classification system which has been derived from the AQLQ, based on Rasch analysis and other psychometric evidence. AQL-5D contains 5 attributes, each with 5 levels.

q) Asthma Symptom Utility Index (ASUI)

This preference-based outcome measure was developed for use in US clinical trials and cost effectiveness studies for asthma interventions. A single index score derives from patient preferences for four symptoms (cough, wheeze, shortness of breath, awakening at night) and two dimensions (frequency and severity). Flood (2006) published results of analysis of differences in multi-symptom states between European including UK and American counties. Statistically significant differences were found and therefore the multi-attribute utility functions derived within countries were different. The authors recommend though that despite these differences, as long

as the same algorithm is used within an international clinical trial, the relative ordering of mean ASUI scores by disease severity is preserved.

r) Asthma Questionnaire 20

The AQ-20/30 has been referred to in the previous review. The total score (expressed as a percentage) for the twenty items are summation of domain scores (Symptoms, Activity and Impacts). High scores indicate a poor quality of life. Several evaluations have been conducted on foreign languages.

s) Royal College of Physicians 3 questions

These questions were developed with clinical experts in collaboration with the Royal College of Physicians (Pearson 1999).

The Three questions are as follows.

In the last week (or month):

1. Have you had difficulty sleeping because of your asthma symptoms (including cough?)

2. Have you had your usual asthma symptoms during the day (cough, wheeze, chest tightness or breathlessness)?

3. Has your asthma interfered with your usual activities (eg housework, work/school etc)?

t) Lara Asthma Symptom Scale

This eight item questionnaire has been developed and evaluated with a English and Spanish paediatric population (Lara et al., 2000). Items assess Symptoms (cough, wheeze, shortness of breath, asthma attacks, chest pain, nocturnal symptoms, and overall perceived severity of asthma) with a five-point Likert response scale with Total scores ranging from 8 to 40. A single factor structure has been empirically confirmed. Item wording has been modified for use with adults

u) Asthma Self-efficacy Scale (ASES)

The ASES is based on self-efficacy and locus of control principles. Patients report levels of confidence in avoiding an asthma attack on a five point Likert scale (1= no confidence, 5=very confident.) for 80 different situations. Mean scores are calculated. This PROM was not identified in the previous review.

v) Work Productivity and Activity Impairment: Asthma (WPAI:Asthma)

This instrument is a modified version of the WPAI: allergy-specific questionnaire. Nine items representing three domains: Work impairment, School impairment, Activity impairment. Patients only complete either the Work or School domain. The impact of their asthma is scored for each domain and a percentage of impairment obtained for each domain

APPENDIX Dii: ASTHMA-SPECIFIC PROMs

PROM	*Domains (items)*	*Response options*	*Score*	*Administration/ Completion (time)*
AQLQ	*4 domains/32 items* 1. Symptoms (12) 2. Emotions (5) 3. Environment (4) 4. Activities (11 including 5 individualised questions	7 point Likert	Summation and domain score Mean score of all items Index: 1 = maximal impairment, 7 = no impairment	Interviewer- and self-administered format 10 minutes to complete at the first visit and 5 minutes at follow-up.
MiniAQLQ	*4 domains/15 items* 1. Symptoms (12) 2. Emotions (5) 3. Environment (4) 4. Activities (4 all generic)	7 point Likert	Summation and domain score Mean score of all items Index: 1 = maximal impairment, 7 = no impairment	Interviewer- and self-administered format 7 minutes to complete at the first visit and 3-5 minutes at follow-up.
AQLQ(S)	*4 domains/32 items* 1. Symptoms (12) 2. Emotions (5) 3. Environment (4) 4. Activities (11 including 5 standardised questions)	7 point Likert	Summation and domain score Mean score of all items Index: 1 = maximal impairment, 7 = no impairment	Interviewer- and self-administered format 10 minutes to complete at the first visit and 5 minutes at follow-up.
Acute AQLQ	*2 domains/11 items* 1. Symptoms (6) 2. Emotions (5)	7 point Likert	Summation and domain score	No details
ACQ	*One domain 8 items* *Symptoms (7) (1 clinician assessed)* Sleep related (2) Breathlessness (1) Wheeze (1) Activity limitations (1) Use of bronchodilators (1) FEV % of predicted-clinician assessed (1)	7 point Likert	Mean score of all items 0= well controlled 6= extremely poor controlled	Self-report and clinician assessed

PROM	***Domains (items)***	***Response options***	***Score***	***Administration/ Completion (time)***
ACD	*Symptoms/7 items* Sleep related (2) Breathlessness (1) Wheeze (1) Activity limitations (1) Use of bronchodilators (1) Morning peak flow expiratory flow rate (PEFR)	7 point Likert	Mean score of all items 0= well controlled 6= extremely poor controlled	Self-report
MAQLQ	*4 domains/20 items* Breathlessness Concerns Mood Social	5 point Likert	Total and domain score	
LWAQ	*5 constructs, 11 domains/68 items* 1. Social/leisure (6) 2. Sports (3) 3. Holidays (3) 4. Sleep (4) 5. Work and other activities (6) 6. Colds (5) 7. Mobility (6) 8. Effect on others (5) 9. Medication usage (6) 10. Sex (1) 11. Dysphoric states and attributes (23)	3 point Likert scale with an option of n/a	Construct and domain scores	Self-report 10 to 20 minutes to complete
SGRQ	*3 domains/17 items* 1. Symptoms (8) 2. Activity and impact (9)	1: 5 point Likert 2: True or False	Weighted scoring Total and domain scores. Percentage of overall impairment: 0= best possible health	Self- report but interview administered recommended 8 to 15 minutes completion

PROM	***Domains (items)***	***Response options***	***Score***	***Administration/ Completion (time)***
ACT	*5 items* Symptoms Role activities Asthma control	5 point Likert	Summation 5= poor control 25=complete control Cut-off for well controlled= ≥20; poorly controlled=≤15.	Self-report
AIS-6	*1 domain/6 items* Impact of asthma (6)	5 point Likert	Norm based methods of scoring Scores range from 36 to 78. Higher scores indicate more impact and reduced quality of life	Self-report
ATAQ	*5 domains/17 items* 1. Control 2. Communication 3. Behaviour/attitude 4. Self-efficacy 5. Knowledge	3 point Likert	5 levels of asthma control are suggested (0=no control, 4= four control problems)	Self-report
PCAQ	*1 domain/11 items* Asthma control (11)	5 point Likert	Scores range from 11 to 55 with higher scores reflecting greater perceived control of asthma	Self-report 5 minutes completion
AOMS	*3 domains* 1. Activity limitation 2. Symptoms 3. Concern or bother	High score (4) represents lower quality of life	No details	No details
ASCC	*3 domains (1 self-report)* 1. Clinical: self-report *2. Physiological response* *3. Inflammatory assessment-clinical measurement*	100% scale	Percentage score High percentage represents higher control	No details

PROM	***Domains (items)***	***Response options***	***Score***	***Administration/ Completion (time)***
AQL-5D	Utility measure derived from the AQLQ and psychometric evidence		5 attributes, each with 5 levels.	
ASUI	*1 domain/11 items* Symptoms (11)	4 point Likert scale	Preference-weighted scores generating a single utility: 0 to 1.0. Lower scores indicate greater symptom problems	Self-report
AQ 20	*3 domains/ 20 items* 1. Symptoms 2. Activities 3. Impacts		Total score expressed as a percentage. High scores indicate poor quality of life.	Self-report
RCP	Three questions assessing impact of asthma	Yes/no	One "yes" indicates medium morbidity and two or three "yes" answers indicate high morbidity	Self-report
LASS	*1 domain/ 8 items* Symptoms (8)	5 point Likert	Total scores range from 8 to 40.	Self-report
ASES	1 domain/80 items Self-efficacy and locus of control	5 point Likert	Patients report level of confidence in avoiding an asthma attack. 1= no confidence, 5= very confident	Self-report
WPAI	*3 domains/ 9 items* 1. Work impairment (4) 2. School impairment (4) 3. Activity impairment (1) Only 1 or 2 is answered	Percentage	Percentage impairment obtained for each domain. Higher scores indicate higher impairment	Self-report

Appendix Diii

Summary of asthma-specific instruments: health status domains ***(after Fitzpatrick et al., 1998)***

Instrument	*Instrument domains*								
	Physical function	**Symptoms**	**Global judgement**	**Psychol. well-being**	**Social well-being**	**Cognitive functioning**	**Role activities**	**Personal construct**	**Treatment satisfaction**
AQLQ		x		x			x		
MiniAQLQ		x		x			x		
AQLQ(S)		x		x			x		
Acute AQLQ		x		x					
ACQ		x							x
ACD		x							
MAQLQ		x		x	x			x	
LWAQ		x		x	x			x	
SGRQ	x	x		x	x		x		x
ACT		x					x	x	x
AIS-6	x	x		x					
ATAQ								x	x
PCAQ								x	
AOMS									
ASCC		x							
AQL-5D									
ASUI		x							
AQ 20	x	x		x					
RCP		x					x		
LASS		x							
ASES								x	
WPAI							x		

APPENDIX E: Licensing and cost

The AQLQ questionnaires are available free of charge from the developers

http://www.qoltech.co.uk/index.htm

APPENDIX F: Methods of working, membership and conclusions of multi-disciplinary panel

Members of the multidisciplinary panel were invited to participate based on their clinical or research experience of asthma and special interest in Patient-reported Outcome Measures.

The panel were sent the following documents:

- A structured review of patient-reported outcome measures for asthma: An update 2009
- A structured review of patient-reported health instruments for people with asthma (2006)
- Copies of the PROMs short-listed for discussion.

The panel were sent by email rating scales to judge the suitability of the questionnaire for use in the NHS for the evaluation of services. There was a section for comments. The rating scale used the following responses:

'not at all suitable' (score 0);
'to some extent unsuitable' (score 1);
'uncertain' (score 2);
'to some extent suitable' (score 3);
'very suitable' (score 4).

Scores for each questionnaire were ranked in order of preference. The Total maximum score=36.

The results and comments were then distributed by email to the panel for further rating should they wish to change their vote.

Ratings and comments

SF-36

It was agreed that a generic instrument is useful to compare disease states across different conditions but that a disease-specific measure is more appropriate for the assessment of asthma disease state. To use both in clinical practice was considered too burdensome.

The SF-36 was considered to be useful in COPD patients but less useful in asthma as patients tend to be younger and less disabled. In addition, the four week time frame for responses was thought to be inadequate due to the nature of asthma disease. Patients often experience periods of good health interspersed with exacerbations. Therefore scores may represent a chronic deterioration. Some questions were considered not relevant to people with asthma and the length would limit use in clinical practice. Despite this, it was thought to have some usefulness in identifying the impact of asthma and how patients have adapted their lifestyle to cope. The

evidence from the review supports its application for the comparison of health states of different conditions, but lacks responsiveness is asthmatic patients. For the evaluation of the quality of services, a disease-specific approach to measurement was more suitable.

FIRST RATING	'not at all suitable' (score 0);	'to some extent unsuitable' (score 1);	'uncertain' (score 2)	'to some extent suitable' (score 3);	'very suitable' (score 4).	TOTAL
SF-36		2	2	12		**16**

Rating and comments
The panel rated the SF-36 using the response categories listed above. Generally it was considered to be suitable to some extent. Several members of the panel suggested the EQ-5D as an alternative despite the lack of evidence in the review to be short-listed. Its usefulness in economic evaluation was an attractive feature although it was acknowledged that utility values could be obtained from the SF-36 but that this was not straightforward.

AQLQ
The AQLQ was considered to be comprehensive in its assessment of health status and performance which was supported in the evidence presented in the review. Furthermore, self-administration and the focus on individualised activities were considered attractive. However, in practice this was deemed to be difficult for some patients and explanation often needed which impedes administration. It was judged to be too long for routine use in clinical practice but that providing supervision could be given; it may be suitable for use in clinical trials.

Despite good evidence of psychometric performance the panel made reference to the standardised and short-version as being more practical.

AQLQ(S)
The standardised version was considered to be easier to complete than the individualised form for some patients. It also has the advantage of being able to compare populations with different cultural characteristics. It was reported to be easy to use and extremely well validated, plus translated and validated in most languages and cultures. Some regarded this as an ideal instrument for formal projects where accurate assessment is needed. There was some doubt though whether it is feasible in clinical settings dues to its length and scoring process. The standardised activity questions were considered limiting by some panel members.

Although the review reports high response rates for the AQLQ(S), one member reports less than ideal response rates with a postal survey including this questionnaire.

MiniAQLQ
Overall, the panel considered the miniAQLQ to be the most promising PROM for people with asthma. This is based on the evidence presented in the review, ease of use and patient acceptability and good concordance with postal and supervised

administration. This was considered to be an important characteristic from an NHS outcome measurement perspective. It was considered to be a useful instrument for use in clinical practice. The reduced responsiveness of the miniAQLQ compared to the AQLQ would limit its use in a research context.

MAQLQ

Despite the MAQLQ fulfilling psychometric criteria for short-listing, most were unfamiliar with it. It was considered to be comprehensive, straightforward and simple to complete. There were similarities noted between the questions from this and the AQLQ. The lack of UK data was disappointing.

Other instruments

It was suggested that in general a range of Questions were needed and something as simple as Royal College of Physicians three questions which has been amended with a 7 day scale be useful. However, it was acknowledged that there were limitations in terms of outcome measurement in the context of NHS service delivery.

Asthma Control Questionnaire (ACQ)/Asthma Control Test (ACT)

The ACQ and ACT were suggested by several members as useful instruments for measuring recent asthma symptom control, although it was accepted that it was narrow in focus. The evidence for this was presented in the update review and the ACQ performs psychometrically as well as the miniAQLQ. Its uni-dimensionality assessed by the PROM group was considered one reason not to include it as a short-listed instrument. However, there are several features to support its use as a measure of asthma control alongside a multi-dimensional outcome measure. It has been reported to be less prone to error when completed unsupervised and therefore very practical for postal or telephone administration. There are also defined cut-off points for quick assessments of control therefore enhancing its use as a pre-consultation tool to ensure therapy is appropriate.

The Asthma Bother Profile was also identified by the panel. This was referred to in the 2006 review and no further evidence was found during the update.

With reference to using adult PROMs for the measurement of outcomes in children and adolescents, it was pointed out that paediatric specific instruments should always be used.

Ratings

FIRST RATING	**'not at all suitable' (score 0)**	**'to some extent unsuitable' (score 1)**	**'uncertain' (score 2)**	**'to some extent suitable' (score 3)**	**'very suitable' (score 4)**	**TOTAL**
miniAQLQ				3	24	**27**
AQLQ(S)				15	8	**23**
AQLQ			2	18		**20**
MAQLQ		1	6	3	8	**18**

Recommendations

The SF-36 is recommended as a generic health status measure for people with asthma. The miniAQLQ was highly rated as an asthma-specific instrument for the measurement of the quality of NHS services.

Several members suggest that for the measurement of asthma control, the ACQ is most favourable option.

Patient-reported Outcome Measure Rating Scale

1. On the basis of the review of evidence and your personal experience, is this questionnaire suitable for the measurement of the quality and outcomes of services for people with asthma? (please tick one box)

☐ Not at all suitable ☐ To some extent unsuitable ☐ Uncertain ☐ To some extent suitable ☐Very suitable

Do you have another questionnaire you could suggest?

Any additional comments

ASTHMA OUTCOMES CONSENSUS GROUP MEMBERS.

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REFERENCES

Aburuz S, Gamble J, Heaney LG. Assessment of impairment in health-related quality of life in patients with difficult asthma: psychometric performance of the Asthma Quality of Life Questionnaire. *Respirology* 2007;12:227-33.

Adams RJ, Ruffin RE, Smith BJ. Validity of a modified version of the Marks Asthma Quality of Life Questionnaire. *Journal of Asthma* 2000; 37:131-43.

Adams RJ, Wilson DH, Taylor AW, Daly A, d'Espaignet ET, Dal Grande E *et al*. Coexistent chronic conditions and asthma quality of life: a population-based study. *Chest* 2006;129:285-91.

Ahmed S, Ernst P, Tamblyn R, Colman N. Validation of The 30 Second Asthma Test as a measure of asthma control. *Canadian Respiratory Journal* 2007;14:105-9.

Ammar D, Gloria CJ, Taningco G, Hammerschlag MR, Weiss S, Gelling M, Roblin PM, Joks R. Monocycline treatment results in reduced oral steroid requirements in adult asthma. *Allergy and Asthma Proceedings* 2008; 29: 286-294

Archea C, Yen IH, Chen H, Eisner MD, Katz PP, Masharani U *et al*. Negative life events and quality of life in adults with asthma.[see comment]. *Thorax* 2007;62:139-46.

Armour C, Bosnic-Anticevich S, Brillant M, Burton D, Emmerton L, Krass I, Saini B, Smith L, Stewart K. Pharmacy Asthma Care Program (PACP) improves outcomes for patients in the community *Thorax*. 2007 Jun;62(6):496-502. Epub 2007 Jan 24

Barley EA,.Jones PW. Adapting to Asthma: Are Some Asthma Effects Acceptable? [References]. *Journal of Asthma* 2006;43:433-8.

Bergner M, Bobbitt RA, Kressel S, et al. (1976) The Sickness Impact Profile: conceptual formulation and methodology for the development of a health status measure. *International Journal of Health Service;* 6: 393-415.

Bergner M, Bobbitt RA, Carter WB et al. (1981) The Sickness Impact Profile: development and final revision of a health status measure. *Medical Care;* 19:787-805.

Blanc PD, Yen IH, Chen H, Katz PP, Earnest G, Balmes JR *et al*. Area-level socio-economic status and health status among adults with asthma and rhinitis. *European Respiratory Journal* 2006;27:85-94.

Boulet LP, Lemiere C, Archambault F, Carrier G, Descary MC, Deschesnes F. Smoking and asthma: clinical and radiologic features, lung function, and airway inflammation. *Chest* 2006;129:661-8.

Bowling A. (1995) Measuring Disease. Open University Press, Buckingham.

Brazier JE, Jones N, Kind P. (1993) Testing the validity of the EuroQol and comparing it with the SF-36 Health Survey questionnaire. *Quality of Life Research;* 2: 169-180.

Brazier JE, Walters SJ, Nicholl JP, Kohler B. (1996) Using the SF-36 and EuroQol on an elderly population. *Quality of Life Research;* 5: 195-204.

Brazier JE, Roberts j, Deverill M: The estimation of a preference-based measure of health from the SF-36. *Journal of Health Economics* 2002; 21 :271-292.

Browne J, Jamieson L, Lewsey J, et al., Patient reported outcome measures (PROMs) in elective surgery. Report to Department of Health 2007.

Busse WW. Anti-immunoglobulin E (omalizumab) therapy in allergic asthma *Am J Respir Crit Care Med*. 2001 Oct 15;164(8 Pt 2):S12-7

Calfee CS, Katz PP, Yelin EH, Iribarren C, Eisner MD. The influence of perceived control of asthma on health outcomes. *Chest* 2006;130:1312-8.

Campbell TS, Lavoie KL, Bacon SL, Scharf D, Aboussafy D, Ditto B. Asthma self-efficacy, high frequency heart rate variability, and airflow obstruction during negative affect in daily life. *Int J Psychophysiol*. 2006 Oct;62(1):109-14. Epub 2006 May 2.

Chaudhuri R, McSharry C, McCoard A, Livingston E, Hothersall E, Spears M, Lafferty J, Thomson NC. Role of symptoms and lung function in determining asthma control in smokers with asthma. *Allergy.* 2008 Jan;63(1):132-5

Chipps B, Buhl R, Beeh KM, Fox H, Thomas K, Reisner C. Improvement in quality of life with omalizumab in patients with severe allergic asthma. *Current Medical Research & Opinion* 2006;22:2201-8.

Chen H, Gould MK, Blanc PD, Miller DP, Kamath TV, Lee JH, Sullivan SD; for the TENOR Study Group. Asthma control, severity, and quality of life: quantifying the effect of uncontrolled disease. *J Allergy Clin Immunol.* 2007 Aug;120(2):396-402. Epub 2007 Jun 11

Chen H, Blanc PD, Hayden ML, Bleecker ER, Chawla A, Lee JH; TENOR Study Group. Assessing productivity loss and activity impairment in severe or difficult-to-treat asthma.*Value Health*. 2008 Mar-Apr;11(2):231-9.

Clark NM, Gong ZM, Wang SJ, Lin X, Bria WF, Johnson TR. A randomized trial of a self-regulation intervention for women with asthma. *Chest.* 2007 Jul;132(1):88-97. Epub 2007 May 15

Cleland JA, Hall S, Price D, Lee AJ. An exploratory, pragmatic, cluster randomised trial of practice nurse training in the use of asthma action plans. *Prim Care Respir J*. 2007 Oct;16(5):311-8.

Cox G, Thomson NC, Rubin AS, Niven RM, Corris PA, Siersted HC *et al*. Asthma control during the year after bronchial thermoplasty.[see comment]. *New England Journal of Medicine* 2007;356:1327-37.

Darzi A. Our NHS Our Future: NHS Next Stage Review Interim Report. Department of Health, London, October 2007.

Darzi A. Our NHS Our Future: High Quality Care for All. NHS Next Stage Review Final Report. Department of Health, London, June 2008.

De Bruin AF, De Witte LP, Stvene F, Diederiks JPM. (1992) Sickness Impact Profile: the state of art of a generic functional status measure. *Social Science and Medicine;* 35: 1003-14.

Department of Health (2008) Guidance on the routine collection of Patient Reported Outcome Measures (PROMs)

Eisner MD, Iribarren C. The influence of cigarette smoking on adult asthma outcomes. *Nicotine Tob Res.* 2007 Jan;9(1):53-6.

Feeny, David, William Furlong, Michael Boyle, and George W. Torrance, "Multi-Attribute Health Status Classification Systems: Health Utilities Index." *PharmacoEconomics*, Vol 7, No 6, June, 1995, pp 490-502

Flood EM, De Cock E, Mork AC, Revicki DA. Evaluating preference weights for the Asthma Symptom Utility Index (ASUI) across countries. *Health & Quality of Life Outcomes* 2006;4:51, 2006.:51, 2006.

FitzGerald JM, Shragge D, Haddon J, Jennings B, Lee J, Bai T, Pare P, Kassen D, Grunfeld A. A randomized, controlled trial of high dose, inhaled budesonide versus oral prednisone in patients discharged from the emergency department following an acute asthma exacerbation. *Can Respir J.* 2000 Jan-Feb;7(1):61-7

Fitzpatrick R, Davey C, Buxton MJ, Jones DR. (1998) Evaluating patient-based outcome measures for use in clinical trials. *Health Technology Assessment;* 2(14).

Fitzpatrick R, Bowling A, Gibbons E, Haywood K, Jenkinson C, Mackintosh A, Peters M. A Structured Review of Patient-Reported Measures in Relation to Selected Chronic Conditions, Perceptions of Quality of Care, and Carer Impact. Oxford: National Centre for Health Outcomes Development, November 2006.

Garratt AM, Schmidt L, Mackintosh A, Fitzpatrick R. (2002a) Quality of life measurement: bibliographic study of patient assessed health outcome measures. *British Medical Journal;* 324 (7351): 1417-1421.

Holloway JW, Barton SJ, Holgate ST, Rose-Zerilli MJ, Sayers I. The role of LTA4H and ALOX5AP polymorphism in asthma and allergy susceptibility. *Allergy.* 2008 Aug;63(8):1046-53. Epub 2008 Jun 10

Hunt SM, McKenna SP, McEwen J, Backett EM, Williams J, Papp E. (1980) A quantitative approach to perceived health status: a validation study. *Journal of Epidemiology and Community Health;* 34: 281-286.

Hyland ME, Finnis S, Irvine SH. A scale for assessing quality of life in adult asthma sufferers. *Journal of Psychosomatic Research* 1991; 35:99-110.

Jenkinson C, McGee H. (1998). Health Status Measurement, a Brief but Critical Introduction. Radcliffe Medical Press Ltd, Oxford.
Jones PW, Quirk FH, Baveystock CM. The St George's Respiratory Questionnaire. *Respiratory Medicine* 1991; 85:25-31.

Juniper EF, Guyatt GH, Epstein RS, Ferrie PJ, Jaeschke R, Hillers TK. Evaluation of impairment of health related quality of life in asthma: development of a questionnaire for use in clinical trials. *Thorax* 1992; 47:76-83.

Juniper EF, Guyatt GH, Ferrie PJ, Griffith LE. Measuring quality of life in asthma. *American Review of Respiratory Disease* 1993; 147:832-8.

Juniper EF, Guyatt GH, Willan AR, Griffith LE. Determining a minimal important change in a disease-specific quality of life questionnaire. *Journal of Clinical Epidemiology* 1994; 47:81-7.

Juniper EF. Assessing health-related quality of life in asthma. *Canadian Respiratory Journal* 1997; 4:145-51.

Juniper EF, Buist AS, Cox FM, Ferrie PJ, King DR. Validation of a standardized version of the Asthma Quality of Life Questionnaire. *Chest: the Cardiopulmonary Journal* 1999; 115:1265-70.

Juniper EF, Guyatt GH, Cox FM, Ferrie PJ, King DR. Development and validation of the Mini-Asthma Quality of Life Questionnaire. *European Respiratory Journal* 1999; 14:32-8.

Juniper EF, O'Byrne PM, Guyatt GH, Ferrie PJ, King DR. Development and validation of a questionnaire to measure asthma control. *European Respiratory Journal* 1999; 14:902-7.

Juniper EF, Svensson K, Mork AC, Stahl E. Measuring health-related quality of life in adults during an acute asthma exacerbation. *Chest* 2004; 125:93-7.

Juniper EF, Bousquet J, Abetz L, Bateman ED, GOAL Committee. Identifying 'well-controlled' and 'not well-controlled' asthma using the Asthma Control Questionnaire. *Respiratory Medicine* 2006;100:616-21.

Katz PP, Yelin EH, Smith S, Blanc PD. Perceived control of asthma: development and validation of a questionnaire. *Am J Respir Crit Care Med.* 1997 Feb;155(2):577-82.

Katz PP, Yelin EH, Eisner MD, Blanc PD. Perceived control of asthma and quality of life among adults with asthma. *Ann Allergy Asthma Immunol*. 2002 Sep;89(3):251-8.

Lafond C, Series F, Lemiere C. Impact of CPAP on asthmatic patients with obstructive sleep apnoea.[see comment]. *European Respiratory Journal* 2007;29:307-11.

Lavoie KL, Bouchard A, Joseph M, Campbell TS, Favreau H, Bacon SL. Association of asthma self-efficacy to asthma control and quality of life. *Ann Behav Med*. 2008 Aug;36(1):100-6.

Lazarus SC, Chinchilli VM, Rollings NJ, Boushey HA, Cherniack R, Craig TJ *et al*. Smoking affects response to inhaled corticosteroids or leukotriene receptor antagonists in asthma.[see comment]. *American Journal of Respiratory & Critical Care Medicine* 2007;175:783-90.

LeBlanc A, Robichaud P, Lacasse Y, Boulet LP. Quantification of asthma control: validation of the Asthma Control Scoring System. *Allergy*. 2007 Feb;62(2):120-5.

Lee JH, Haselkorn T, Borish L, Rasouliyan L, Chipps BE, Wenzel SE. Risk factors associated with persistent airflow limitation in severe or difficult-to-treat asthma: insights from the TENOR study. *Chest.* 2007 Dec;132(6):1882-9.

Lloyd A, Price D, Brown R. The impact of asthma exacerbations on health-related quality of life in moderate to severe asthma patients in the UK. *Prim Care Respir J.* 2007 Feb;16(1):22-7.

Lowery EP, Henneberger PK, Rosiello R, Sama SR, Preusse P, Milton DK. Quality of life of adults with workplace exacerbation of asthma. *Qual Life Res.* 2007 Dec;16(10):1605-13. Epub 2007 Oct 24.

Mancuso CA, Rincon M, McCulloch CE, Charlson ME. Self-efficacy, depressive symptoms, and patients' expectations predict outcomes in asthma. *Med Care*. 2001 Dec;39(12):1326-38.

Mancuso CA, Choi TN, Westermann H, Briggs WM, Wenderoth S, Charlson ME. Measuring physical activity in asthma patients: two-minute walk test, repeated chair rise test, and self-reported energy expenditure. *J Asthma*. 2007 May;44(4):333-40.

Marks GB, Dunn SM, Woolcock AJ. A scale for the measurement of quality of life in adults with asthma. *Journal of Clinical Epidemiology* 1992;45:461-72.

Markson Markson LE, Vollmer WM, Fitterman L, O'Connor E, Narayanan S, Berger M, Buist AS. Insight into patient dissatisfaction with asthma treatment. *Arch Intern Med*. 2001 Feb 12;161(3):379-84.

McDowell I, Jenkinson C. (1996) Development standards for health measures. *Journal of Health Service Research Policy;* October. 1(4): 238-246.

McDowell I, Newell C. (1996) Measuring Health: a guide to rating scales and questionnaires. Oxford University Press, New York.

McTaggart-Cowan HM, Marra CA, Yang Y, Brazier JE, Kopec JA, FitzGerald JM, Anis AH, Lynd LD. The validity of generic and condition-specific preference-based instruments: the ability to discriminate asthma control status. *Qual Life Res*. 2008 Apr;17(3):453-62. Epub 2008 Feb 15.

Metz SM, Wyrwich KW, Babu AN, Kroenke K, Tierney WM, Wolinsky FD. A comparison of traditional and Rasch cut points for assessing clinically important change in health-related quality of life among patients with asthma. *Quality of Life Research* 2006;15:1639-49.

Morjaria JB, Chauhan AJ, Babu KS, Polosa R, Davies DE, Holgate ST The role of a soluble TNFalpha receptor fusion protein (etanercept) in corticosteroid refractory asthma: a double blind, randomised, placebo controlled trial *Thorax.* 2008 Jul;63(7):584-91. Epub 2008 Feb 1

Murphy Murphy K, Nelson H, Parasuraman B, Boggs R, Miller C, O'Dowd L. The effect of budesonide and formoterol in one pressurized metered-dose inhaler on patient-reported outcomes in adults with mild-to-moderate persistent asthma. *Curr Med Res Opin.* 2008 Mar;24(3):879-94. Epub 2008 Feb 8.

Nathan RA, Sorkness CA, Kosinski M, Schatz M, Li JT, Marcus P, Murray JJ, Pendergraft TB. Development of the asthma control test: a survey for assessing asthma control. *J Allergy Clin Immunol.* 2004 Jan;113(1):59-65.

Nathan JA, Pearce L, Field C, Dotesio-Eyres N, Sharples LD, Cafferty F, Laroche CM. A randomized controlled trial of follow-up of patients discharged from the hospital following acute asthma: best performed by specialist nurse or doctor? *Chest.* 2006 Jul;130(1):51-7.

Nathan RA, Meltzer EO, Derebery J, Campbell UB, Stang PE, Corrao MA, Allen G, Stanford R. The prevalence of nasal symptoms attributed to allergies in the United States: findings from the burden of rhinitis in an America survey. *Allergy Asthma Proc.* 2008 Nov-Dec;29(6):600-8.

Nelson E, Landgraf J, Hays R, Wasson J, Kirk J. (1990) The functional status of patients. How can it be measured in physicians' offices? *Medical Care;* 28: 1111-1126.

Niven Niven R, Chung KF, Panahloo Z, Blogg M, Ayre G. Effectiveness of omalizumab in patients with inadequately controlled severe persistent allergic asthma: An open-label study. *Respir Med*. 2008 Oct;102(10):1371-8. Epub 2008 Jul 26.

Olajos-Clow J, Costello E, Lougheed MD. Perceived control and quality of life in asthma: impact of asthma education. *J Asthma*. 2005 Nov;42(9):751-6.

Patrick D and Peach H (eds) (1989) Disablement in the Community: A Sociomedical Press Perspective. Oxford, U.K.: Oxford University Press

Pavord ID, Cox G, Thomson NC, Rubin AS, Corris PA, Niven RM, Chung KF, Laviolette M; RISA Trial Study Group. Safety and efficacy of bronchial thermoplasty in symptomatic, severe asthma. *Am J Respir Crit Care Med.* 2007 Dec 15;176(12):1185-91. Epub 2007 Sep 27.

Peters D, Chen C, Markson LE, Allen-Ramey FC, Vollmer WM. Using an asthma control questionnaire and administrative data to predict health-care utilization. *Chest.* 2006 Apr;129(4):918-24.

Pettit T, Livingston G, Manela M, Kitchen G, Katona C, Bowling A. (2001) Validation and normative data of health status measures in older people: the Islington study. *International Journal of Geriatric Psychiatry;* 16: 1061-1070.

Pogson ZE, Antoniak MD, Pacey SJ, Lewis SA, Britton JR, Fogarty AW. Does a low sodium diet improve asthma control? A randomized controlled trial *Am J Respir Crit Care Med.* 2008 Jul 15;178(2):132-8. Epub 2008 May

Post MWM, de Bruin AF, de Witte et al (1996) The SIP68: a measure of health related functional status in rehabilitation medicine Archives of Physical Medicine and Rehabilitation 77, 440

Price DB, Williams AE, Yoxall S.Salmeterol/fluticasone stable-dose treatment compared with formoterol/budesonide adjustable maintenance dosing: impact on health-related quality of life. *Respir Res.* 2007 Jul 4;8:46.

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* 1990; 79: 17-21.

Quirk FH, Baveystock CM, Wilson RC, Jones PW. Influence of demographic and disease related factors on the degree of distress associated with symptoms and restrictions on daily living due to asthma in six countries. *Eur Respir J* 1991; 4: 167-71.

Quittner AL, Modi A, Cruz I. Systematic review of health-related quality of life measures for children with respiratory conditions. *Paediatr Respir Rev*. 2008 Sep;9(3):220-32.

Resnick B, Nahm ES. (2001) Reliability and validity testing of the revised 12-item Short-Form Health Survey in older adults. *Journal of Nursing Measurement;* Fall. 9(2): 151-61.

Resnick B, Parker R. (2001) Simplified scoring and psychometrics of the revised 12-item Short-Form Health Survey. *Outcomes Management for Nursing Practice;* Oct-Dec. 5(4): 161-6.

Ritz T, Steptoe A, Bobb C, Harris AHS, Edwards M. The Asthma Trigger Inventory: Validation of a Questionnaire for Perceived Triggers of Asthma. [References]. *Psychosomatic Medicine* 2006;68:956-65.

Schaffer SD, Tian L. Promoting adherence: effects of theory-based asthma education. *Clin Nurs Res.* 2004 Feb;13(1):69-89.

Schatz M, Zeiger RS, Vollmer WM, Mosen D, Apter AJ, Stibolt TB *et al*. Development and validation of a medication intensity scale derived from computerized pharmacy data that predicts emergency hospital utilization for persistent asthma. *American Journal of Managed Care* 2006;12:478-84.

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. *Journal of Allergy & Clinical Immunology* 2006; 117:549-56.

Schatz M, Zeiger RS, Vollmer WM, Mosen D, Mendoza G, Apter AJ *et al*. The controller-to-total asthma medication ratio is associated with patient-centered as well as utilization outcomes.[see comment]. *Chest* 2006;130:43-50.

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. *Quality of Life Research* 2007;16:345-55.

Schatz M, Mosen DM, Kosinski M, Vollmer WM, Magid DJ, O'Connor E, Zeiger RS. The relationship between asthma-specific quality of life and asthma control. *J Asthma*. 2007 Jun;44(5):391-5.

Schatz M, Mosen DM, Kosinski M, Vollmer WM, Magid DJ, O'Connor E, Zeiger RS. Validity of the Asthma Control Test completed at home. *Am J Manag Care*. 2007 Dec;13(12):661-7.

Schatz M, Mosen DM, Kosinski M, Vollmer WM, Magid DJ, O'Connor E, Zeiger RS. Predictors of asthma control in a random sample of asthmatic patients. *J Asthma.* 2007 May;44(4):341-5.

Schatz M, Zeiger RS, Drane A, Harden K, Cibildak A, Oosterman JE, Kosinski M. Reliability and predictive validity of the Asthma Control Test administered by telephone calls using speech recognition technology. *J Allergy Clin Immunol*. 2007 Feb;119(2):336-43. Epub 2006 Dec 27

Schatz M, Zeiger RS, Mosen D, Vollmer WM. Asthma-specific quality of life and subsequent asthma emergency hospital care. *Am J Manag Care*. 2008 Apr;14(4):206-11.

Schofield M, Mishra G. (1998) Validity of the SF-12 compared with the SF-36 health survey in pilot studies of the Australian longitudinal study on women's health. *Journal of Health Psychology;* 3: 259-271.

Shaheen SO, Newson RB, Rayman MP, Wong AP, Tumilty MK, Phillips JM, Potts JF, Kelly FJ, White PT, Burney PG. Randomised, double blind, placebo-controlled trial of selenium supplementation in adult asthma. *Thorax.* 2007 Jun;62(6):483-90. Epub 2007 Jan 18.

Shedd AD, Peters JI, Wood P, Inscore S, Forkner E, Smith B, Galbreath AD. Impact of home environment characteristics on asthma quality of life and symptom scores. J Asthma. 2007 Apr;44(3):183-7.

Slader CA, Reddel HK, Spencer LM, Belousova EG, Armour CL, Bosnic-Anticevich SZ *et al*. Double blind randomised controlled trial of two different breathing techniques in the management of asthma.[see comment]. *Thorax* 2006;61:651-6.

Siu AL, Reuben DB, Ouslander JG, Osterweil D. (1993a) Using multidimensional health measures in older persons to identify risk of hospitalisation and skilled nursing placement. *Quality of Life Research;* 2: 253-261.

Smith S, Cano S, Lamping D, et al., Patient reported outcome measures (PROMs) for routine use in treatment centres: recommendations based on a review of the scientific literature. Final Report to Department of Health, 2005

Solans M, Pane S, Estrada MD, Serra-Sutton V, Berra S, Herdman M, Alonso J, Rajmil L Health-Related Quality of Life Measurement in Children and Adolescents: A Systematic Review of Generic and Disease-Specific Instruments. *Value Health*. 2007 Dec 17.

Stewart AL, Hays RD, Ware JE. (1988) The MOS Short-Form General Health Survey: reliability and validity in a patient population. *Medical Care;* 26: 724-735.

Streiner DL, Norman GR. (1995) Health Measurement Scales. A practical guide to their development and use. Oxford Medical Publications, Inc. Second Edition.

Sullivan SD, Wenzel SE, Bresnahan BW, Zheng B, Lee JH, Pritchard M *et al*. Association of control and risk of severe asthma-related events in severe or difficult-to-treat asthma patients. *Allergy* 2007;62:655-60.

Surette ME, Stull D, Lindemann J. The impact of a medical food containing gammalinolenic and eicosapentaenoic acids on asthma management and the quality of life of adult asthma patients. *Curr Med Res Opin.* 2008 Feb;24(2):559-67.

The EuroQol Group. (1990) EuroQol: a new facility for the measurement of health-related quality of life. *Health Policy;* 16:199-208.

Thomas M, Sheran J, Smith N, Fonseca S, Lee AJ. AKL1, a botanical mixture for the treatment of asthma: a randomised, double-blind, placebo-controlled, cross-over study. *BMC Pulmonary Medicine* 2007;7:4, 2007.:4, 2007.

Vollmer WM, Markson LE, O'Connor E, Sanocki LL, Fitterman L, Berger M, Buist AS. Association of asthma control with health care utilization and quality of life. *Am J Respir* Crit Care Med. 1999 Nov;160(5 Pt 1):1647-52

Wallenstein GV, Carranza-Rosenzweig J, Kosinski M, Blaisdell-Gross B, Gajria K, Jhingran P. A psychometric comparison of three patient-based measures of asthma control. *Current Medical Research & Opinion* 2007;23:369-77.

Ware JE, Sherbourne CD. (1992) The MOS 36-Item Short-Form Health Survey (SF-36). I. Conceptual framework and item selection. *Medical Care;* 30: 473-483.

Ware J, Kosinski M, Keller SD. (1994) SF-36 Physical and Mental Health Summary Scales: A User's Manual. Boston, MA: The Health Institute, New England Medical Centre.

Ware JE, Kosinski M, Keller SD. (1995) SF-12: How to Score the SF-12 Physical and Mental Health Summary Scales. The Health Institute, New England Medical Center. Boston, MA. Second Edition.

Ware JE. (1997) SF-36 Health Survey. Manual and Interpretation Guide. The Health Institute, New England Medical Centre. Boston, MA. Nimrod Press. Second Edition.

Ware JE, Gandek B. (1998) Methods for testing data quality, scaling assumptions and reliability: the IQOLA project approach. *Journal of Clinical Epidemiology;* 51(11): 945-952.

Win T, Pearce L, Nathan J, Cafferty F, Laroche C. Use of the Airway Questionnaire 20 to detect changes in quality of life in asthmatic patients and its association with the St George's Respiratory Questionnaire and clinical parameters. *Can Respir J.* 2008 Apr;15(3):133-7

Wood PR, Smith B, O'Donnell L, Galbreath AD, Lara M, Forkner E, Peters JI. Quantifying asthma symptoms in adults: the Lara Asthma Symptom Scale. *J Allergy Clin Immunol.* 2007 Dec;120(6):1368-72. Epub 2007 Nov

Wyrwich KW, Tierney WM, Babu AN, Kroenke K, and Wolinsky FD. A comparison of clinically important differences in health-related quality of life for patients with chronic lung disease, asthma, or heart disease. *Health Services Research* 2005;4 0:577-