Validation of Subscales of the Severe Asthma Questionnaire (SAQ) Using Exploratory Factor Analysis (EFA)

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Research

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Abstract

Background

The Severe Asthma Questionnaire (SAQ) is a health related quality of life (HRQoL) questionnaire validated for use in severe asthma. It is scored using the mean value of 16 items (SAQ score) in addition to a single item global rating of HRQoL (SAQ-global). The aim was to validate clinically relevant subscales by following best practice guidelines of exploratory factor analysis (EFA).

Methods

The SAQ was completed, along with measures of asthma control and EQ5D-5L by patients attending six UK severe asthma centres. Clinical data were included in the analysis. EFA using principal axis factoring and promax rotation was used to achieve best fit to data.

Results

460 patients participated, 65% women, mean age 51 (16-83) yrs. A three factor solution achieved best fit and showed that the SAQ items formed three distinct but inter-correlated groups of items where items were grouped in a way that was consistent with item content. The three subscales were differentially associated with clinically relevant variables (lung function and mood). Males and females interpreted the question of night disturbance in different ways.

Conclusions

The 16 items of the SAQ can be scored as a single overall score or as three subscales with content reflecting three different constructs people with severe asthma use when making judgements about their lives. The subscale ‘My Life’ assesses the impact of severe asthma on different life activities, ‘My Mind’ assesses the perceived emotional impact and ‘My Body’ the impact of extra-pulmonary symptoms and side effects.

Plain English Summary

The Severe Asthma Questionnaire (SAQ) measures health related quality of life in severe asthma. 460 patients attending severe asthma clinics completed the SAQ and other questionnaires. Using the available clinic data, we validated three subscales of the SAQ: ‘My Life’ assesses the impact of severe asthma on different life activities, ‘My Mind’ assesses the perceived emotional impact and ‘My Body’ the impact of symptoms and side effects not directly related to breathing or the lung. We followed best practice guidelines for exploratory factor analysis and showed that these three subscales were differentially related to clinically relevant variables. The understanding provided by these subscales should help facilitate better communication between patient and healthcare workers and allow more detailed assessment regarding response to different treatments and management strategies. We found that males and females interpreted a question about night disturbance in different ways. This paper provides a blueprint for carrying out exploratory factor analysis in health related questionnaires, a technique that can be used to show whether or not clinically relevant subscales can be formed from a questionnaire.

Background

Validated health-related quality of life (HRQoL) questionnaires are used in clinical practice and research to evaluate the impact of disease and/or treatment responses. They consist typically of several items the responses to which are
aggregated to form an overall HRQoL score. Subscales can be formed from groups of items as subscales provide information that can be useful in clinical trials and clinical practice.

Guidelines for validating questionnaires recommend a two stage process where content validity is followed by construct validity [1], but these recommendations were published after the publication of four asthma specific HRQoL questionnaires. Validation of the asthma quality of life questionnaire's (AQLQ) subscales is based only on content validity [2,3] as the subscales are formed by grouping items on the basis of an examination of content alone. However, in three other asthma specific HRQoL questionnaires subscales are validated by both content validity and construct validity. This is done by showing that items initially grouped on the basis of content have similar statistical properties, using either principal component analysis [4,5] or principal factor analysis [6]. The advantage of construct validation is that it can show whether patients’ interpretation of the meaning of items is the same as that of the researchers.

The number of subscales in existing asthma specific HRQoL varies between three [5], four [2], five [6] and six [4], but despite this variation, there is consensus that activity restriction and mood should be measured in different subscales. Activity-related items are assessed in subscales labelled ‘activity limitation’ [2], ‘activity’ [5], and ‘activities’ and ‘avoidance’ [6]. Items relating to the emotional impact of asthma are assessed in subscales labelled ‘emotional function’ [2], ‘mood’ [4] and ‘distress’ and ‘preoccupation’ [6].

The Severe Asthma Questionnaire (SAQ) is the only validated HRQoL questionnaire for severe asthma [7]. It comprises 16 inter-correlated items measuring the impact of disease and medical interventions, and the mean of those items forms the SAQ score [8]. In addition, the questionnaire has a single question measuring the impact of disease and its treatment on the patient’s overall perception of quality of life, the SAQ-global score. Content validity for the questionnaire was established in two qualitative studies [7,9], and construct validity for the SAQ score demonstrated by factor analysis. The content of the 16 items fall into three categories. Items 1 – 7 ask patients to rate the impact of their asthma and its treatment on seven different types of life activity, and have content consistent with items in the activity subscales of earlier questionnaires. Items 8 – 11 ask patients about various aspect of mood and have content consistent with that in the emotional subscales of earlier questionnaires. Items 12-16 assess the impact on life of extra-pulmonary symptoms and side effects. These last five items measure quality of life deficits that are typically found only in severe asthma where qualitative research shows them to have play a major role [7,9-11]. They are rare in mild and moderate asthma and have limited representation in earlier asthma specific HRQoL questionnaires [9].

Content derived subscales for the SAQ and one consistent with earlier scales would therefore be based on three subscales (a) impact on life's activities (b) impact on emotional well-being, and (c) impact of extra-pulmonary symptoms including those caused by side effects of treatment.

Although there is a rationale for having three subscales of the SAQ on the basis of content, that subscale structure has not been construct validated. The aim of this study is to provide construct validation of the subscales of the 16 items of the SAQ by showing that the different subscales are associated with different constructs. In this study, construct validity is achieved by providing evidence that (a) the 16 items fall into statistically distinct clusters; (b) that items in the statistically formed subscales are consistent with classification based on content; (c) that the subscales formed from these clusters have different associations with clinically relevant variables and therefore provide additional information compared to the overall scores.

Methods

Design

This was a cross-sectional study with questionnaire and clinic data each collected at one time point.
Participants

Patients aged ≥16 years of age and diagnosed with severe asthma as defined by the ERS/ATS guidelines were invited to participate [12]. Participants were recruited from six UK severe asthma centres and were excluded if they were diagnosed with another condition that significantly contributed to their respiratory health, e.g. lung cancer, heart disease or chronic obstructive pulmonary disease.

Questionnaires

Severe Asthma Questionnaire (SAQ)

The SAQ is a HRQoL designed for patients with severe asthma. The questionnaire consists of 16-items scored from 1 to 7, with a higher score indicating better quality of life. The mean of the 16 items is calculated to provide the SAQ score. The SAQ also contains a separate, Borg-type scale ranging from 0-100 and based on the Global Quality of Life Questionnaire [13] which provides the SAQ-global score [8].

Asthma Control Test (ACT)

The ACT consists of five asthma symptom and medication use items, which are totalled to provide an indication of asthma control. The sum of the five items, scale = 5, is calculated to give the ACT score, with a higher number indicating better asthma control [14].

Asthma Control Questionnaire-6 (ACQ-6)

Contains six items concerning asthma symptoms and daily use of rescue bronchodilator. Patients respond to these items on a 0-6 scale (0 = no impairment, 6 = maximum impairment). The mean of the six items is calculated to provide the ACQ-6 score with a lower number indicating better asthma control [15].

EQ-5D-5L and mood measurement

Consists of 5 items scored from 1 to 5 with a higher score indicating greater impairment, and a 0-100 visual analogue score, the EQ-5D VAS [16]. Index scores are calculated using the 2012 value set for England [17] and these index scores are presented here. For this study we used item 5 of the questionnaire as a proxy measure of mood. Participants indicate the degree to which they feel "anxious or depressed" on a five point scale of severity.

Clinical data

Clinical data included body mass index (BMI) and asthma severity as measured by the following items: GINA treatment step, spirometry (forced expiratory volume in 1 second (FEV₁) and FEV₁ % predicted), prednisolone dose (mg/day), health care utilisation in the least 12 months including number of hospital admissions, emergency department visits and exacerbations requiring oral corticosteroids (OCS). An estimate of cumulative OCS exposure (mg/year) was calculated by multiplying a patient’s maintenance OCS dose by 365 and adding an estimated use of OCS following each exacerbation. British Thoracic Society and GINA guidelines suggest that 40mg of prednisolone for 7 days should be prescribed for the treatment of exacerbations [18]. This equates to 280mg of OCS per exacerbation.

Procedure

Patients with severe asthma at five specialist treatment centres were approached for recruitment to this study. Questionnaires were completed in clinic once written informed consented was given. Spirometry was conducted either at the time of questionnaire completion or at any point within the previous 6 months. Participating sites collected either
ACT or ACQ data as a measure of asthma control for this study as per their normal clinical practice. The same data collected for a previous study [8] from a sixth specialist centre were also included for analysis.

Ethical Approval

This study received ethical approvals from the Research Ethics Committee/Health Research Authority (REC reference: 19/WA/0011, IRAS project ID: 250167) and was sponsored by University Hospitals Plymouth NHS Trust. Data from a previous study received ethical approval number 16/NE/0188, IRAS ID: 207601) [8].

Statistical analysis

Exploratory factor analysis (EFA) is an exploratory procedure for examining patterns of correlations between a set of variables. The aim is to discover groups of variables that have variation in common. The common variation is used to create an artificial variable called a factor. The factor represents a construct whose causal influence is assumed to create the common variation amount the variables. According to guidelines for good practice [19,20], parameters of EFA should be chosen to achieve a “good fit” to the data, and the meaning of good fit and the rationale for choosing those parameters for this analysis are described below.

There are two main forms of data extract: principal component analysis and factor analysis. Principal component analysis is a simpler and older form of analysis that became popular when computers were slower and is the default option in many statistical packages. Principal component analysis is a method of data reduction only, it does not distinguish between unique and shared variance and therefore does not identify causal factors (psychological constructs). The method risks overestimating variance. Factor analysis analyses only shared variance and in so doing provides information about underlying causal structures, it does not inflate estimates of variance and for most purposes is the recommended form of extraction [20]. We used factor analysis rather than principal component extraction because we wanted to identify causal constructs and estimate variance, and we used principal axis factor analysis as a commonly used type of factor analysis [20].

EFA is an exploratory tool that provides choice in the numbers of factors to be extracted. When used for subscale construction in HRQoL, the primary determinant of factor number and hence subscale number is a number that is both theoretically plausible and clinically useful. If that number produces best fit (see later), then that number can be accepted as the final solution. If that number fails to produce good fit, then alternatives should be considered. In our case, a plausible and useful number based on content is that there should be three factors, corresponding to activity, emotion and extra-pulmonary symptoms.

There are four data driven methods of determining factor number that can be used in addition to the primary, theoretical determination, but these methods typically produce different results and are therefore advisory only [19]. The eigenvalue is a measure of variance explained, and because of the way factors are extracted eigenvalues decrease with the number of factors extracted. The default setting in many statistical packages is to select the number of factors with eigenvalues greater than one (the Kaiser-Guttman rule) [21]. Because eigenvalues increase with the number of items analysed this method provides limited information and is widely held to be the least useful data driven method of advising on factor number [19,20]. However, the overall pattern of all eigenvalues is useful not only by providing data for another test of factor number (the scree test), but also providing information about the proportion of total variance explained by various numbers of factors. In the analysis carried out here, eigenvalues are used to estimate proportion of variance explained in order to characterise the relationship between the overall score, subscale scores and individual items.
Once the number of factors is set, principal axis extraction first identifies groups of items as factors, and then achieves a best fit of items to those factors by a process called rotation. The technique of rotation can be done either by forcing the factors to be uncorrelated (called orthogonal rotation, e.g., varimax) or allowing the factors to be correlated (called oblique rotation, e.g., promax), each type of orthogonal or oblique rotation having slightly different properties. Orthogonal rotation should be used only when uncorrelated factors are predicted on theoretical grounds or when there is evidence from an earlier oblique rotation that the factors are largely uncorrelated. Varimax (i.e., orthogonal) rotation became popular through its use in psychology where there was a theoretical requirement for personality factors to be uncorrelated [22], but this form of rotation is often used incorrectly in situations where factors may be correlated. In the present case, factors are predicted to be correlated as the three content derived domains of the SAQ all form part of the overall HRQoL. We used promax rotation.

EFA produces a factor matrix where each item of a questionnaire has a value, called a loading, on each of the factors. The item loadings vary between -1 and 1 and can be considered equivalent to correlations between the item and the artificial variable represented by the factor. We adopted the convention that items that load at or greater than 0.3 should be allocated to that factor [19,20]. Orthogonal rotations produce only one factor matrix whereas oblique (i.e., correlated) rotations produce two matrices of which the pattern matrix is commonly reported. The pattern matrix expresses the relationship between items and a factor after removing the effect of the correlations between the factors, and therefore provides a clearer picture of the separation of items between factors, should that be the case, compared to the alternative matrix, the structure matrix. However, in order to interpret the pattern matrix it is necessary to know the degree of correlation between the factors produced by the rotation. These factor correlations are reported separately from the pattern matrix, and are similar but not identical to subscale correlations because factor correlations are based on response to weighted items whereas subscales are based on unweighted items [19].

The solution provided by any EFA depends on the correlation matrix between the variables. Differences in that matrix resulting from low correlations and small sample sizes can produce large differences in solution, i.e., factor instability. The Kaiser-Meyer-Olkin measure of sampling adequacy provides a way of measuring the level of factor stability. The Kaiser-Meyer-Olkin varies between zero and one, values above 0.8 indicating that the factor solution is likely to be stable, and above 0.9 highly stable. However, if sample size allows, factor stability can be checked by separate analysis of subgroups. In the analysis conducted here, we examined factor solutions for males and females separately, a technique that also checks that males and females interpret every item in the same way.

The aim of an EFA, as a statistical tool, is to find a solution where there is a “good fit” to the data. Good fit is summarised as “item loadings above .30, no or few item crossloadings, no factors with fewer than three items” [20]. Validation of HRQoL subscales has an additional requirement, that the subscales so produced are both theoretically plausible in terms of content as well as clinically useful. An EFA solution producing 10 subscales may achieve good fit but is unlikely to have much clinical use. Cross-loading items (i.e., where the loading is > 0.3 on more than one factor) indicate either that response to the item is affected by more than one construct, or that the solution provides a poor fit for data. Either way, the presence of cross-loading items is undesirable and absence of all but a bare minimum of cross-loading items is a primary requirement for construct validation of subscales of a HRQoL questionnaire [20]. Validation requires a “clean” factor matrix, namely one where there is good separation between loadings for every item. An item that loads 0.32 on one factor and 0.25 on another is a poor item. Items with loadings of 0.32 and 0.01 and 0.25 and 0.60 are acceptable, but the goal is for the largest possible separation.

Although a HRQoL questionnaire may fail to provide validated subscales according to the criteria described above, the overall scale score will still be valid so long as all items load significantly on the first unrotated factor. This last requirement is easy to achieve as most items co-vary with severity. An HRQoL item must by definition be related to
health. Subscale construct validation is more demanding as it requires specificity of items to constructs, rather than specificity to severity.

Following EFA, subscales were constructed on the basis of the factor loadings by taking the mean of items loading on any factor. The relationship between the subscales and other variables was examined using Pearson correlations. EFA and correlations were conducted using SPSS version 25. Tests of difference between correlations were carried out using Psychometrica (https://www.psychometrica.de/correlation.html).

Results

The total sample size was 460 consisting of data from 160 participants who provided data for a previous validation study [8] and 300 participants who provided new data. Two hundred and ninety-nine (65%) of the participants were female. Further patient demographics are shown in table 1 and the mean questionnaire scores are shown in table 2.

The Kaiser-Meyer-Olkin measure of sampling adequacy was 0.96 for the total sample and was 0.94 for both the male and female subgroup analyses. For the total sample, the first five eigenvalues were 10.5, 1.1, 0.87, 0.64 and 0.45. All 16 items loaded > 0.64 on the first unrotated factor of a principal axis factor analysis. The first factor accounted for 66% of the variance, and the first three factors accounted for 78% of the variance. The remaining 22% of the variance represents variance unique to any of the 16 items. The pattern matrix is shown in Table 3. The factor correlations were: factors 1 and 2 $r = 0.72$, factors 1 and 3 $r = 0.74$, factors 2 and 3 $r = 0.73$.

Fifteen of the 16 items loaded on only one of the three factors with item grouping consistent with the content derived domains. Item 14 (night disturbance) loaded on two factors: factor 1 and factor 3. When EFA was repeated separately for males and females, then any item loading on a factor in the overall analysis was replicated in these sub-analyses, with one exception. For males item 14 loaded only on factor 1 (0.58) but not on factor 3 (0.24) or 2 (0.02), whereas for females item 14 loaded only on factor 3 (0.58) but not on factor 1 (0.24) or factor 2 (0.03). These results indicate that the cross-loading of item 14 in the total sample is due to males and females responding in different ways to that item, but that the underlying three factor solution is preserved.

Table 4 shows the correlations between clinically relevant variables and the three subscales created from the mean of items allocated to that subscale. Table 5 shows the correlations between all questionnaires. Together these two tables illustrate differences in correlations between subscales and theoretically relevant variables. Using tests of difference between correlations, the correlation between FEV$_1$ % predicted and My Life was significantly different ($p = 0.016$) from the correlations between FEV$_1$ % predicted and either My Mind or My Body. The correlation between Anxiety/depression and My Mind was significantly different ($p < 0.001$) from the correlations between Anxiety/depression and either My Life or My Body.

Discussion

According to current recommendations, measures of patient reported outcomes should be validated first by content validity and then by construct validity [1]. In the case of subscales it is possible to group items on the basis of content alone, and this is a feature of some of the earlier scales [2]. Construct validation provides an additional level of certainty by showing that there is a statistical basis for grouping items. In this study we used EFA to show that the 16 items of the SAQ fall into three groups, with all but one the items loading only on one factor, that one item (night disturbance) loading on two factors and therefore not performing according to prediction. On the basis of item content, of the single loading items, the groups of items are given the domain labels, My Life as the items refer to activities and other aspects of a person’s life, My Mind as the items refer to self-perceptions of mental state and My Body as the
items refer to the perceived impact of extra-pulmonary symptoms including side effects on the body. The relationship between items and subscales is shown in Figure 1.

The reason that the night disturbance item cross-loads on the My Life and My Body factors is because males and females interpret the question differently. For females, the night disturbance item loads only on the My Body factor, suggesting that females may report night disturbance predominantly in terms of bodily perceptions, for example, fatigue and appearance. By contrast, for males, the item night time disturbance loads only on the My Life factor indicating that for males, night disturbance may be preferentially interpreted in terms of limitation in daily activities. These results show the value of EFA in providing insight into the way people interpret items, and how that interpretation of the same item can be different for different groups of people. Although there is a trend for males to interpret the night disturbance item one way and females a different way, it is uncertain how night disturbance is interpreted by any particular patient, so the night disturbance item (item 14) is scored to contribute to both the My Life and My Body subscales, consistent with the data from the total sample.

Principal axis extraction provides information about the relationship between the overall score, subscales and individual items. Sixty six percent of the variance of the questionnaire is common variance between all 16 items. An additional 12% of variance is unique to and distributed between the three factors. The remaining 22% of variance is unexplained and is unique to and distributed between the 16 items (see Figure 1).

The factor structure obtained in this analysis can be compared to that obtained with the earlier three HRQOL scales for mild and moderate asthma that also used component or factor analysis. Although all three scales provide evidence of a distinction between activity restriction and emotional impact, the results are very different. Only one study that used oblique rotation achieved best fit producing five factors with minimal cross-loading items [6]. One using varimax rotation and produced a very poor fit of six factors with 28 out of 31 items cross-loading [4]. One reported “good separation” of three factors but without reporting any factor loadings [5] or any other data. One used the scree test to determine the number of factors but without presenting the eigenvalues on which the test is based [4], one reported eigenvalues and, after demonstrating that the scree test could not be used, used pragmatic examination to give five factors [6], and one used three factors on the basis of content alone [5]. The scree test requires inspection of the eigenvalues to determine the point at which eigenvalues reduce in a similar way – the analogy is with the scree at the bottom of a cliff. By definition all HRQoL items must correlate with health, and because of this items form a hierarchical structure where all items load on a first factor. In the present data, all items loaded > 0.6 on a first factor. The result is that in all HRQoL questionnaires the scree test is likely to indicate a one factor solution, and will do so long as the items are good measures of health. High loadings on a first principal axis factor are also a feature of some biomarkers because they also reflect an underlying dimension of health [23]. Although the scree test is recommended instead of the Kaiser-Guttman test [16] and is a useful statistical guide for factor number when factors are uncorrelated or weakly correlated, it cannot be used for determining the number of factors in the case of HRQoL questionnaires because of the hierarchical structure of the items. Nevertheless, whether or not a scree test is used, eigenvalues should always be reported, either to support the use of a scree test or to show that it can not be used. Eigenvalues provide information about the underlying structure of a set of items.

Despite evident weaknesses in EFA, the subscales of earlier asthma specific HRQoL questionnaires reflect a common distinction of activity versus emotions, a distinction consistent with the theory that HRQoL judgements are affected by both symptoms (affecting activities) and underlying personality (affecting mood) [24]. The activity versus emotion distinction is found both in subscales are based only on content [2,4] and those using statistical analysis [4-6]. In the case of severe asthma, however, there is an additional group of items relating to the impact of non-asthma symptoms. These symptoms arise partly due to the polysymptomatic nature of severe asthma [25] and partly due to side effects
caused by more aggressive treatment. The three factor solution provides subscales presented here are consistent with
guidelines that questionnaires and their subscales should be fit for purpose [1], something that is not achieved with five
or six factor solutions [4,5].

Although the subscale specific variance is relatively low (12% of the total variance), it differentiates between clinically
relevant variables. The My Life subscale is more strongly related to lung function as measured by FEV₁ % predicted
compared to the other two subscales, and the My Life subscale also has higher correlations with symptoms than the
other two subscales. It is possible that the My Life subscale is more sensitive to change in respiratory function in a
clinical trial as activity subscales have been shown to more sensitive to pharmaceutical interventions in two other
asthma specific HRQoL scales [6,26]. By contrast, the My Mind subscale is more strongly associated with participants’
response to a question on the severity of anxiety and depression compared to the other two subscales. This finding
would indicate that the My Mind subscale may be most sensitive to change for interventions that affect mood. Finally,
the content and statistical properties of the My Body subscale would indicate that this subscale may be most sensitive
to changes in drug treatments that alter side effects and the experience of extra-pulmonary symptoms.

Quality of life and health are concepts used in clinical practice and research, but they are also words that are used by
the general public in everyday speech. The SAQ asks people to evaluate the impact of asthma on ‘quality of life.’ The
EQ5D asks people to rate their ‘health.’ Examination of Table 5 shows that both types of global estimate correlate most
strongly with the My Life subscale compared to the other two subscales. When people are asked to make global
estimates of ‘quality of life’ or ‘health’ they interpret these words and judge them by preferentially using the activity
limitation construct as measured by the My Life subscale of the SAQ.

Although construct validity is an important part of subscale validation, the use of EFA for validating the overall score
should be treated with caution. Items should not be selected on the basis of high factor loadings on a first factor as so
doing can lead to overly restrictive set of items. Content validity through qualitative methods is an essential first step in
establishing the items of a scale, as recommended by current guidelines [1]. Construct validation of subscales is
carried out only after content validity is established. Although cross-loading items can be removed, such removal has
the potential to weaken the breadth of the questionnaire.

A limitation of this study is that data were collected from only English speaking participants and not from participants
responding to any of the validated translations of the SAQ. Those taking part were not randomly selected but selected
by virtue of being under the care of a specialist severe asthma service. Estimated cumulative OCS dose is an estimate
only. Additional longitudinal data collection is needed to establish the usefulness of subscales.

Conclusions

There are two conclusions to be drawn from this study, one respiratory and the other methodological. The respiratory
conclusion is that the SAQ has three subscales measuring three different constructs: impact on different life activities
(measured by the My Life subscale), self-perceived mood disturbance (measured by the Mind subscale) and the impact
of extra-pulmonary symptoms including side effects (measured by the My Body subscale). Each of these subscales
relate to clinically distinct clinical measures.

The methodological conclusion is that there are best practice guidelines for EFA that should be adopted in preference
to default values in statistical packages, and that construct validation of HRQoL questionnaire subscales requires
more than just running an EFA and reporting how items load on factors. Factor number should be determined on
theoretical (fit for purpose) not statistical grounds, and the factor loadings of construct validated subscales must
achieve best fit. Not all HRQoL questionnaires can have construct validated subscales.
Declarations

Ethics: Patients provided written informed consent. Ethical approval references are: 19/WA/0011, IRAS project ID: 250167 and 19/WA/0011, IRAS project ID: 250167

Consent for publication: All authors give consent for publication in Health and Quality of Life Outcomes

Availability of data: Full data set is available on request from the authors.

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**Tables**

Table 1 Participant Demographics

|                        | N  | Mean (CI)         | n (%)       |
|------------------------|----|-------------------|-------------|
| **Age, yrs.**          | 460| 51 (50 - 53)      |             |
| **Female, n**          | 460| 299 (65)          |             |
| **FEV<sub>1</sub>, L** | 457| 2.12 (2.05 – 2.20)|             |
| **FEV<sub>1</sub>, % predicted** | 454| 71.75 (69.79 – 73.71) |             |
| **Caucasian, n**       | 460| 416 (91)          |             |
| **BMI, kg/m<sup>2</sup>** | 459| 31.10 (30.39 – 31.81)|             |
| **Prescribed maintenance OCS, n** | 460| 218 (47)        |             |
| **Exacerbations in the last 12 months requiring OCS, n** | 460| 3.74 (3.35 – 4.12) |             |
| **Emergency Department visits** | 460| 0.91 (0.66 – 1.15) |             |
| **Hospital visits**    | 460| 0.64 (0.42 – 0.86) |             |
| **Cumulative prednisolone, mg/yr** | 460| 3148 (2814 - 3483) |             |
| **Receiving biologics, n** | 456| 180 (39)        |             |

Sample sizes vary as a function of data availability.
Table 2 Mean questionnaire scores (95% confidence intervals)

|                        | n  | Mean  |               |               |
|------------------------|----|-------|---------------|---------------|
| **SAQ score**          | 449| 3.99  | (3.84 – 4.14) |               |
| **SAQ My Life**        | 449| 4.16  | (3.99 – 4.32) |               |
| **SAQ My Mind**        | 449| 4.04  | (3.87 – 4.21) |               |
| **SAQ My Body**        | 449| 3.58  | (3.43 – 3.73) |               |
| **SAQ-global score**   | 452| 53.88 | (51.66 – 56.10)|               |
| **ACQ score**          | 258| 2.68  | (2.50 – 2.86) |               |
| **ACT total**          | 200| 14.32 | (13.49 – 15.14)|               |
| **EQ-5D-5L**           | 381| 0.69  | (0.67-0.72)   |               |
| **EQ-5D VAS**          | 383| 61.03 | (58.74 – 63.13)|               |
| **EQ-5D-5L item 5 – Anxiety/Depression** | 381| 2.12  | (2.06 – 2.89) |               |

Sample sizes vary as a function of data availability

Table 3. Factor loadings of the pattern matrix of a principal axis factor extraction.
|                          | Factor 1 | Factor 2 | Factor 3 |
|--------------------------|----------|----------|----------|
| My Life                  |          |          |          |
| 1. My social life        | 0.88     | -0.07    | 0.11     |
| 2. My personal life      | 0.82     | 0.10     | -0.07    |
| 3. My leisure activities | 0.83     | -0.11    | 0.18     |
| 4. My jobs around the house | 0.96    | -0.11    | 0.04     |
| 5. My work or education | 0.76     | 0.04     | 0.08     |
| 6. My family life - how it affects me | 0.86  | 0.17     | -0.13    |
| 7. My family life - how it affects others | 0.70 | 0.29     | -0.10    |
| Depression               | 0.06     | 0.88     | 0.02     |
| 9. Irritable             | 0.08     | 0.78     | 0.05     |
| 10. Anxiety in general   | -0.08    | 0.92     | 0.08     |
| 11. Worry that asthma may get worse | 0.17  | 0.41     | 0.27     |
| 12. Worry about long term side effects of medicines | 0.08 | 0.11     | 0.54     |
| 13. Getting tired        | 0.20     | 0.11     | 0.59     |
| 14. Problems at night    | 0.36     | 0.02     | 0.48     |
| 15. The way I look       | -0.08    | -0.01    | 0.89     |
| 16. Problems with food   | 0.02     | 0.14     | 0.66     |

Table 4. Correlations between different scores of the SAQ, EQ-5D-5L Index value and other variables.
|                        | FEV₁ % predicted | BMI   | Cumulative prednisolone, mg/yr | Exacerbations in the last 12 months requiring OCS | Hospital admissions in the last 12 months |
|------------------------|------------------|-------|-------------------------------|-----------------------------------------------|----------------------------------------|
| **SAQ score**          | 0.23**           | -0.28** | -0.34**                      | -0.37**                                      | -0.17**                                |
|                        | (443)            | (448)  | (449)                         | (449)                                        | (449)                                  |
| **SAQ My Life**        | 0.29**           | -0.29** | -0.35**                      | -0.37**                                      | -0.16**                                |
|                        | (443)            | (448)  | (449)                         | (449)                                        | (449)                                  |
| **SAQ My Mind**        | 0.15**           | -0.21** | -0.23**                      | -0.33**                                      | -0.16**                                |
|                        | (443)            | (448)  | (449)                         | (449)                                        | (449)                                  |
| **SAQ My Body**        | 0.15**           | -0.28** | -0.34**                      | -0.33**                                      | -0.13**                                |
|                        | (443)            | (448)  | (449)                         | (449)                                        | (449)                                  |
| **SAQ global score**   | 0.28**           | -0.25** | -0.37**                      | -0.36**                                      | -0.23**                                |
|                        | (446)            | (451)  | (452)                         | (452)                                        | (452)                                  |
| **EQ-5D-5L Index value** | 0.22**       | -0.36** | -0.31**                      | -0.25**                                      | -0.19**                                |
|                        | (375)            | (380)  | (381)                         | (381)                                        | (381)                                  |
| **EQ-5D VAS**          | 0.24**           | -0.24** | -0.34**                      | -0.36**                                      | -0.18**                                |
|                        | (377)            | (382)  | (383)                         | (383)                                        | (383)                                  |

*p<0.05, **p<0.01.

Table 5. Correlations (N¹) between study questionnaires
|                      | SAQ score | SAQ My Life | SAQ My Mind | SAQ My Body | SAQ global score | EQ-5D-5L Index value | EQ-5D-5L item 5 – Anxiety/Depression | EQ-5D VAS |
|----------------------|-----------|-------------|-------------|-------------|------------------|----------------------|--------------------------------------|----------|
| SAQ My Life          | 0.95**    |             |             |             |                  |                      |                                      |          |
|                      | (449)     |             |             |             |                  |                      |                                      |          |
| SAQ My Mind          | 0.90**    | 0.77**      |             |             |                  |                      |                                      |          |
|                      | (449)     | (449)       |             |             |                  |                      |                                      |          |
| SAQ My Body          | 0.91**    | 0.80**      | 0.77**      |             |                  |                      |                                      |          |
|                      | (449)     | (449)       | (449)       |             |                  |                      |                                      |          |
| SAQ global score     | 0.77**    | 0.79**      | 0.64**      | 0.66**      |                  |                      |                                      | (441)   |
|                      | (441)     | (441)       | (441)       | (441)       |                  |                      |                                      |          |
| EQ-5D-5L Index value | 0.72**    | 0.73**      | 0.64**      | 0.59**      | 0.66**           |                      |                                      | (374)   |
|                      | (374)     | (374)       | (374)       | (374)       | (376)            |                      |                                      |          |
| EQ-5D-5L item 5 –   | -0.64**   | -0.54**     | -0.73**     | -0.56**     | -0.50**          | -0.72**              |                                      | (376)   |
| Anxiety/Depression   | (376)     | (376)       | (376)       | (376)       | (378)            | (381)                |                                      |          |
| EQ-5D VAS            | 0.73**    | 0.74**      | 0.63**      | 0.62**      | 0.79**           | 0.72**               | -0.52**                             | (375)   |
|                      | (375)     | (375)       | (375)       | (375)       | (379)            | (379)                | (381)                               |          |
| ACQ score            | -0.75**   | -0.79**     | -0.62**     | -0.60**     | -0.77**          | -0.66**              | 0.48**                             | -0.73** |
|                      | (253)     | (253)       | (253)       | (253)       | (256)            | (240)                | (241)                               | (240)   |
| ACT total            | 0.71**    | 0.72**      | 0.62**      | 0.64**      | 0.68**           | 0.59**               | 0.50**                             | 0.63**  |
|                      | (195)     | (195)       | (195)       | (195)       | (194)            | (139)                | (140)                               | (141)   |

**p<0.01.

1N varies due to availability of data.

Figures
Overall HRQoL

66% of variance is common to all items

Subscales

12% of variance is specific to and shared between the three subscales

Items

22% of variance is unique to and shared between the 16 items

My social life
My personal life
My leisure activities
My jobs around the house
My work or education
My family life - how it affects me
My family life - how it affects others
Depression
Irritable
Anxiety in general
Worry that asthma may get worse
Worry about long term side effects of medicines
Getting tired
Problems at night
The way I look
Problems with food

Figure 1