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Development and valuation of a vision bolt-on to EQ-5D

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ABSTRACT

Background and aims: EQ-5D is commonly used for measuring health outcomes for economic evaluation. It has been widely studied and validated; however, there are concerns about its validity and responsiveness in some specific conditions, including vision impairment. One potential solution to this problem is to develop 'bolt-on' items to the EQ-5D. Three potential bolt-on dimensions were developed following a systematic review of the validity and responsiveness of EQ-5D and tested in an exploratory valuation study. The results indicated that a bolt-on for vision would have a significant impact on EQ-5D values. The aims of this study were to estimate a value set for the EQ-5D+Vision measure and to compare the values with a value set for EQ-5D without the bolt-on.

Method: Based on an orthogonal design, 20 health states for EQ-5D+Vision were selected for valuation. A comparable set of EQ-5D states without the bolt-on was also selected. The time trade-off method was used to value the health states in a sample of the general public: one group valued EQ-5D and the other EQ-5D+Vision. Random effects models were used to analyse the data for EQ-5D and EQ-5D+Vision separately. The impact of the bolt-on on EQ-5D values was assessed by comparing the coefficients for dummy variables representing each level and dimension between the models.

Results: A total of 312 TTO interviews were conducted, which generated 1550 and 1570 TTO observations for the EQ-5D and EQ-5D+Vision states. The two groups of respondents were broadly comparable in terms of age, gender, and self-reported health status. Mean values for EQ-5D states ranged from 0.05 to 0.96, and for the EQ-5D+Vision from -0.04 to 0.94. The random effects model showed that inclusion of a vision bolt-on item has a significant impact on EQ-5D health state values. The largest difference in coefficients between the models was observed for level 2 (moderate problems) on the usual activities dimension (difference = 0.044; $p=0.059$); but this did not reach the pre-defined 5% level for statistical significance.

Conclusion: The vision bolt-on item had a significant impact on EQ-5D health state values. Although statistically significant differences were not observed between the models, the comparison of the coefficients suggests that inclusion of the bolt-on could affect the valuation of the five EQ-5D dimensions.

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INTRODUCTION

Generic preference-based measures (GPBM) of health-related quality of life (HRQL) are commonly used in the economic evaluation of health interventions. These instruments have many advantages, including the ability to reflect health on a multi-dimensional scale and that they measure HRQL on a scale that can be combined with data on length of life to form of quality adjusted life years (QALYs). Furthermore, they facilitate comparison between conditions, which is important if there is a need to compare cost-effectiveness estimates to a common benchmark or cost-effectiveness threshold. The questionnaires can usually be easily administered to patients for self-completion, and the data can incorporate an assessment of the value associated with different levels of health (usually based on values from members of the general population).

In the UK, the National Institute for Health and Clinical Excellence (NICE) has specified that health technology assessments (HTAs) submitted to its Technology Appraisal programme should be reported using an incremental cost per QALY framework, and recommends the use of the EQ-5D as the preferred GPBM.⁽¹⁾ The EQ-5D descriptive classification consists of five dimensions of health: mobility; self-care; usual activities; anxiety/depression; and pain/discomfort.⁽²⁾ In the older and most commonly used version, each dimension of health has three levels of severity. A new five-level version has recently been published.⁽³⁾ The 3-level version can describe 243 unique health states, to which a preference value can be assigned based on a set of values obtained from a large UK general population survey.^(4;5)

The decision by NICE to recommend the EQ-5D was in part a pragmatic decision.⁽⁶⁾ It is now established that the various GPBMs produce different values⁽⁷⁻⁹⁾. This can be problematic for an organisation wanting to make consistent and predictable decisions. The recommendation of a single reference-case GPBM is therefore appealing, and the EQ-5D is an easy to use instrument and the most widely used and studied of all the GPBMs. Whilst NICE recommends the use of the EQ-5D for its HTAs, it also recognises that it may not be an appropriate measure for all conditions.⁽¹⁾ In these circumstances, NICE requests that the alternative preference-based measure used has been validated and valued using methods that are comparable with those used to value the EQ-5D.⁽¹⁾

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Recently research has been conducted to develop preference-based measures from validated condition-specific measures of HRQL.(10-13) There have, however, been concerns raised that these condition-specific preference-based measures produce very different values to the GPBMs(14); and these differences may continue arise even when the methods of valuation are designed to be similar with GPBMs. One possible solution to this problem is to not only use comparable methods of valuation, but also to keep the health state classification systems as similar as possible. Previous research has examined the impact of modifying the EQ-5D descriptive system to include additional dimensions of health. Krabbe *et al* valued EQ-5D health states including a 'cognition' dimension and found that it significantly impacted upon health state values.(15) More recently Yang *et al* developed a 'sleep' dimension to add to EQ-5D but found that its inclusion did not affect the valuation of health states.(16)

'Bolt-ons' are dimension/s that can be appended to another instrument and to which utility values can be assigned to the health states described jointly by the instrument and the bolt-on. The worth of any potential 'bolt-on' dimension to EQ-5D depends crucially on whether its inclusion significantly impacts on the values given to the EQ-5D health states. The development of bolt-ons to EQ-5D raises several issues relating to their valuation. For example, it is not clear if the bolt-on itself could be simply valued and an adjustment made to the existing tariff of EQ-5D values (for example, through a simple additive model). In addition, it is not clear if the inclusion of the bolt-on affects the relative valuation of the EQ-5D dimensions. For example, if having some problems with self-care is valued differently depending on whether vision problems are present. These issues will affect the appropriate design of future bolt-on valuation studies.

The study reported here was conducted as part of a larger project: the NICEQoL study. In addition to the study reported here, this included a series of systematic reviews of the performance of GPBMs in various conditions, a study of 'mapping' methods for when EQ-5D data are not available and an exploratory study of bolt-on valuation. This paper reports the results of a study to value a Vision bolt-on to EQ-5D. Brief details of some of the preparatory studies leading to the development and valuation of the Vision bolt-on are also provided.

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The primary aim of this study was to develop to a model for valuing EQ-5D with a Vision bolt-on (EQ+Vision). Secondary aims included testing the impact of the bolt-on to (i) health states described by the EQ-5D and (ii) the coefficients representing the five EQ-5D dimensions.

METHODS

Development and initial testing of the vision bolt-on

The bolt-on item was developed to address vision impairment. This broadly defined condition was chosen following a series of related studies. Firstly, a series of systematic reviews were conducted to assess the performance of EQ-5D and two other commonly used generic preference-based measures of HRQL (the Short Form-6D(17;18) and Health Utilities Index(19)) in several different conditions (hearing impairment, vision impairment, cancer and skin conditions). Performance was assessed in terms of responsiveness, reliability and validity using standard psychometric methods. The results of the review in vision impairment found that the evidence for EQ-5D was mixed according to the specific vision condition. Specifically, there was good evidence to support the use of EQ-5D in conjunctivitis and cataracts, but the evidence suggested poor performance for age-related macular degeneration and diabetic retinopathy. Further details of vision systematic reviews have been reported elsewhere.(20)

After considering the results of the systematic reviews, three separate bolt-on items were developed: vision impairment; hearing impairment; and fatigue. The bolt-ons were designed for inclusion with the three-level version of the EQ-5D and the labels phrased to be consistent with the labels of the EQ-5D so that they include categories of 'no problems', 'some problems' and 'extreme problems'. The dimension heading for the Vision bolt-on explicitly referenced the use of supportive equipment (glasses and contact lenses) so that the bolt-on instrument captures vision severity *after* taking into account their use. The use and provision of equipment such as these are common place in developed countries and in most cases, easily address vision problems. If the use of equipment was not explicitly addressed, the bolt-on item would fail to distinguish more severe problems that cannot be corrected using standard equipment. The references to equipment were developed to follow a similar format to that for the 'Usual activities' dimension of EQ-5D which includes a

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clarification in parentheses in the heading of the item: “Vision (using glasses or contact lenses if needed)”. The Vision bolt-on item is shown in Figure 1.

Figure 1: The vision bolt-on item

Vision (using glasses or contact lenses if needed)	
I have no problems seeing	<input type="checkbox"/>
I have some problems seeing	<input type="checkbox"/>
I have extreme problems seeing	<input type="checkbox"/>

The Vision bolt-on (EQ+Vision) and the two other bolt-on items for hearing and fatigue were tested in an exploratory study. Briefly, a set of health states with and without the bolt-ons were valued by 300 members of the general population using the time trade-off (TTO) method in face-to-face interviews. The TTO values for the health states including each bolt-on were compared to TTO values for EQ-5D states without the bolt-on. All three bolt-on were found to have a significant impact on EQ-5D health states. The Vision bolt-on was chosen for further evaluation based on having slightly more consistent results in the pattern of TTO values and showing a slightly larger number of statistically significant differences in paired comparisons of EQ+Vision values and EQ-5D values. No changes to the labelling or format of the Vision bolt-on were made following the exploratory study.

Valuation of the EQ+Vision

Data collection was undertaken to obtain TTO values for a selection of EQ+Vision states. To facilitate comparison, data were also obtained for a corresponding selection of EQ-5D states (with no bolt-on). Health states were selected for valuation based on an orthogonal design of EQ+Vision. This required values for 18 health states (for a six dimension instrument) assuming a main effects additive model. As the orthogonal design included mainly severe health states, two additional mild states were added to the orthogonal set. The set of EQ-5D states was selected from dropping the sixth dimension of the 20 EQ+Vision states. Both sets of 20 health states were randomly halved to produce four groups of 10 states for valuation. The health states valued within the survey are shown in Table 1.

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Table 1: Health states selected for valuation

EQ-5D states		EQ+Vision states	
Group 1	Group 2	Group 3	Group 4
23133	32231	23133+3	32231+1
13122	21221	13122+1	21221+2
23212	22323	23212+2	22323+1
21332	13331	21332+1	13331+2
31133	31312	31133+2	31312+3
12232	12313	12232+3	12313+2
22111	33321	22111+3	33321+3
32122	33213	32122+2	33213+1
11121	11223	11121+1	11223+3
33333	11112	33333+3	11112+2

A sample of 300 members of the general public in South Yorkshire was recruited to participate in face-to-face interviews. Recruitment aimed to achieve a good spread across age, gender, ethnicity and social class. The sample was selected on the basis of postal address within South Yorkshire using the Names and Numbers software.(21) Five trained interviewers undertook the interviews.

Survey respondents were randomly allocated to one of the four groups (n=75). In order to minimise any interviewer effect, each interviewer undertook valuations of each questionnaire variant in turn. The format for the interviews was based on a similar format to the three-level EQ-5D valuation protocol recommended by the EuroQol Group. After agreeing to participate in the study, respondents were asked to describe their own health using the EQ-5D (EQ+Vision for Groups 3 and 4), then rated their own health using the EQ-Visual Analogue Scale (VAS). Respondents then ranked four EQ-5D states (EQ+Vision for Groups 3 and 4) plus the state 'dead' as a warm-up task to familiarise them with the health state cards and the process of stating their preferences towards the health states.

Respondents then completed the main valuation exercise using the TTO. The respondent was asked to imagine ten years of life in the health state under valuation, relative to a shorter duration in 'full health' followed by the state 'dead'. A TTO board was used as a visual aid to assist respondents with one side for valuing health states considered to be better than dead and the other side for those states considered worse than being dead. Respondents valued a practice health state and then each of the ten health states described

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in Table 1. Finally, respondents completed some background questions and described their health status using the Vision bolt-on item (Groups 1 and 2 only). The study was approved by the Research Ethics Committee at Brunel University.

Analysis

TTO valuations were transformed using the transformation reported for the UK EQ-5D tariff to ensure all health state values are bounded between -1 and +1.(4) Tests for differences in the socio-demographic characteristics were compared using a Chi-square test for categorical variables, a Chi-square Gamma statistic for ordered variables and ANOVA for continuous variables. Mean TTO values of EQ-5D states with and without the bolt-on were compared using a paired t-test. Two models were estimated for both instruments separately (EQ-5D and EQ+Vision) using random effects models to account for repeated observations. The dependent variable in each model was '1-TTO value'. Explanatory dummy variables were used to represent the levels on each dimension. Alternative model specifications were explored including models published for the standard EQ-5D value sets from UK and USA.(4;22) The coefficients of the EQ-5D dimension dummy variables in the final model were compared using the z-statistic in order to make an assessment of the impact of the Vision bolt-on to the values given to the EQ-5D dimensions. A level of statistical significance was assumed where $p < 0.05$. STATA version 10(23) was used for all regression analysis, and SPSS 18(24) was used for the descriptive statistical analysis.

RESULTS

In total 302 people completed the interviews: 155 for EQ-5D alone and 157 for EQ+Vision. The socio-demographic characteristics and self-reported health status of respondents are presented in Table 2. There were no statistically significant differences in the socio-demographic characteristics or the self-reported health between the two groups. A summary of the TTO values for each health state is reported in table 3.

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Table 2: Socio-demographic characteristics and self-reported health of respondents

	EQ-5D (n=155)	EQ+Vision (n=157)
Age (%):		
18-24	10	10
25-34	14	15
35-44	19	23
45-54	21	15
55-64	17	17
65+	19	21
Gender: Male (%)	46	39
Relationship status (%)		
Single	17	26
Married	57	59
Separated	3	2
Divorced	12	7
Widowed	11	6
Experience of serious illness (%):		
In yourself	25	30
In your family	75	72
In caring for others	51	42
Employment status(%)		
Employed	53	46
Retired	25	26
Housework	12	14
Student	0	2
Seeking work	4	8
Other	6	5
Educated after minimum school leaving age (%)	56	57
Degree (%)	33	37
Home ownership (%)		
Own home	73	75
Rent (local authority)	19	15
Rent (private sector)	8	11
Self- reported EQ-5D (%)		
Mobility: Level 1/2/3	84 / 16 / 0	75 / 24 / 1
Self-care: Level 1/2/3	94 / 7 / 0	90 / 9 / 1
Usual activities: Level 1/2/3	82 / 16 / 2	76 / 20 / 3
Pain/discomfort: Level 1/2/3	67 / 30 / 3	61 / 33 / 6
Anxiety/depression: Level 1/2/3	80 / 17 / 3	78 / 22 / 1
Vision: Level 1/2/3	61 / 36 / 3	69 / 29 / 2
Self-reported VAS: Mean (SD)	79 (18)	76 (20)
EQ-5D index: Mean (SD)	0.85 (0.24)	0.82 (0.26)

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Table 3: Summary of time trade-off values

EQ-5D				EQ+Vision			
state	Mean	SD	Median	state	Mean	SD	Median
11121	0.961	0.097	1.000	111211	0.942	0.124	1.000
32231	0.283	0.454	0.375	322311	0.348	0.431	0.400
13122	0.746	0.299	0.850	131221	0.802	0.228	0.900
21332	0.553	0.300	0.600	213321	0.601	0.348	0.625
22323	0.551	0.357	0.513	223231	0.579	0.390	0.700
33213	0.261	0.468	0.350	332131	0.337	0.459	0.350
13331	0.389	0.447	0.400	133312	0.476	0.414	0.500
21221	0.823	0.231	0.900	212212	0.886	0.167	1.000
11112	0.934	0.171	1.000	111122	0.954	0.103	1.000
23212	0.720	0.321	0.800	232122	0.714	0.270	0.750
32122	0.500	0.375	0.525	321222	0.430	0.409	0.500
12313	0.623	0.320	0.675	123132	0.632	0.358	0.700
31133	0.354	0.404	0.375	311332	0.312	0.439	0.300
22111	0.904	0.150	1.000	221113	0.769	0.254	0.825
33321	0.209	0.469	0.200	333213	0.247	0.478	0.213
12232	0.570	0.318	0.625	122323	0.530	0.339	0.525
31312	0.462	0.400	0.500	313123	0.424	0.455	0.500
11223	0.671	0.368	0.775	112233	0.593	0.404	0.700
23133	0.421	0.377	0.425	231333	0.297	0.450	0.325
33333	0.048	0.419	0.000	333333	-0.041	0.449	0.000

SD (standard deviation)

Mean TTO values ranged from 0.05 (state 33333) to 0.96 (state 11121) for the EQ-5D (Table 3). For the EQ+Vision mean values ranged from -0.04 (state 33333+3) to 0.95 (state 11112+2). Between 76 and 80 valuations were obtained for each health state. The inclusion of the vision bolt-on affected the ordering of the states ranked by value for each of the measures. For example, the state with the third highest value was state 22111 for EQ-5D but was state 21221+2 for EQ+Vision. Standard deviations were generally higher for states considered to be most severe, and reported ranges for all of the health states were large.

The impact of the Vision bolt-on when compared to the EQ-5D values does not appear to be straight forward. As expected, the values for the EQ+Vision states with a level 3 Vision bolt-on included had, on average, lower values than the corresponding EQ-5D health state. However, when the included bolt-on item was a level 1 (no problems seeing), most mean

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values for the EQ+Vision states were higher than those given to the corresponding EQ-5D states. The differences between EQ-5D and EQ+Vision with a level 2 bolt-on item included were mixed.

A description of the explanatory variables considered for inclusion in the multivariate analyses are presented in Table 4. All were included as dummy variables unless reported otherwise. Models were estimated with and without background characteristics included.

Table 4: Variables considered in the multivariate analysis

Variable	Description
Mobility	EQ-5D Mobility dimension: level 1 (ref); level 2; level 3
Self-care	EQ-5D Self-care dimension: level 1 (ref); level 2; level 3
Activities	EQ-5D Usual activities dimension: level 1 (ref); level 2; level 3
Pain	EQ-5D Pain/discomfort dimension: level 1 (ref); level 2; level 3
Anxiety	EQ-5D Anxiety/depression dimension: level 1 (ref); level 2; level 3
Vision	EQ+ Vision dimension: level 1 (ref); level 2; level 3
Gender	Male (ref) or female
Age	Age categories: 1) 18-24 years (ref); 2) 25-34 years; 3) 35-44 years; 4) 45-54 years; 5) 55-64 years; 6) 65+ years
Marital	Marital status: 1) single (ref); 2) married; 3) separated; 4) divorced; 5) widowed
Yourself	Reporting experience serious of illness in yourself (0 reporting experience; 1 otherwise)
Family	Reporting experience serious of illness in your family (0 reporting experience; 1 otherwise)
Carer	Reporting experience serious of illness in caring for others (0 reporting experience; 1 otherwise)
Activity	Main activity: 1) employed or self-employed (ref); 2) retired; 3) homemaker; 4) student; 5) seeking work; 6) other
Education	Educated beyond school leaving age (0 yes; 1 no)
Home	Housing status: 1) own home (ref); 2) rent in public sector; 3) rent privately
SRVision	Self-reported level vision problems: level 1 (ref); level 2; level 3
N3	1 if any level 3 problems included in the health state; 0 otherwise
I2	Number of dimensions at level 2 beyond the first
I3	Number of dimensions at level 3 beyond the first
D1	Number of dimensions not at level 1 beyond the first

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The regression models for the EQ-5D and EQ+Vision excluding socio-demographic variables included are presented in Tables 5a and 5b respectively. The terms representing interactions (e.g. N3) were not statistically significant. The preferred models are those including main effects only for both EQ-5D and EQ+Vision (Model 1).

In the model for EQ-5D all the coefficients followed a logical ordering (e.g. the decrement in TTO value was higher for level 3 problems compared to level 2 problems). The coefficients for all dimensions were statistically significant, except for the dummy variables representing some mobility problems and moderate anxiety/depression. The largest impact on EQ-5D values was level 3 mobility problems (being confined to bed), followed by level 3 problems with pain/discomfort and self-care.

The model for EQ+Vision demonstrated a similar pattern to that for EQ-5D. Again all coefficients followed a logical ordering, including the coefficients for the vision bolt-on. The vision coefficients were statistically significant. This indicates that vision has a significant impact on the values given to the health states beyond any impact captured within the five EQ-5D dimensions. Similarly to the model for EQ-5D, the coefficients representing some mobility problems and moderate anxiety/depression were not statistically significant; and this also applied to the coefficient representing some problems carrying out usual activities. The coefficients with the largest impacts were level 3 problems on the mobility dimension and the pain/discomfort dimension; the coefficient for level 3 vision problems was the fifth largest, ahead of level 3 problems performing usual activities.

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Table 5a: Models estimated for EQ-5D

	Model 1: Main effects only			Model 2: Including N3 term			Model 3: Including D1 terms		
	Coef.	Std. Err.	P value	Coef.	Std. Err.	P value	Coef.	Std. Err.	P value
Mobility 2	0.019	0.018	0.309	0.021	0.018	0.253	0.017	0.049	0.726
Mobility 3	0.315	0.017	<0.001	0.308	0.018	<0.001	0.293	0.083	<0.001
Self care 2	0.079	0.018	<0.001	0.067	0.020	0.001	0.083	0.033	0.012
Self care 3	0.185	0.018	<0.001	0.170	0.022	<0.001	0.166	0.069	0.016
Activities 2	0.076	0.020	<0.001	0.066	0.022	0.002	0.091	0.035	0.011
Activities 3	0.150	0.021	<0.001	0.136	0.024	<0.001	0.136	0.071	0.056
Pain 2	0.071	0.018	<0.001	0.060	0.020	0.003	0.082	0.030	0.006
Pain 3	0.236	0.020	<0.001	0.221	0.024	<0.001	0.220	0.078	0.005
Anxiety 2	0.036	0.020	0.070	0.014	0.027	0.610	0.039	0.031	0.206
Anxiety 3	0.120	0.018	<0.001	0.100	0.025	<0.001	0.101	0.062	0.103
Vision 2	-	-	-	-	-	-	-	-	-
Vision 3	-	-	-	-	-	-	-	-	-
N3	-	-	-	0.043	0.038	0.259	-	-	-
D1	-	-	-	-	-	-	0.020	0.041	0.635
I2	-	-	-	-	-	-	-0.029	0.069	0.675
squaredI2	-	-	-	-	-	-	-0.001	0.022	0.970
I3	-	-	-	-	-	-	0.023	0.102	0.821
squaredI3	-	-	-	-	-	-	-0.007	0.011	0.509
Constant	0.009	0.031	0.768	0.017	0.032	0.598	-	-	-
Number of obs.	1550			1550			1550		
Number of groups	155			155			155		
Log likelihood	-340			-339			-338		
P (chi squared)	<0.001			<0.001			<0.001		

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Table 5b: Models estimated for EQ+Vision

	Model 1: Main effects only			Model 2: Including N3 term			Model 3: Including D1 terms		
	Coef.	Std. Err.	P value	Coef.	Std. Err.	P value	Coef.	Std. Err.	P value
Mobility 2	0.034	0.018	0.062	0.032	0.018	0.079	0.025	0.039	0.533
Mobility 3	0.320	0.017	<0.001	0.314	0.018	<0.001	-0.069	0.354	0.846
Self care 2	0.091	0.018	<0.001	0.077	0.022	<0.001	0.104	0.051	0.042
Self care 3	0.158	0.018	<0.001	0.147	0.021	<0.001	-0.255	0.379	0.501
Activities 2	0.032	0.020	0.118	0.029	0.021	0.165	0.090	0.071	0.204
Activities 3	0.104	0.021	<0.001	0.097	0.022	<0.001	-0.209	0.306	0.495
Pain 2	0.062	0.019	0.001	0.062	0.019	0.001	0.071	0.038	0.062
Pain 3	0.219	0.020	<0.001	0.216	0.020	<0.001	-0.100	0.324	0.756
Anxiety 2	0.038	0.020	0.056	0.029	0.021	0.170	0.070	0.053	0.193
Anxiety 3	0.159	0.018	<0.001	0.150	0.020	<0.001	-0.161	0.319	0.612
Vision 2	0.037	0.018	0.040	0.039	0.018	0.031	0.030	0.034	0.389
Vision 3	0.130	0.018	<0.001	0.127	0.018	<0.001	-0.246	0.361	0.495
N3	-	-	-	0.035	0.033	0.293	-	-	-
D1	-	-	-	-	-	-	0.444	0.381	0.244
I2	-	-	-	-	-	-	-0.555	0.429	0.196
squaredI2	-	-	-	-	-	-	0.026	0.017	0.128
I3	-	-	-	-	-	-	-0.236	0.168	0.160
squaredI3	-	-	-	-	-	-	0.042	0.036	0.237
Constant	-0.018	0.035	0.608	-0.026	0.036	0.477	-	-	-
Number of obs.	1570			1570			1570		
Number of groups	157			157			157		
Log likelihood	-361			-361			-361		
P (chi squared)	<0.001			<0.001			<0.001		

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Table 6: Final models (including background characteristics)

	EQ-5D			EQ+Vision		
	Coef.	Std. Err.	P value	Coef.	Std. Err.	P value
Mobility 2	0.020	0.019	0.270	0.036	0.019	0.051
Mobility 3	0.318	0.017	<0.001	0.320	0.017	<0.001
Self-care 2	0.079	0.018	<0.001	0.091	0.018	<0.001
Self-care 3	0.185	0.018	<0.001	0.163	0.018	<0.001
Activities 2	0.076	0.020	<0.001	0.033	0.021	0.105
Activities 3	0.149	0.021	<0.001	0.108	0.021	<0.001
Pain 2	0.072	0.018	<0.001	0.060	0.019	0.002
Pain 3	0.238	0.020	<0.001	0.216	0.020	<0.001
Anxiety 2	0.039	0.020	0.051	0.037	0.020	0.062
Anxiety 3	0.122	0.018	<0.001	0.158	0.018	<0.001
Vision 2	-	-	-	0.033	0.018	0.068
Vision 3	-	-	-	0.127	0.018	<0.001
Gender	-0.040	0.043	0.352	-0.071	0.045	0.117
Age 1	-	-	-	-	-	-
Age2	-0.104	0.090	0.248	-0.212	0.087	0.014
Age3	-0.202	0.098	0.040	-0.316	0.088	<0.001
Age4	-0.188	0.103	0.069	-0.226	0.102	0.027
Age5	-0.160	0.111	0.149	-0.208	0.105	0.048
Age6	-0.147	0.132	0.264	-0.122	0.129	0.344
Marital_1	-	-	-	-	-	-
Marital_2	0.010	0.069	0.890	0.057	0.062	0.356
Marital_3	-0.001	0.124	0.991	0.449	0.148	0.002
Marital_4	0.078	0.091	0.390	0.058	0.097	0.549
Marital_5	0.089	0.097	0.359	0.044	0.103	0.666
Yourself	0.022	0.052	0.681	-0.031	0.050	0.54
Family	0.031	0.048	0.522	0.057	0.045	0.207
Carer	-0.046	0.043	0.290	0.101	0.044	0.022
Activity_1	-	-	-	-	-	-
Activity_2	0.055	0.085	0.518	-0.123	0.087	0.159
Activity_3	-0.076	0.066	0.247	0.013	0.063	0.839
Activity_4	-	-	-	-0.027	0.149	0.856
Activity_5	-0.046	0.103	0.653	-0.191	0.084	0.024
Activity_6	0.058	0.087	0.505	0.032	0.105	0.759
Education	-0.017	0.043	0.697	-0.045	0.046	0.331
Home_1	-	-	-	-	-	-
Home_2	-0.021	0.056	0.705	-0.031	0.064	0.626
Home_3	-0.077	0.080	0.339	-0.142	0.072	0.047
SRVision 1	-	-	-	-	-	-
SRVision 2	0.008	0.047	0.860	-0.031	0.044	0.478
SRVision 3	-0.036	0.113	0.748	0.037	0.195	0.848
Constant	0.159	0.097	0.101	0.217	0.101	0.032

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Table 6 shows the results of the analysis including background characteristics. People who reported that they had some or extreme vision problems did not value the health states significantly differently from people who reported no vision problems. There were some statistically significant differences in the health state values according to age with the youngest age group giving lower values than the other age groups. Some differences were also seen in the valuation of the EQ+Vision health states according to experience of caring for others and those seeking work compared to employed respondents.

The model coefficients for the EQ-5D dimensions were compared between the EQ-5D model and the EQ+Vision model. The results of the *z test* are presented in Table 7. There were no statistical differences in the coefficients at the pre-defined level for statistical significance. However, some of the coefficients appeared to be qualitatively different and approached the level for significance. In particular, the coefficients for levels 2 and 3 on the usual activities dimension differed by almost 0.05.

Table 7: Comparison of the model coefficients

	EQ-5D model	EQ+vision model	p(z-test)
Mobility 2	0.0186	0.0344*	0.271
Mobility 3	0.315***	0.320***	0.428
Self-care 2	0.0787***	0.0909***	0.313
Self-care 3	0.185***	0.158***	0.140
Activities 2	0.0764***	0.0318	0.059*
Activities 3	0.150***	0.104***	0.062*
Pain 2	0.0710***	0.0619***	0.367
Pain 3	0.236***	0.219***	0.285
Anxiety 2	0.0356*	0.0377*	0.468
Anxiety 3	0.120***	0.159***	0.062*
Vision 2	-	0.0368**	
Vision 3	-	0.130***	

*p<0.1 **p<0.05 ***p<0.001

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Discussion

The results of this study show that the Vision bolt-on had a significant impact on EQ-5D state valuations. A full valuation model for EQ+Vision is reported. The comparison of the values given to EQ+Vision states with the values given to EQ-5D states show that the impact on EQ-5D of including a Vision bolt-on are not straight-forward. Health states with a level 3 (extreme) vision problems included are unsurprisingly lower than the corresponding EQ-5D health state. However; the values given to EQ+Vision health states which explicitly describe no problems seeing (level 1 bolt-on) are higher than those for the corresponding EQ-5D state where vision problems are not mentioned at all. The values including a level 2 bolt-on are more mixed. Given these results, a simple additive model to represent decrements associated with levels 2 and 3 problems on the bolt-on would not be appropriate.

There is frequently a concern whether people who do not experience a specific health problem can give meaningful valuations of health states. In this study we found that people who reported problems with their own vision did not value the health states differently from those who reported no problems with their own vision.

One of the aims of the study was to establish whether the inclusion of the bolt-on with the EQ-5D health state description had a significant impact on the valuation of the five EQ-5D dimensions. This is an important question as it has significant implications for future bolt-on valuations both in terms of study design and the extent of the resources required for the valuation of bolt-ons. If the bolt-on impacts on the existing dimensions then it further suggests that the bolt-on valuation needs to be conducted alongside valuation of EQ-5D states and can't be valued in isolation. Unfortunately, the results from the analysis were not conclusive. Although, the differences were not significant at the predefined 5% level for statistical significance, we were unable to conclude that the impact was not qualitatively different. In particular the vision bolt-on appeared to affect the coefficients for the usual activities dimension and the most severe level of anxiety and depression.

There were a few similarities in the estimated models presented here when compared to the model most commonly used for EQ-5D (3 level) values in the UK.(4) That study also found that level 3 mobility and pain/discomfort had the largest impact on EQ-5D values; however overall respondents in this study reported higher TTO values.

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The vision bolt-on item included explicit reference to the use of equipment such as glasses and contact lenses. This was in order to detect serious vision problems that cannot be corrected by the use of standard equipment. As a result, it is possible that the bolt-on items may not be responsive for some interventions which remove the need for the use of that equipment; for example, laser eye surgery to remove the need for wearing glasses. Whilst accepting this limitation, this was considered preferable to the alternative of excluding the use of equipment, as this could drive differences between levels of severity and would not pick up the most severe levels of vision and hearing problems which are not readily correctable using standard equipment.

Further research is required to establish conclusively if the inclusion of a bolt-on affects the relative valuations of the other dimensions. In addition further research is needed to establish whether the estimates from bolt-ons are more comparable with alternative approaches for establishing health state utility values when EQ-5D is considered to be inappropriate (such as the use of other GPBMs or preference based condition-specific measures of health). The EuroQol Group has recently established a five-level version of EQ-5D. It remains to be seen if that version will perform better in conditions relating to Vision impairment.

It is not clear if the results presented here would be generalisable to other bolt-ons. Previous research on the inclusion of bolt-ons has shown mixed results. The inclusion of a cognition bolt-on was found to have a significant upon values.⁽¹⁵⁾ A study designed to assess the impact of a sleep bolt-on found that it did not have a significant impact.⁽¹⁶⁾ The results of this study offer support for a Vision bolt-on. In addition the results of the exploratory study suggest that the fatigue and hearing bolt-ons warrant further investigation.

The vision bolt-on item had a significant impact on EQ-5D health state values. Although statistically significant differences were not observed between the models, the comparison of the coefficients suggests that inclusion of the bolt-on could affect the valuation of the five EQ-5D dimensions. With regard to the future development of bolt-ons, the impact on EQ-5D values and the coefficients for the individual EQ-5D dimensions is likely to be specific to each bolt-on depending on the condition represented. The results presented here suggest

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that a simple valuation of the bolt-on item in isolation cannot be assumed to be appropriate; rather it should be tested empirically.

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