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A review of studies mapping (or cross walking) non-preference based measures of health to generic preference-based measures — Source link [2]

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A review of studies mapping (or cross walking) from non-preference based measures of health to generic preference-based measures

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INTRODUCTION

A common approach to assessing the outcomes of health care is to obtain patient reported descriptions of health status across various dimensions and then to apply a standardised numerical scoring system. There are many different measures of health, including several hundred condition specific measures of health designed for use in specific medical conditions or groups of condition (Spilker et al, 1990), and a number of generic measures designed to cover the core dimensions of health that are relevant across all medical conditions. Health measures can also be distinguished in terms of whether they generate a profile of dimension scores or a single index and if they produce a single index, whether or not the index has been derived using simple summation of item scores or by using preference weights obtained from patients or the general public (known as preference-based measures or multi-attribute utility scales).

Patient reported measures of health have become widely used in clinical trials as primary or secondary outcomes. There is little agreement on which specific instruments should be used for this purpose. For assessing clinical efficacy, there is disagreement on whether to use a generic or condition specific measure, and between condition specific measures there is often disagreement amongst clinical researchers on the most appropriate instrument. As a result clinical trials around the world often use different measures for the same patient groups. This presents a substantial barrier to the synthesis of evidence.

Preference-based measures of health are necessary to generate the health state utility values required to calculate QALYs for assessing the cost effectiveness of interventions. These are usually based on generic instruments (e.g. EQ-5D) that permit comparisons between patient groups, though there are examples of condition specific preference-based measures (Revicki et al 1998). Even for assessing clinical effectiveness, it could be argued that a preference-based index is necessary to deal with trade-offs made between outcomes. There has been a debate amongst health economists about the most appropriate preference-based generic measure to use in cost effectiveness analyses. Whilst the EQ-5D is the most widely applied in recent years (Brooks et al, 1996), the HUI3 (Feeny et al,

2002), QWB (Kaplan and Andersen, 1988), SF-6D (Brazier et al, 2002) and others continue to be used. However, different preference-based measures have been shown to generate different values on the same sample of patients (Marra et al, 2005; Feeny et al, 2004; Barton et al, 2004). Furthermore, many key clinical trials on the efficacy of new interventions do not have a generic measure and the recent FDA Guidance on using Patient Reported Outcome measures seems to further discourage the use of generic measures for pivotal trials designed for seeking licensing approval (FDA, 2006). This presents a barrier to populating economic models with the best evidence on effectiveness.

One solution to the problem of having different measures of health has been to try to 'map' between measures. This can be done, for instance, by using the judgement of 'experts'. The use of judgement based methods, however, has been criticised for its arbitrariness (Coast, 1992). Furthermore, it does not involve any attempt to estimate the uncertainty around the mapping. The validity of such mappings is questionable and the only way to test them is by empirically comparing the judgements against real data. Ultimately, a better approach is to estimate the relationship between the measures empirically by statistical inference. This approach involves estimating the relationship between a health measure and a generic preference-based measure (also known as 'cross-walking' or estimating exchange rates between instruments) and requires the two measures to be administered on the same population.

There are different estimation models that can be used in mapping studies (see Table 1, adapted from Tsuchiya et al, 2002). Model (1) is the simplest additive model, which regresses the target measure (such as the EQ-5D) onto the total score of the starting measure (e.g. SF-36, HAQ, HAD etc.). This is also the most limiting specification since it assumes that the dimensions of the starting measure are equally important; all items carry equal weight; and response choices to each item lie on an interval scale (so for example the intervals between 'all of the time', 'most of the time', 'some of the time', 'a little of the time' and 'none of the time' are equal). These assumptions can be relaxed by modelling either dimension scores (model 2), item scores (model 3), or item responses (model 4) as independent variables. For these models dimension and item scores will be

treated as continuous variables and item responses are modelled as discrete dummy variables (e.g. 'all the time' is one, other wise zero, and so forth). Using item responses can, however, result in a large number of independent variables (over 100 for SF-36) and so it may be useful to be selective in the items included in the model. In this case, items can be excluded for having coefficients that are non-significant or counter-intuitive in their sign prior to estimating a model with item responses (model 4).

The assumptions of a simple additive model can be relaxed by including squared terms for dimension or item scores and interaction terms. Again these can generate a large number of variables and so researchers may also limit them to variables with significant main effects, at least for the item level models. A more complex approach to modelling the relationship would be to estimate separate models for each dimension of the target instrument (such as the 5 EQ-5D dimensions) (i.e. models 5 and 6). For the EQ-5D this creates a dependent variable that can be treated as continuous (model 5), but is more accurately treated as a discrete variable (model 6). These can be estimated using any of the previous 4 specifications.

This paper presents a systematic review of current practice in mapping between nonpreference based measures and generic preference-based measures. It reviews the studies identified by a systematic search of the published literature and the grey literature. This review seeks to address the feasibility and overall validity of this approach, the circumstances when it should be considered and to bring together any lessons for future mapping studies.

LITERATURE REVIEW

Search

A systematic literature search was carried out. Based on a few core papers identified by the research group a citation search was carried out using the Science Citation Index, Social Science Citation Index and Web of Science citation database. The citation search was undertaken both forwards and backwards. The forward search ensures that all papers that cite the core papers are reviewed. The backwards search ensures that all papers cited by the core papers are reviewed. A key words search was also undertaken using the titles and abstracts in 15 electronic bibliographic databases covering biomedical and healthrelated sciences, social science, and the grey literature. Key words were combinations of: 'mapping / cross walking' and 'EQ-5D / SF-36 / HUI / QWB / NHP / SIP / health status / health profile'. The following databases were searched: Cinahl, Cochrane Central Database of Controlled Trials (CENTRAL), Cochrane Database of Systematic Reviews (CDSR), DH-Data, Embase, Kings Fund, Medline, Medline Plus, NHS Database of Abstracts of Reviews of Effectiveness (DARE), NHS Economic Evaluations Database (NHS EED), NHS Health Technology Assessment (HTA) Database, OHE Health Economic Evaluations Database (HEED), Science Citation Index, Scopus, Social Sciences Citation Index, UK HESG. Where possible, the searches were not restricted by publication type, language, or date of publication. These searches were supplemented by contacting known experts in the field.

Review

The overall aims of the review were to examine the feasibility and validity of the mapping approach, the circumstances when it should be considered and to bring together any lessons for future mapping studies. These questions were addressed by extracting data on 56 items listed in Table 2 on each model presented. These items cover a description of the instruments used, the population completing the instruments, model specification, methods of estimation, model fit and predictive performance within and outside the estimation sample. In addition any important comments from the author(s) were noted. Data extraction on all 28 papers was undertaken by a member of the research team and summarized in Excel using headings shown in Table 2 that had been agreed by all team members.

Findings

Studies included

One thousand three hundred and eleven papers were identified. The number of relevant papers was reduced to 34 based on a review of abstracts. Among these 34 papers, 3 papers were excluded as only conference abstracts could be found (after contacting the

authors). Another 3 papers were excluded because they were not based on empirical methods. This left a total of 28 papers for review that covered 119 different models. A 30-page Appendix tabulating all the estimation models is available on request from the corresponding author.

Details of the 28 studies are presented in Table 3. Mapping between measures is a new research area with most papers (26 out of 28) published or produced after 2000, with the remaining 2 papers published in 1997 and 1998. Out of the 28 papers, 20 have been published in non-clinical journals including: *Medical Decision Making* (6 papers), *Value in Health* (3 papers), *Health Economics* (2 papers), *Medical Care* (2 papers), *Quality of Life Research* (2 papers); and the others (5 papers) were published in specific clinical journals. Out of the remaining 8, 3 were conference papers (with sufficient detail), 2 were published discussion papers and 3 were unpublished project reports.

General description of studies

Twenty-seven out of the 28 studies involved the mapping of a non-preference based measure of health (the "starting measure") onto to a preference-based measure of health (the "target measure"); the exception being a study mapping between two preference-based measures (SF-6D to EQ-5D). The most popular target measure used for mapping was the EQ-5D with 16 studies (15 used the UK MVH value set and one used the US value set), followed by HUI2/HUI3 with 6 studies, SF-6D with 5 studies, and QWB with one study. On the right hand side of the mapping equation, the most widely used starting measures were SF-12 (n=7) and SF-36 (n=5). The remainder consisted of various condition specific instruments intended to capture patient-perceived quality of life covering asthma, rheumatoid arthritis, osteoarthritis, overactive-bladder, irritable bowl syndrome, intermittent claudication, dental, dyspepsia, obesity, cancer and heart disease. One study mapped clinical measures onto EQ-5D in angina patients.

The sample size (number of people giving responses) used in the mapping studies ranged from 98 to 23,547. Clinical trials were the most common source of data. Respondents were also recruited from populations in the community, hospital and primary care. Six

studies used large panel survey data, such as the US Medical Expenditure Panel Survey and the Health Survey for England.

Model specification

The most widely used was the additive model. Most studies used total, dimension and item scores as the independent variables and some entered dummy variables representing the level of each item. Out of the 119 models reviewed: 33 models included interaction terms; 19 models incorporated transformations of the main effect such as square terms; 6 models included other health measures; 15 models included clinical measure; and 34 models considered respondents' personal characteristics, such as age, gender, race and income. Quite modest or negligible improvements were achieved from increasing model complexity. Moving from total to dimension, to item level models or adding interaction and other terms also improved the model fit. Only rarely was a major impact on the range of scores being predicted and goodness of fit. One example is the mapping between IBDQ to EQ-5D where R^2 increased from 0.45 to 0.69 after incorporating squared terms of dimension scores (Buxton, et al, 2007). Furthermore, some studies included additional variables, such as other clinical indicators (Grootendorst et al, 2007; Buxton et al, 2007) and demographic variables (Brazier et al, 2004). Only 4 studies used dimension scores or responses as the target measure and in all cases these were the 5 dimensions of the EQ-5D (Tsuchiya et al, 2002; Edlin et al, 2002, Gray et al, 2004; 2006).

Estimation

Most mapping functions have been estimated by OLS, though some researchers have explored Generalised Linear Models with random effects, Adjusted Least Square Regression Model (ALS), Tobit Model, Censored Least Absolute Deviation Model (CLAD) and non-linear models. For models with a discrete dependent variable (e.g. EQ-5D dimension level) then researchers have used Ordinal Logit and Multi-nomial Logit regression models. These latter models generate a probability distribution across dimension levels and there is a subsequent stage of imputing a single level for calculating a single index value for the respondent. One way for doing this has been to choose the

highest probability level (Tsuchiya et al, 2002). In a recent study, researchers used a Monte Carlo procedure to select from the distribution (Gray et al, 2006).

Performance

Studies commonly report the model's explanatory power in terms of adjusted R-Squared. Overall, models mapping a generic onto a generic preference-based measure (e.g. SF-12/36 to EQ-5D, NHP to SF-6D, and SF-36 to QWB) achieved an R^2 or adjusted R^2 of more than 0.5 within sample. There was little reduction in the goodness of fit from testing the mapping function on samples randomly selected from the same data set as the estimation samples. The fit of functions mapping from condition specific to generic measures is more variable. One of the poorest fitting models was for the Overactive Bladder Questionnaire (OABq) onto the SF-6D which achieved an adjusted R^2 of 0.17 (Roberts et a, 2005). One of the better models was between the International Weight Quality of Life Questionnaire (IWQoL) and the SF-6D that managed 0.51 (Brazier et al, 2004). Figure 1 shows the distribution of R^2 statistics for generic to generic measures and condition-specific to generic measures. Explanatory power, however, has little value in comparing models estimated using different methods of estimation (see below for details).

Authors have also assessed performance in terms of the sign, significance and consistency of the estimated coefficients. At least for main effects, coefficients should be negative (i.e. the more severe the health problem the lower the preference index) and the more severe the item levels in model (4) the larger the negative coefficient. However, for some descriptive systems there is some ambiguity regarding the ordering of statements (e.g. between 'your health limits you a little in bathing and dressing' versus 'your health limits you a lot in moderate activities' in the SF-6D). Furthermore, interaction terms would interfere with these orderings and so are not reliable. For some models, item levels were merged to remove inconsistencies.

Explanatory power is not a useful basis for assessing model performance, since the purpose of mapping functions is to predict values in other data sets. A better method used in many of these studies has been to examine the difference between predicted and

observed values at either the aggregate level by calculating Mean Error (ME) or at the individual level by calculating the Mean Absolute Error (MAE) or the Root Mean Squared Error (RMSE). Models can also be compared in terms of the numbers or proportion of absolute errors greater than some cut-off (e.g. 0.05 or 0.10) or within 5% or 10% of the observed value at the individual level. The mean error for the 119 models ranged from 0.0007 to 0.042 and was nearly zero for the OLS models (as would be predicted). MAE at the individual level ranged from 0.0011 to 0.19 and RMSE ranged from 0.084 to 0.2. These typically represented a percentage error of up to 15% of the overall scale of the dependent variable.

The normality of prediction errors by the Jarque-Bera test, but this is not used in OLS models since these are unbiased by definition. What is potentially more important is the pattern of errors across the range of the dependent variable. Only a few studies have examined this and some of those have found that the degree of error is not evenly distributed across the scale of the dependent variable. This problem was shown in two studies, one using a condition specific (Tsuchiya et al, 2002) and the other a generic instrument (Gray et al, 2006) as the start measure. Overall, the level of error is far greater at the lower (or severer) end. Gray et al (2006), for example, found that the MAE varied from 0.065 to 0.109 for EQ-5D index values from 0.7 to 1.00, but for values less than 0.7 the MAE was over 0.30. Scatter plots have found that there was a tendency for EQ-5D models to over predict values at the lower end and under predict at the upper end of the EQ-5D. This was despite the inclusion of interaction and squared terms. These papers also found that the predicted values from the mapping functions tend to have lower levels of variance than the original observed values.

Model performance is often assessed on the same data set as that used to estimate the model and referred to in the literature as within-sample testing. Another strategy which was occasionally used is to estimate the model on a sub-sample of the full data (the 'estimation' sample) and then to test the model on the remaining sample (the 'validation' sample). These-out-of-sample tests found little reduction, if any, in the performance of

the models. However, these tests do not examine the performance of the model in truly independent samples nor did they examine them across subgroups.

DISCUSSION

This review found 28 studies reporting a total of 119 different models. The studies undertook a range of different modelling methods, but the most common was a simple additive model with the preference-based index as the dependent variable and the independent variables being dimension or item scores and estimated by OLS. More complex specifications were examined that included interaction and squared terms, non-health variables (e.g. socio-demographics) and different methods of estimation. These studies clearly show that this approach is feasible, but the validity of the models in terms of goodness of fit and error of prediction at the individual level was highly variable. Explanatory power ranged from 0.17 to 0.51 and RMSE from 0.084 to 0.2. For those studies that examined the pattern of the error, they found the RMSE increased with the severity of the condition while mappings from SF-12 or SF-36 onto EQ-5D.

The question of whether mapping is a valid method for generating preference-based indices depends on the circumstances. In a situation where the analyst does not have any other data, some of the poorer models might still be acceptable. This may happen in economic evaluations alongside clinical trials where a non-preference-based condition specific measure has been used or where an analyst is seeking to synthesise data across studies and does not want to limit the evidence base to those studies using a particular preference-based measure. However, the potential degree of uncertainty and likely error must be fully explored. At the individual level, the RMSE was often quite high and larger than published minimally important differences for these measures of between 0.041 and 0.071 (Walters and Brazier, 2004). However, the purpose of mapping functions is to predict differences across groups of patients or differences between arms over time in clinical trials, and not individual level index values. Work undertaken after this review was completed indicates that the size of the errors in predicting mean EQ-5D indices for patient groups from SF-36 data may be quite modest (Ara and Brazier et al, 2007). However, this was only for a limited range of patient groups. Patients with more severe

problems may have gains under-estimated by the mapping function on the basis of existing evidence relating SF-36 to EQ-5D. Most published studies have not even examined whether such systematic patterns exist in the predictions of their models. This may have important implications for cost effectiveness.

For prospective decisions about the instruments to use in future studies the decision maker also needs an estimate of the error relevant to the population of interest (e.g. disease, severity and size of sample) to decide whether the error in these models is acceptable. The likely implications of any error in the estimation of differences or changes over time must be weighed against the additional cost of using a generic preference-based measure directly in the study or application being considered.

For mapping from conditions specific measures the degree of error tended to be larger, although it varied across patient groups and/or conditions. However, the use of mapping to derive preference-based generic indices from condition specific measures raises a more fundamental concern. Mapping assumes that the preference-based target measure covers all important aspects of health of the non-preference-based start measure. In other words, the strength of the mapping function depends on the degree of overlap between the two descriptive systems. Where there are important dimensions of one instrument not covered by the other, then this may undermine the model. Where the generic measure does not cover certain dimensions of the non-preference based condition specific measures that are regarded as important this could be an important weakness. EO-5D does not, for example, contain a dimension for energy or vitality. So it is not surprising that in published mapping functions from any of the SF instruments to EQ-5D, energy has a small and non-significant coefficient. Another source of weakness can arise from differences in the severity range covered for given health dimension. The SF-36 physical functioning dimension, for example, has been demonstrated to suffer from floor effects (i.e. large numbers of patients at, or are near, the lowest score) and so it is not likely to be as good at predicting at the lower end. These problems can be more dramatic in condition specific measures.

Where generic measures are not regarded as appropriate for the condition, either due to a lack of relevance or insensitivity, then mapping from the condition specific measure onto a generic measure does not solve this problem. Indeed the mapping function is likely to perform poorly, as was found in the case of the Over-Active Bladder Questionnaire (Roberts et al, 2005). An alternative approach in these circumstances is to estimate a preference-based index directly from the condition specific measure, as has been done with the King's Health Questionnaire (Brazier et al, 2007) or the Overactive Bladder Questionnaire (Yang et al, 2007).

There are important lessons to be learnt about the methodology for undertaking mappings. The first is that the population used in the mapping process should cover the range of clinical and demographic characteristics of the sample on which the mapping function is ultimately going to be applied. In terms of model specification, most studies found that a simple additive model with an index score as the dependent variable and main effects of either total or dimension scores as independent variables, performed nearly as well as those for more complex models. Greater complexity came with little gain in most cases, but small gains come at little cost in terms of computing time.

The most common method of estimation was OLS. There is a concern in the literature that the standard OLS regression models under-estimate the level of uncertainty in the estimates (Briggs et al, 2004). This results from a centering around the mean caused by assuming that respondents who complete the start measure (e.g. SF-36) in the same way would also complete target instrument in the same way (EQ-5D). The result is a lower variance around the mean estimates. The importance of this problem depends on the way the data are going to be used. In large pooled analyses this may be of little importance. More of a problem is the systematic pattern referred to earlier of over-predicting at the lower end and under-predicting at the upper end may be partly a result of this. This problem still existed for the multinomial model used to predict the probability of response across the dimension levels of the EQ-5D. There may be other solutions to the problem, such as the application of a Bayesian approach (as has been successfully used in modelling health state values (Kharroubi et al, 2007)).

This review addressed a number of questions about the use of functions to map between non-preference based and generic preference-based measures. It found a surprisingly large body of literature. The performance of the mappings functions in terms of goodness of fit and prediction was variable and so it is not possible to generalise across instruments. Performance is related to the degree of overlap in content between the instruments being mapped. The current literature is also limited in the way these models have been tested, since most testing has focused on their use at the individual level and yet the main purpose of these functions is to predict mean values for subgroups of patients (such as arms of trials). Further work is required to test the accuracy of these functions in more relevant contexts and over a larger range of instruments. The use of mapping functions is always a second best solution to using a preference-based generic measure in the first place (or arguably using preference-weighted condition specific measure), but it is often necessary for pragmatic reasons and so this remains an important of area of research.

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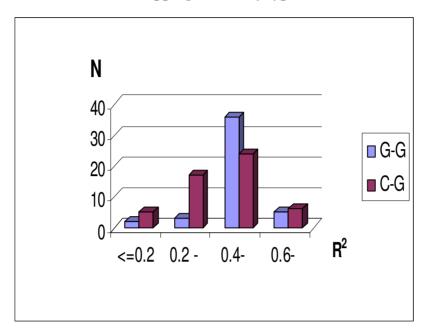


Figure 1 Distribution of R² of mapping models by type of start measure

N: Number of models relevant

G-G: Mapping from a generic health measure to another generic measure

C-G: Mapping from a condition-specific measure to a generic health measures

Table 1: Alternative specifications of mapping functions

Мо	dependent	D/C †	independent variables				
del	variable	2101	Main effects	D/C †	Interactions	Other measures	
(1)	index	С	overall score	С		For any model:	
(2)	index	C	dimension scores	С	dimensions	squared terms, other health	
(3)	index	С	item levels	С	items	measures, clinical measures,	
(4)	index	C	item levels	D	items level	demographics	
(5)	Dimension level	С	Models 1-4	C/D	Models 1-4		
(6)	Dimension level	D	Models 1-4	C/D	Models 1-4		

† C, continuous; D, discrete

Table 2 : Items extracted from papers

Author name Start Measure **Target Measure** Population, method of recruitment and setting **Estimation sample size Estimation method** Dependent variable (C/D) Main effects independent variable(C/D) Method of selection of main effects variable Main effects interactions **Transformations** Other measures Independent variables in model (βs) Proportion of β s (P<0.1) Proportion of β s unexp. sign (P<0.1) Proportion of Inconsistent βs (P<0.1) **R² and Adjusted R2** Uncertainty In-sample tests: Mean error Mean absolute error (MAE) (95% CI) **Proportion MAE>0.05** Proportion MAE>0.10 MAE by sev./cat. MAE /obs (%) RMSE Maximum predicted score compared to observed Minimum predicted score compared to observed Correlation Intra class correlation Use of plots **External-sample size** Source Setting R² and Adjusted R2 Mean error MAE (95% CI) Prop. MAE>0.05 Prop. MAE>0.10 MAE /obs (%) RMSE(95%CI) Max. prediction vs. observation Min prediction vs. obervation MAE by severity group or category Correlation Intraclass correlation coefficient Plots Authors' comments on the study

Table 3: Summary of mapping studies

ID	First Author	Year	Journal	Start Measure	Target	Population	Sample size ³
1	Bansback N	2007	Arthritis Care Research	HAQ-DI (Health Assessment Questionnaire Disability Index)	EQ-5D	Rheumatoid Arthritis (RA) patients	923
2	Bartman BA	1998	Quality of Life Research	SF-36	HUI3	Older patients with intermittent claudication (>=55)	510
3	Brazier J	2004	Value in Health	BI (Barthel Index)	EQ-5D	Older patients of intermediate care - admission	964
4	Brazier J	2004	Health Economics	IWQOL- Lite	SF-6D	 Community volunteers; 2. Participants in clinical trials for obesity; 3.gastric bypass surgery taker 	468
5	Brennan DS	2006	BMC Health Services Research	SF-6D	EQ-5D	7 samples of patients with different diseases	2192
6	Buxton MJ	2007	Value in Health	OHIP-14 (14 item version of the oral Health Impact Profile)	EQ-5D	Dental patients	248
7	Dixon S	2003	Journal of Outcomes Research	IBDQ (Inflammatory Bowel Disease Questionnaire)	SF-6D	Moderate to severe Crohn's disease patients	905
8	Dobrez D	2007	Value in Health (In press)	NHP (Nottingham Health Profile)	SF-6D	Primary care patients	1327
9	Dooslaser E	2003	Journal of Health Economics	FACR-G (Functional Assessment of Cancer Therapy - General)	TTO utilities	Cancer patients	717
10	Edlin R	2002	Unpublished manuscript	SAH (self-assessed health question)	HUI3	General public >=12	15539
11	Edlin R	2002	Unpublished manuscript	NDI (Nepean Dyspepsia Index)	SF-6D	Dyspepsia patients	271
12	Franks P	2004	Medical Decision Making	MLWHF (Minnesota Living with Heart Failure Questionnaire)	EQ-5D	Heart patients	3000
13	Franks P	2003	Medical Care	SF-12	EQ-5D	General public (>=18)	12988
14	Fryback DG	1997	Medical Decision Making	SF-12	EQ-5D	Patients >=18	240

15	Gray A	2006	Medical Decision Making	SF-36	QWB	General public >=45 years	1356
16	Gray A	2004	HESG ¹ , January 2004, Paris	SF-12	EQ-5D	General public adults >=18	12967
17	Grootendorst P	2007	The journal of Rheumatology	SF-36	EQ-5D	General public adults >=18	12753
18	Kaambwa B	2006	HESG ¹ , July 2006, York	WOMAC(Western Ontario and McMaster University Osteoarthritis Index)	HUI3	Knee Osteoarthritis (OA) patients	168
19	Lauridsen J	2004	Health Economics	SAH (self-assessed health question)	15D	Finnish General public >=15	2697
20	Lawrence WF	2004	Medical Decision Making	SF-12	EQ-5D	General public (>=18)	7313
21	Longo M	2000	HESG ¹ , July 2000, Nottingham	SF-36	EQ-5D	Women with breast disorder	271
22	Longworth L	2005	European Journal of Health Economics	CCS (Canadian Cardiovascular Society Score) & the Breathlessness Grade	EQ-5D	Patients with stable angina	533
23	Nichol MB	2001	Medical Decision Making	SF-36	HUI2	Managed care patients with at least 1 prescription in the previous year, >18	6921
24	Roberts J	2005	Unpublished manuscript	OABQ (Overactive-bladder Questionnaire)	SF-6D	Over-Active Bladder patients	688
25	Sengupta N	2004	Medical Care	SF-12	HUI3	Managed care patients,>18, with at least one prescription in the previous year	6323
26	Sullivan PW	2006	Medical Decision Making	SF-12	EQ-5D (US)	Representative sample of US population >=18	23647
27	Tsuchiya A	2006	HEDS ² discussion paper	AQLQ (Asthma Quality of Life Questionnaire)	EQ-5D	Asthma patients	3059 - 6939
28	Tsuchiya A	2002	HEDS ² discussion paper	IBS_QoL (Irritable Bowel Syndrome questionnaire)	EQ-5D	IBS patients	121

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 Sample size is the respondents included in the dataset. The number of observations used for model estimation may vary if repeated observations are used.