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Estimating a preference-based single index from the Asthma Quality of Life Questionnaire (AQLQ)

Yaling Yang, Aki Tsuchiya, John E. Brazier, Tracey A. Young
HEDS, ScHARR University of Sheffield, S1 4DA

Corresponding author: Yaling Yang (cmp04yy@sheffield.ac.uk)

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Introduction

A cost-effectiveness study may employ Quality adjusted life years (QALYs) as the outcome measure to allow valid comparisons across different health interventions or different medical conditions. Generic preference-based measures, such as EQ-5D (Dolan et al, 1997), HUI3 (Feeny et al, 2002) and SF-6D (Brazier et al, 2002) have been increasingly used in clinical trials to obtain health state utility values for calculating QALYs. However, for some specific medical conditions, generic measures maybe considered inappropriate due to their lack of sensitivity. An alternative approach would be to directly obtain preference weights for a condition specific measure to ensure that the final health state utility values properly reflect the medical condition. Asthma could be such a medical condition.

The Asthma Quality of Life Questionnaire (AQLQ) has been designed to assess health related quality of life in patients with asthma (Juniper et al, 1993; also see Juniper et al, 1999). However, the AQLQ cannot be directly used in economic evaluation in its current form because it does not incorporate preference information. The aim of this study is to derive a preference-based single index from the AQLQ to calculate QALYs for use in economic evaluation.

To derive a preference-based single index measure from the AQLQ, we applied the hypothetical health state valuation method, which has been successfully used on the SF-36 by Brazier et al (2002) to generate the SF-6D. The first stage is to derive a reduced health state classification system from the AQLQ that is amenable to valuation exercises using a preference elicitation technique. The second stage is a valuation survey of a selection of states defined by this reduced classification system, by a sample of the UK general population. The third stage is to estimate a range of econometric models for predicting the health state values for all states defined by the new classification system, which in turn will enable the calculation of QALYs based on AQLQ data.

This paper concentrates on the valuation survey and the econometric modelling, which are based on the reduced classification system (reported in Young et al, 2005). The current paper also presents the results of applying the regression coefficients from the valuation study to actual AQLQ data to compare these with the EQ-5D indices, using a dataset where both AQLQ and EQ-5D were administered on the same patients at the same administration. The next section describes the AQLQ. This is followed by a brief description of the reduced classification system. Section 3 describes the methods involving in the valuation survey, modelling, and application of the results to real data. Section 4 presents the results of the study including the survey, the models and the application of the results to the trial data.

1. The AQLQ and the reduced classification system

The AQLQ consists of 32 items with 7 levels each, covering 4 domains: symptoms (12 items), activity limitations (11 items), emotional function (5 items) and environmental stimuli (4 items). Table 1 shows the 32 items in the AQLQ.

The original AQLQ is too large to be amenable to valuation. Therefore, based on Rasch analysis and a set of psychometric tests, the AQLQ has been reduced to a 5- dimension classification system which we callAQL-5D (see Table 2). The dimensions are: concern about asthma, short of breath, weather and pollution stimuli, sleep impact and activity limitations. These dimensions are selected directly from the original AQLQ. Each dimension has 5 levels of severity with level 1 denoting no problem and level 5 indicating extreme problem. All AQLQ health states can be mapped on to the newly defined AQL-5D.

2. Methods

2.1 Valuation survey

The aim of the valuation survey is to elicit preference values from the general public for a sample of health states defined by the AQL-5D. The key methodological issues are the selection of health state sample to be valued, sampling of respondents and overall size of the sample, the technique for eliciting preferences.

2.1.1 Selection of health states

The selection of health states was determined by the specification of the model to be estimated. In this study, 98 health states were selected out of the 3125 possible health states defined by the classification. The selection was on the basis of a balanced design, which ensured that any dimension-level (level λ of dimension δ) had an equal chance of being combined with all levels of the other dimensions. These states chosen were stratified into severity groups based on their total level score across the dimensions, and then randomly allocated into 14 blocks, so that each block has 7 health states. This procedure ensured that each respondent, who were allocated one of the 14 blocks, received a set of states balanced in terms of severity and that each state is valued the same number of times apart from the worst possible state, or the ‘pits’ state which is valued by all respondents.

2.1.2. Respondents and the presentation of information on asthma

An important methodological issue is whether to sample a group of patients or use a sample of the general population (Drummond et al, 1997). Past studies have used samples drawn from both constituencies. However, health policy bodies such as NICE have recommended using general public values. It was decided to elicit the preference values of general public although this instrument is a condition specific questionnaire. Given that it might be a problem for members of the general public to imagine what it is like to live with asthma, two different ways in which to present information on asthma were piloted. One was based on around 180 words of textual information (taken from the British Thoracic Society website), and the other was based on two brief video clips (provided by Asthma UK, and Wellington Asthma Research) showing the mechanism of asthma and patients with asthma symptoms. Piloting established that the textual information and the video clips lead to no difference in valuation results, and thus the less resource intensive, textual information was used for the main survey (See Appendix 1).

The respondents are members of the general population randomly selected using the electoral register of names and address from within South Yorkshire, UK. Based on previous experience, we decided to interview a sample of 300 participants providing valuations for 98 health states, which were deemed sufficient to estimate a reliable additive model.

2.1.3 Preference elicitation task

The time trade off (TTO) technique was chosen for eliciting preference values, which asks respondents to trade off between length of life and quality of life. This survey used the TTO-prop method developed by the York Measurement and Valuation Health Group, which uses a 'time board' as a visual aid (Gudex, 994). This version was selected because it has been showed to be reliable (Dolan et al, 1996).

2.1.4 Interviews

Trained interviewers visited and interviewed respondents at their home during April, 2005. The interviews consisted of five stages:

1. Self-reported health in EQ-5D.
2. Part A: self-reported health in AQL-5D for those respondents who replied they have asthma;

Part B: fill in the AQL-5D, imagining that they had asthma, for those respondents who replied they do not have asthma

3. Ranking task of 7 intermediate AQLQ health states, full health (AQL-5D health state 11111), worst health state defined by the AQL-5D ('pits' state 55555) and immediate death.
4. TTO valuation of the 7 intermediate AQL-5D health states and 'pits'. The upper anchor of the TTO exercise is 11111.
5. Questions on respondent background characteristics

2.2 Modelling health state values

The overall aim is to construct a model for predicting health state valuations based on the reduced AQLQ health state classification, or the AQL-5D. The data are skewed and are likely to be clustered by respondent. Respondents did not value the same set of states. Although allocation of states to respondents was essentially random, differences between health state values may be partly due to differences in the preferences of the respondents, rather than the attributes of those states.

A number of alternative models were explored for predicting the TTO scores generated in the valuation survey (take from Brazier et al, 2002). The general model is:

$$y_{ij} = g(b'\mathbf{x}_{ij} + q'\mathbf{r}_{ij} + d'\mathbf{z}_j) + e_{ij} \qquad (1)$$

where i = 1, 2, …, n represents individual health state values and j = 1,2, …, m represents respondents. The dependent variable, y_{ij}, is the TTO score for health state i valued by respondent j. x is a vector of binary dummy variables ($x_{\delta\lambda}$) for each level δ of dimension λ of the classification. Level λ = 1 acts as the baseline for each dimension.

The r term is a vector of terms to account for interactions between the levels of different attributes. z is a vector of personal characteristics, which is only examined in terms of respondents' asthma condition in this paper. g is a function specifying the appropriate functional form. ε_{ij} is an error term whose autocorrelation structure and distributional properties depend on the assumptions underlying the particular model used.

The starting point is an OLS estimation of model (1), with g as a linear function. An improved specification, which takes account of variation both within and between respondents, is the one-way error components random effects model. Estimation is via generalized least squares (GLS) or maximum likelihood estimation (MLE).

There is evidence that preferences for different dimensions of health may not be additive. Therefore it is important to try to estimate interactions. Adapting the approach used in other studies (Brazier et al, 2002), interaction variable C3_2 was created as a dummy variable which takes a value of 1 if two or more dimensions in the health state are at level 4 or 5, and 0 otherwise.

To avoid negative values, all models were estimated using a dependent variable defined as 1-TTO. Given 1 denoting full health, this variable dis_TTO indicates the extent to which a given health state moves away from full health. Thus, the severer the health state is, the greater the coefficient should be, and the expected signs of the dummy coefficients should be positive.

Given the fact that we used AQL-5D full health 11111 as our upper anchor for TTO, the choice of the best model should be between models without a constant term. This is due to the fact that we do not have AQL-5D 11111 valued against some generic full health such as “no health problems at all”. If AQL-5D 11111 had been valued against generic full health, then AQL-5D 11111 can be represented by the intercept term and the best model can be selected using the with-constant model. Thus the choice of the best model is based on theoretical concerns, rather than the empirical performance though other performance criteria are helpful. For instance, models were compared in terms of their overall diagnosis by R squared, goodness of fit, likelihood ratio, the size and significance of individual parameter estimates, as well as their predictive ability by mean absolute errors (MAE) and the numbers of errors greater than 0.05 and 0.10 in absolute value.

All modelling was carried out using STATA 9.0 and SPSS for Windows 12.0.

2.3 Applying the regression results in real data

Based on the best regression model identified, the regression coefficients were applied to actual AQLQ data and the AQL-5D utility values were obtained. Then, the asthma specific AQL-5D utility values were compared with the generic EQ-5D utility values where the two instruments were administered alongside each other.

2.3.1. The AQLQ data.

The AQLQ data used in the application section came from a random controlled trial which examined the effectiveness of computerized decision support in primary care, covering a wide range of patients with asthma. A sample of 3000 patients was identified with general practice morbidity and prescribing registers. Among other information, EQ-5D, AQLQ, SF-36 and Newcastle Asthma Symptom Questionnaire were administered in the trial using postal questionnaires, which make the comparison between EQ-5D and AOL-5D possible.

2.3.2. The statistical analysis.

Descriptive statistics for the EQ-5D and AQL-5D utility values were computed using mean, standard deviation (SD), median, minimum, maximum, range and inter-quartile range. The paired t-test was used to examine the within-subject difference in mean utility scores. The two utility scores were presented graphically using a scatter plot. Given the assumption that the EQ-5D and AQL-5D are measuring the same thing on the same scale, we also computed the intraclass correlation coefficient using one way random effects models. The relationship between EQ-5D and AQL-5D utility values was also tested using Pearson's product moment correlation coefficient and bivariate linear regression estimated by Ordinary Least Square (OLS).

In order to examine the discriminative ability of the EQ-5D and AQL-5D to detect difference in external indicators of health status, patients were divided into 5 groups according to self-reported SF-36 general health question with response categories "excellent", "very good", "good", "fair", and "poor". Given the SF-36 is a generic instrument, patients were also divided into quintiles of the Newcastle Asthma Symptom Score which ranges from 0 for best and 100 for worst asthma symptoms. After the grouping, ANOVA was carried out using the F test to check for differences in means between groups and to test for linear trend. Effect sizes of mean utility values of EQ-5D

and AQL-5D between groups according to both SF-36 and the Newcastle Asthma Symptom Score groups were calculated and compared using Cohen's definition and Rosnow, R. L and Rosenthal's adjusted formula. (Cohen, J 1988; Rosnow, R. L et al, 1996).

3. Results

3.1 Valuation survey

3.1.1 Respondents

A sample of 307 members of the public (response rate 40%) in South Yorkshire was interviewed. They were all included in the final dataset for analysis. The description of the sample is shown in table 3. Among the respondents, more than half are female, between 36 to 65 years old, married or living with partner, and experienced serious illness in their family. In this sample, 53 (17.3%) have asthma, 22.5% respondents have a degree or equivalent, and 45.6% respondents receive full-time education after 17. The self-reported EQ-5D health states of the respondents are also shown in table 3.

3.1.2 Health state values

In all there were 2455 health state valuations generated by the respondents. Average number of valuations per intermediate health state was 22 (range from 19 to 22) where as the 'pits' state (AQL-5D state 55555) was valued 307 times, by every respondent. The mean health state values ranged from 0.39 to 0.94 and generally have fairly large standard deviations (around 0.2 to 0.4). The distribution of the values was negatively skewed. Table 4 presents health valuation values in blocks 1 to 7 as examples (results of remaining states are available from the corresponding author on request).

3.2 Modelling

The results of modelling are presented in table 5, with summary statistics for internal sample predictions presented in the lower half of the table. Except model (6) with the interaction variable C3_2, all models were estimated on the basis of the main effects dummies; and except mean models (3) and (7), models were estimated in individual level.

For theoretical reason, 'the best model' should be chosen between models that exclude the constant term, which are model (5) (6) and (7). Among them, model (5) and (6) are slightly better in terms of inconsistency and significance of the coefficients but in turn, model (7) is slightly better on prediction. After trading off between the different patterns, model (5) has been chosen as the best model and be applied it in the patient AQLQ data.

Introducing an additional dummy variable of 'do you have asthma' with 1 denoting 'yes' and 0 'no', we rerun 'the best model' (5). The coefficients stayed almost unchanged compared to the original one, with the coefficient of the 'do you have asthma' dummy as 0.010 ($p = 0.776$).

3.3 Applying to patient data and comparing with EQ-5D

The overall aim of the application of the AQL-5D to patient data is to compare the utility values based on AQL-5D with those derived from EQ-5D. Table 6 presents descriptive statistics of AQL-5D and EQ-5D utility values. It can be seen that the EQ-5D has a larger range than the AQL-5D, with minimum value -0.32 compared to 0.46, and their maximum values are the same. The inter-quartile range also showed a similar pattern. AQL-5D has twice as many missing values compared to EQ-5D. Mean utility value of the AQL-5D is 0.82 with a standard deviation of 0.13, and for the EQ-5D, mean value is 0.73 with higher standard deviation 0.27. There is not much difference between medians. The result of paired t-test suggests statistically significant difference between AQL-5D and EQ-5D mean values.

Figure 1 is a plot of AQL-5D to EQ-5D values. It shows a fair to weak linear relationship between the two values. The trend line can be drawn with an intercept at 0. 63, a regression coefficient 0.261, and R-square 0.318, which is far from the 45º line denoting perfect correlation. Between the utility values of AQL-5D and EQ-5D, the Pearson correlation coefficient is 0.564 and significant at the 0.01 level. The intraclass correlation coefficient is 0.376 and though significant at the 0.01 level this is regarded as poor level of agreement.

Table7 compares mean utility values of AQL-5D and EQ-5D according to the general health question of the SF-36, and the Newcastle Asthma Symptom scores. For the SF-36 response categories, the EQ-5D mean values range from 0.93 to 0.305, and the AQL-5D from 0.927 to

0.645. The mean AQL-5D values show consistently smaller standard deviations compared to EQ-5D. Both mean values show a decreasing trend following the decline of general health. The EQ-5D mean values have a big jump from the "good" group to the "poor" group, especially between the "fair" to the "poor" group while the AQL-5D values decline more smoothly. One-way ANOVA tests indicate statistically significant differences in mean values and a linear trend between SF-36 groups in both instruments. In general, the effect sizes of mean EQ-5D and AQL-5D utility values are similar which would suggest similar ability of the two measures to detect differences between the SF-36 general health groups.

For the Newcastle Symptom Scores, observations are broken up into quintile groups, with cut off values at 17, 28, 42, and 61. Again, the EQ-5D mean values have a larger range than the AQL-5D values, with consistently greater standard deviations. One-way ANOVA also tests significant difference and linear trend between groups in both instruments. In terms of effect size, the effects sizes based on EQ-5D range from 0.251 to0.641 with AQL-5D range from 0.551 to 1.253. Furthermore, the effect sizes of AQL-5D are consistently larger than those of EQ-5D in all Newcastle Asthma Symptom Score based groups, which implied better detection ability of AQL-5D between groups than EQ-5D.

4. Discussion and conclusion

This paper has presented a study to estimate a preference-based single index from a condition specific quality of life instrument, using the AQLQ. An approach used in the development of SF-6D was also used in the current study. This paper is very much work in progress and so the discussion is incomplete, but the following emerge as important issues to discuss at HESG (though we welcome any others that HESG/CES members choose to raise).

Since the preference indices for a specific medical condition was valued by members of the general public, one concern is the extent to which the majority of respondents who have no direct experience of asthma managed to understand and/or imagine what it is like to live with asthma. Asthma related information was provided to respondents in the form of brief verbal text, after it was established through piloting that this resulted in similar values to showing short video clips. The additional regression analysis using a variable to represent whether or not the respondent has

asthma resulted in its coefficient being non-significant (with no effect on the values of the other coefficients). This is encouraging since it suggests that there was no statistically significant difference between the way respondents with and without asthma perceived the hypothetical asthma states.

Another concern is the choice of condition specific full health (AQL-5D state 11111) as opposed to generic "full health" as the upper anchor for TTO valuation. Given that it is quite possible to conceive of health states that involve no respiratory problems (and hence correspond to AQL-5D 11111), and yet involve other health problems (e.g. pain), an alternative design would be to use a generic description such as "no health problems" as the upper TTO anchor and to directly evaluate AQL-5D 11111 against this and death. The difficulty with this is that since the other dimensions of health are not explicitly mentioned, it could be confusing to respondents. Related is the issue of other domains of health. In contrast to generic instruments, AQL-5D is focused on asthma. We do not know what respondents were thinking during the interview: did they only think of the condition as described by AQL-5D, or did they extend their imagination to other aspects of health not included by in the descriptive system, such as depression or pain. Even if respondents made references to other domains of health, if these were constant across all the health states valued (e g. Moderate pain and moderately depressed, regardless of the asthma state) or completely at random, then it will be minor issue. However, if the levels given to these other domains of health were related to the main asthma specific domains of health (e g. no pain and not depressed for the mild asthma states, but severe pain and very depressed for the severe asthma states), then this would clearly introduce bias to the modelling results.

The selection of the health state sample for valuation and modelling is another issue. The selection was based on balanced design regardless of the prevalence of health state in population, which may cause difficulty for respondents to imagine those health states happened rarely in real life.

And, finally, the sample size of 300 might be thought to be small compared the original EQ-5D valuation survey with a sample of 3000, given the AQL-5D descriptive system defines 13 times more health states than the EQ-5D. Since different regression methods were used, a direct

comparison of the best models of these two studies is not straightforward. However, in terms of MAE, the results are both around 0.5. Certainly, we suspect that perhaps a larger model could have been estimated with more resources.

There are two observations to make on the results, both regarding the application exercise. Firstly, the main differences between AQL-5D and EQ-5D utility scores are quite modest at the upper end of the scales and this is reflected in smaller differences between median scores, but as we move down the scale the differences become larger as the EQ-5D continues to generate values below 0.4. This may suggest that the EQ-5D is reflecting co-morbidities in the population which we have mentioned earlier. On the other hand, it has been known that the EQ-5D values generated by the MVH study tends to have very low utility scores for the severe states, and the pattern observed here may be partly explained by study-specific variation.

Secondly, at the beginning of this study, it was expected that a condition specific measure will be more sensitive. The results are consistent with this as the relative sensitivity of the AQL-5D as measured by the effect size has proven to be better than the EQ-5D. Further work is needed to compare the responsiveness of the two instruments in data across multiple time points. However, it is important to note that the standard deviations of AQL-5D scores are consistently smaller than the corresponding EQ-5D scores across all groups, with implications for sample size calculation and study design. So for example, based on the observed standard deviations, in order to establish a difference in health benefit of 0.1 (with a p value of 0.05 and power of 0.9), a study using EQ-5D needs 154 patients in the treatment and placebo arms, whereas a study using AQL-5D needs 36 in each arm.

Overall, this paper is one of the first to generate a condition specific preference based measure. While the exercise has provided to be a technical success, it does raise some interesting issues for discussion about the nature of condition specific measures compared to generic measures.

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Table 1: Standardized AQLQ items (taken from Juniper, 1993)

Item No.	Question (during the last 2 weeks) as a result of your asthma	Domain	Wording
1	Limited strenuous activities	Activity	Limitations
2	Limited moderate activities	Activity	Limitations
3	Limited social activities	Activity	Limitations
4	Limited work-related activities	Activity	Limitations
5	Limited sleeping	Activity	Limitations
6	How much discomfort or distress as a result of chest tightness	Symptoms	Quantity
7	Feel concerned about having asthma	Emotional	Time
8	Feel short of breath as a result of your asthma	Symptoms	Time
9	Experience asthma symptoms as a result of being exposed to cigarette smoke	Environment	Time
10	Experience a wheeze in your chest	Symptoms	Time
11	Feel you had to avoid a situation or environment because of cigarette smoke	Activity	Time
12	How much discomfort or distress have you felt as a result of coughing	Symptoms	Quantity
13	Feel frustrated as a result of your asthma	Emotional	Time
14	Experience a feeling of chest heaviness	Symptoms	Time
15	Feel concerned about the need to use medication for your asthma	Emotional	Time
16	Feel the need to clear your throat	Symptoms	Time
17	Experience asthma symptoms as a result of being exposed to dust	Environment	Time
18	Experience difficulty breathing out as a result of your asthma	Symptoms	Time
19	Feel you had to avoid a situation or environment because of dust	Activity	Time
20	Wake up in the morning with asthma symptoms	Symptoms	Time
21	Feel afraid of not having your asthma medication available	Emotional	Time
22	Feel bothered by heavy breathing	Symptoms	Time
23	Experience asthma symptoms as a result of the weather or air pollution outside	Environment	Time
24	Were you woken at night by your asthma	Symptoms	Time
25	Avoid or limit going outside because of the weather or air pollution	Activity	Time
26	Experience asthma symptoms as a result of being exposed to strong smells or perfume	Environment	Time
27	Feel afraid of getting out of breath	Emotional	Time
28	Feel you had to avoid a situation of environment because of strong smells or perfume	Activity	Time
29	Has your asthma interfered with a good night's sleep	Symptoms	Time
30	Have a feeling of fighting for air	Symptoms	Time
31	How much has your range of activities you would like to have done been limited by your asthma	Activity	Limitations
32	Among all the activities you have done how limited have you been by your asthma	Activity	Limitations

Table 2 the reduced asthma quality of life classification (AQL-5D)

CONCERN

5. Feel concerned about having asthma all of the time.
4. Feel concerned about having asthma most of the time.
3. Feel concerned about having asthma some of the time.
2. Feel concerned about having asthma a little or hardly any of the time.
1. Feel concerned about having asthma none of the time.

SHORT OF BREATH

5. Feel short of breath as a result of asthma all of the time.
4. Feel short of breath as a result of asthma most of the time.
3. Feel short of breath as a result of asthma some of the time.
2. Feel short of breath as a result of asthma a little or hardly any of the time.
1. Feel short of breath as a result of asthma none of the time.

WEATHER & POLLUTION

5. Experience asthma symptoms as a result of air pollution all of the time.
4. Experience asthma symptoms as a result of air pollution most of the time.
3. Experience asthma symptoms as a result of air pollution some of the time.
2. Experience asthma symptoms as a result of air pollution a little or hardly any of the time.
1. Experience asthma symptoms as a result of air pollution none of the time.

SLEEP

5. Asthma interferes with getting a good night's sleep all of the time.
4. Asthma interferes with getting a good night's sleep most of the time.
3. Asthma interferes with getting a good night's sleep some of the time.
2. Asthma interferes with getting a good night's sleep a little or hardly any of the time.
1. Asthma interferes with getting a good night's sleep none of the time.

ACTIVITIES

5. Overall, totally limited with all the activities done.
4. Overall, extremely or very limited with all the activities done.
3. Overall, moderate or some limitation with all the activities done.
2. Overall, a little limitation with all the activities done.
1. Overall, not at all limited with all the activities done.

Table 3 Characteristics of respondents in evaluation survey (N=307)

	Count	Percentage	
Age			
< 35	91	29.7	
36 - 65	156	50.9	
>66	60	19.5	
Female	168	54.7	
Have asthma	53	17.3	
Married or living with partner	214	69.8	
Experienced serious illness:			
in family	194	63.4	
themselves	94	30.6	
Degree or equivalent	69	22.5	
Education after 17	140	45.6	
Renting property	64	20.8	
Found valuation task difficult:			
very difficult	24	7.9	
quite difficult	82	26.7	
Neither difficult nor easy	52	16.9	
Self-reported EQ-5D health state	No problem (%)	Moderate problem (%)	Extreme problem (%)
Mobility	225(73.8)	78(25.6)	2(0.7)
Self-care	281(92.7)	21(6.9)	1(0.3)
Usual activities	241(78.8)	56(18.3)	9(2.9)
Pain/discomfort	203(66.3)	85(27.8)	18(5.9)
Anxiety/depression	250(82.2)	50(16.4)	4(1.3)

Table 4 Descriptive statistics for AQL-5D health state values (blocks 1 to 7)

health state	N	Minimum	Maximum	Mean	Median	Std. Deviation
12144	25	0.03	1.00	0.70	0.78	0.29
12314	21	-0.08	1.00	0.80	0.85	0.26
13251	23	-0.38	1.00	0.80	0.99	0.36
14225	25	0.00	1.00	0.76	0.83	0.25
15131	19	0.38	1.00	0.79	0.83	0.22
15251	23	0.00	1.00	0.78	0.88	0.26
15311	21	0.38	1.00	0.79	0.93	0.24
15355	23	-0.95	1.00	0.62	0.83	0.48
21223	25	0.00	1.00	0.82	0.93	0.26
23235	23	0.38	1.00	0.73	0.75	0.21
24133	21	-0.78	1.00	0.63	0.63	0.40
24422	19	0.00	1.00	0.66	0.75	0.30
25112	23	0.00	1.00	0.73	0.73	0.24
25313	21	0.38	1.00	0.79	0.83	0.21
25425	23	-0.98	1.00	0.57	0.55	0.49
31155	19	-0.30	1.00	0.61	0.68	0.38
31531	19	0.00	1.00	0.73	0.93	0.33
32235	21	0.38	1.00	0.73	0.80	0.23
32435	19	-0.38	1.00	0.63	0.73	0.38
33132	23	0.00	1.00	0.80	0.93	0.27
34254	21	-0.50	1.00	0.47	0.50	0.43
34351	21	-0.48	1.00	0.70	0.78	0.34
34554	19	-0.45	1.00	0.50	0.53	0.41
35422	25	0.33	1.00	0.76	0.88	0.23
41211	23	0.50	1.00	0.85	1.00	0.20
41322	21	0.40	1.00	0.86	0.93	0.19
41442	23	0.00	1.00	0.79	0.95	0.29
42214	21	0.00	1.00	0.72	0.80	0.28
42234	2	0.57	0.63	0.60	0.60	0.04
42245	21	-0.28	1.00	0.66	0.80	0.35
42325	21	0.30	1.00	0.80	0.83	0.22
42542	19	0.00	1.00	0.69	0.78	0.30
43234	23	0.08	1.00	0.71	0.78	0.27
45532	21	-0.73	1.00	0.64	0.88	0.52
45553	25	-0.95	1.00	0.59	0.73	0.50
51214	21	-0.38	1.00	0.68	0.83	0.39
51451	23	-0.70	1.00	0.78	0.93	0.38
51454	23	-0.38	1.00	0.58	0.70	0.39
51522	25	0.18	1.00	0.82	0.93	0.25
53532	25	-0.95	1.00	0.71	0.80	0.43
54123	21	-0.48	1.00	0.73	0.88	0.33
54245	21	-0.23	1.00	0.69	0.80	0.32
54333	23	0.38	1.00	0.72	0.78	0.22
55555	132	-0.98	1.00	0.43	0.50	0.45

Table 5 Estimated models

	With constant				No constant		
	OLS(1)	RE (2)	Mean (3)	FE (4)	RE(5)	RE with C3_2 (6)	Mean (7)
Constant	**0.095**	**0.080**	**0.098**	0.076	N/A	N/A	N/A
Concern2	0.024	0.032	0.023	**0.034**	**0.047**	0.046	0.044
Concern3	0.038	**0.048**	0.039	**0.051**	**0.064**	**0.066**	**0.064**
Concern4	0.047	**0.053**	**0.049**	**0.055**	**0.074**	**0.072**	**0.078**
Concern5	**0.066**	**0.078**	0.054	0.080	**0.095**	**0.085**	**0.080**
Breath2	-0.007	0.004	-0.003	0.008	0.024	0.025	0.020
Breath3	0.014	0.028	0.011	0.032	**0.045**	**0.046**	0.036
Breath4	**0.087**	**0.092**	**0.089**	**0.094**	**0.107**	**0.105**	**0.108**
Breath5	**0.086**	**0.097**	**0.077**	**0.101**	**0.116**	**0.109**	**0.103**
Weather2	-0.018	-0.001	-0.010	0.003	0.017	0.019	0.014
Weather3	-0.021	0.007	-0.022	0.016	0.028	0.028	0.008
Weather4	0.035	**0.049**	0.037	**0.053**	**0.063**	**0.060**	**0.063**
Weather5	**0.077**	**0.088**	**0.070**	**0.091**	**0.099**	**0.090**	**0.090**
Sleep2	0.035	-0.000	0.045	-0.011	0.013	0.016	**0.064**
Sleep3	0.054	0.012	**0.062**	0.001	0.029	0.031	**0.084**
Sleep4	**0.057**	**0.040**	**0.059**	0.034	**0.054**	**0.052**	**0.082**
Sleep5	**0.087**	**0.056**	**0.082**	**0.047**	**0.069**	**0.061**	**0.103**
Activity2	-0.014	0.013	-0.015	0.019	0.029	0.029	0.006
Activity3	0.017	0.025	0.014	0.027	**0.044**	**0.046**	**0.041**
Activity4	**0.122**	**0.122**	**0.124**	**0.122**	**0.139**	**0.136**	**0.147**
Activity5	**0.140**	**0.156**	**0.122**	**0.160**	**0.164**	**0.149**	**0.138**
C3_2	N/A	N/A	N/A	N/A	N/A	0.011	N/A
N	2455	2455	100	2455	2455	2455	100
Adj R^2	0.114	N/A	0.632	0.1167	N/A	N/A	0.948
Likelihood	N/A	-452.71	N/A	N/A	-456.50	-455.82	M/A
inconsistencies	6	2	8	1	0	0	4
significant	8	12	10	10	14	13	14
MAE	0.044	0.047	0.043	0.049	0.051	0.051	0.047
No>|0.05|	37	14	33	35	44	44	40
No>|0.10|	14	5	8	12	17	17	10
T(mean=0)	-0.098	0.010	***	0.006	**2.467**	**12.085**	***

Note: Independent variable: dis_TTO = 1 – TTO

Estimates showed in bold are significant at the 0.05 level

***: mean error is zero by definition

Table 6 Descriptive statistics of EQ-5D and AQL-5D utility scores in real data

		eq5d values	Aql-5d values
N	Valid	2953	2847
	Missing	106	212
Mean (SD)		0.73(0.27)	0.82(0.13)
Median		0.80	0.84
Inter-quartile range		(0.66, 1.00)	(0.75, 0.84)
Minimum		-0.32	0.46
Maximum		1.00	1.00
Range		1.32	0.54
Mean difference (95% CI)		0.084(0.075, 0.092)*	

CI: confidence interval * : $p < 0.001$

Figure 1 Scatter plots of EQ-5D and AQL-5D utility values

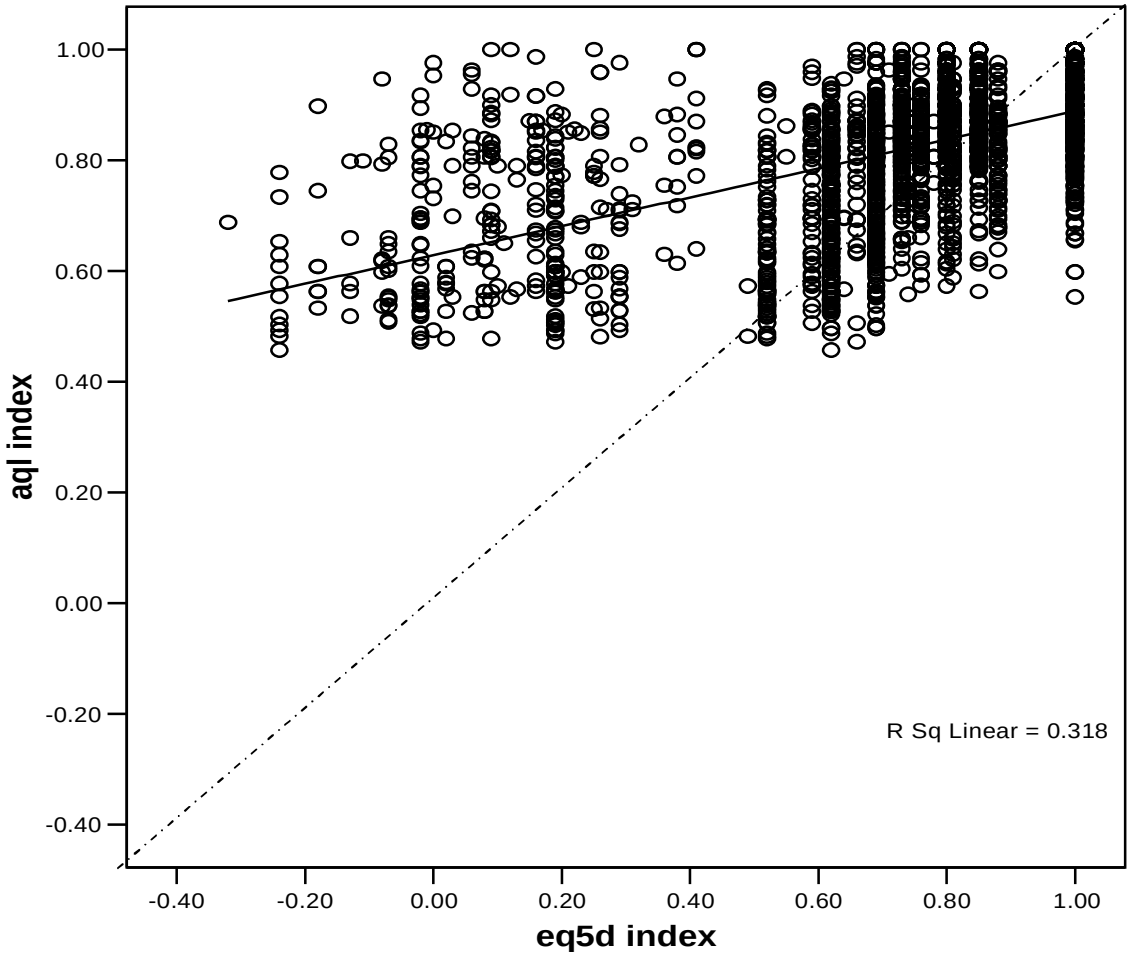

Table7 Mean (SD) utility values according to tSF-36 general health question, and the Newcastle Symptom Score

		EQ-5D			AQL-5D	
SF-36 general health question	N	Mean (SD)	ES	N	Mean(SD)	ES
Excellent	97	0.930(0.125)		92	0.927(0.079)	
Very good	571	0.900(0.149)	0.218	568	0.898(0.084)	0.356
Good	1141	0.812(0.182)	0.529	1111	0.851(0.095)	0.524
Fair	828	0.627(0.257)	0.831	793	0.765(0.117)	0.807
Poor	263	0.305(0.314)	1.122	254	0.645(0.118)	1.021
ANOVA between groups		F=368.8 (p<0.001) *			F=434.8 (P<0.001)*	
Newcastle Asthma Symptom Score	N	Mean (SD)	ES	N	Mean (SD)	ES
<17	669	0.883(0.176)		641	0.935(0.060)	
17-	548	0.821(0.193)	0.336	534	0.874(0.065)	0.975
28-	612	0.768(0.228)	0.251	593	0.831(0.082)	0.581
42-	503	0.682(0.256)	0.355	483	0.783(0.092)	0.551
61-	576	0.498(0.315)	0.641	555	0.658(0.107)	1.253
ANOVA between groups		F=266.3(p<0.001)*			F=914.5 (p<0.001)*	

ES: effect size = (mean1- mean2) / $\sqrt{(SD1^2 + SD2^2)}$

*: p<0.05 in ANOVA F test for linear trend

Appendix 1: the information on asthma shown to respondents

What is asthma?

Asthma is a condition that affects the airways - the small tubes that carry air in and out of the lungs. If you have asthma your airways are almost always sensitive and inflamed.

When you come in to contact with something you are allergic to, or something that irritates your airways (a trigger), you airways will become narrower, making it harder to breathe. The muscles around the walls of your airways tighten. The lining of the airways becomes inflamed and starts to swell and often sticky mucus or phlegm is produced. This will lead to you experiencing asthma symptoms.

Asthma symptoms can vary. You may find that you start to cough or wheeze, get short of breath, or have a tight feeling in your chest. Despite what many people think, wheezing does not always occur. In fact, coughing is the most common asthma symptom.

Asthma can start at any age. Some people get symptoms during childhood which then disappear in later life. Others develop 'late-onset' asthma in adulthood, without ever having had symptoms as a child.

Taken from the British Thoracic Society (BTS) website