Monograph:
Ara, R. and Brazier, J. (2009) Health related quality of life by age, gender and history of cardiovascular disease: results from the Health Survey for England. Discussion Paper. (Unpublished)

HEDS Discussion Paper 09/12

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Health Economics and Decision Science Discussion Paper Series

No. 09/12

Health related quality of life by age, gender and history of cardiovascular disease: results from the Health Survey for England

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Key words: health-state utility, health economics methods, cardiovascular, decision models, health surveys

Running title: Cardiovascular disease health state utility values

Abstract

Introduction: While there is an increasing volume of literature describing the health state utility values (HSUV) individuals with angina, heart attack or stroke, research comparing HSUVs for these conditions within the same study is sparse. This hinders analysts wishing to explore the benefits of interventions in cardiovascular disease (CVD). The objective of this study was to obtain EQ-5D scores to inform health states in CVD economic models using the same source for each health state.

Methods: EQ-5D data (N = 26,679) from individuals aged 16 to 98 years taking part in the Health Survey for England (2003, 2006) was used. Regressions were employed to explore the significance of age, gender and history of CVD on HSUVs taking into account the number and type of cardiovascular condition(s) and time since event. The predictive ability of the model was assessed using errors in predicted values on both the individual and the sub-group levels.

Results: Our results show HSUVs differ by age, gender, CV history, time since CV event and the number of concurrent CV conditions. The regression model is reasonably accurate when predicting mean values for sub-groups stratified by age, CV condition and time since event, with 67% of predicted values within the minimal important difference for the EQ-5D index.

Conclusions: The results provide a consistent basis for analysts to populate the most frequently defined health states (no CVD, heart attack, angina and stroke) in CVD models. Further research is required to validate these results in other datasets.

INTRODUCTION

Policy decisions on reimbursement within health care are frequently informed by economic evaluations describing the cost-effectiveness of interventions in terms of the cost per quality adjusted life year. The mathematical models used to generate these results are constructed to replicate the clinical pathway of the disease under consideration. Models can vary from simple decision trees with just two health states (alive or dead) to more complex forms where each health event associated with a disease is described by a distinct health state.

Economic models require health state utility values (HSUV) obtained from preference-based measures for each of the health states and the data needs to be obtained from patients whose health condition corresponds to the definition of the individual health state. Depending on the health condition or the particular health related event, health related quality of life (HRQoL) can either improve or deteriorate over time. As respondents are asked to describe their HRQoL during the immediately preceding time period (frequently the last seven days), long term studies are required to describe any changes over time. While the evidence base describing HSUVs in different samples and settings is growing, patient demographics, definitions of health conditions, and the follow-up period can all differ considerably between studies. The heterogeneity in study design hinders analysts when the data required to populate the different health states within a model is not available from a single study.

Cardiovascular disease (CVD) encompasses a number of distinct but related conditions including angina, heart attack, stroke, transient ischaemic attack, peripheral arterial disease and peripheral vascular disease. Depending on the intervention under evaluation, an economic model in CVD would typically include health states for a number or all of these sub-conditions and events.[1,2] If the intervention is for primary prevention of CVD, individuals would enter the model with no history of CVD and the events modelled would be first ever CV events.[3] Conversely, if evaluating a secondary intervention, individuals would enter the model with a history of one or more CV conditions and the events modelled would include subsequent CV events.[2] As individuals with a history of one CV condition are at high risk of developing another CV condition, secondary prevention models can include health states for individuals with a history of a several CV conditions. Events such as strokes

and heart attacks are frequently fatal thus a lifetime horizon is required to quantifying the benefits associated with avoiding these.[4] While CV events have a large detrimental effect on HRQoL during the period immediately following the event, the magnitude of the initial detriment may diminish over time. Consequently CV health states are frequently defined to differentiate between the first year and subsequent years after the event.[1]

Studies exploring the HSUVs associated with coronary heart disease and related conditions are generally conducted in individuals who have recently experienced just one of the CV events. The inclusion criteria frequently exclude individuals who have a history of the other related conditions. For example, studies exploring the effect of heart attacks may exclude individuals with a history of stroke. Long term data describing changes in HRQoL beyond the immediate period following a CV event are also scarce. These limitations in the evidence base make it difficult to obtain HSUVs for the numerous health states in CVD models, many of which include co-morbidities and different histories.

The objective of this study is to estimate HSUVs which can be used to populate the most frequently defined health states used in conventional CVD models. Data collected during the Health Survey for England (HSE) provide an opportunity to explore the HRQoL reported by individuals in the general population. In particular, there is sufficient detail to investigate if HSUVs differ by age, gender, type of cardiovascular condition (angina, heart attack or stroke), number of cardiovascular conditions and time since CV event. While an analysis of US data showed differences between the HSUVs for angina, heart attack and stroke,[5] to our knowledge, this is the first publication which provides all these data from a single source for a UK population and also shows a change in HSUVs over time.

METHODS

Health Survey for England

The Health Survey for England (HSE) is an annual nationwide survey which uses a random sample of the population living in private households in England.[6-7] The surveys conducted in 2003 (N = 18,553) and 2006 (N = 21,399) focused on CVD and included questions on the respondent's history of

angina, heart attack or stroke. The positive responses (i.e. "yes") to the questions "doctor diagnosed angina"; "doctor diagnosed heart attack" or "doctor diagnosed stroke" were used to identify individuals who had a history of CVD. Given a doctor's diagnosis of CVD, the positive responses to the questions "angina in the last year", "heart attack in the last year", "stroke in the last year", were used to identify individuals who had experienced a CV event in the previous 12 months. These responses were then used together with positive responses to the questions "ever had angina", "ever had a heart attack" or "ever had a stroke", and a doctor's diagnosis, to identify individuals who had a history of a CV condition prior to the previous 12 months.

These data allow us to estimate EQ-5D scores for health states defined in both primary prevention models (no history of CVD; angina, heart attack or stroke within the previous 12 months given a history of just one CV condition; angina, heart attack or stroke but no event within the previous 12 months given a history of just one CV condition), and secondary prevention models (given a history of more than one CV condition, angina, heart attack or stroke within the previous 12 months given a history of more than one CV condition; angina, heart attack or stroke but no event within the previous 12 months given a history of more than one CV condition).

The EQ-5D preference-based instrument

A random sample of the HSE respondents were asked to complete the EuroQol questionnaire (N = 26,679).[8] This is a generic preference-based measure of health commonly used to obtain health state valuations. It has five health dimensions with three levels each describing a total of 243 health states. Patients complete a one page questionnaire to assign them to a health state and the preference-weighted algorithm is then applied to obtain the corresponding EQ-5D index score. The weights for the EQ-5D preference-based index used in the current study were obtained (based on time trade off valuations) from the UK general public.[9] The index covers the range -0.594 to 1 whereby -0.594 represents the most severe impairment on all five dimensions and 1 represents no problems on any dimension. The minimal important difference (MID), defined as the smallest difference in score which patients perceive as beneficial, is |0.074|.[10] The EQ-5D has to be completed by patients with different health conditions in order to obtain mean values for each condition.

Statistical methods

Standard descriptive techniques were used (mean, range, standard error) and the significance of any potential difference in mean EQ-5D values for either gender, presence of CVD, type of CV condition, or time since event was assessed using independent t-tests ($p = 0.05$). The EQ-5D index was regressed onto age, sex and history of CVD using ordinary least square (OLS) techniques. The model is of the form:

$$EQ = \beta + \beta_1 x_i + \beta_2 y_i + \beta_3 z_i + \varepsilon \text{ whereby}$$

EQ represents the EQ-5D preference-based index, *i* represents individual respondents, β represents the vector of unknown variables, *x* represents the vector of demographs (age and sex), *y* represents the vector of health conditions (given a history of just one CV condition: angina within the previous year, heart attack within the previous year, stroke within the previous year, angina prior to the previous year, heart attack prior to the previous year, stroke prior to the previous year; given a history of greater than one CV condition: angina within the previous year, heart attack within the previous year, stroke within the previous year, angina prior to the previous year, heart attack prior to the previous year, stroke prior to the previous year), *z* represents the vector of cross-products and ε represents the stochastic error term of the regression (the residual).

History of CVD and sex were entered as dummy variables with zero representing no history of a CV condition and female respectively. As no history of CVD was the reference category a negative coefficient was expected for the regression coefficients for the various health conditions. Based on evidence in the literature suggesting males have a higher QoL than females, the coefficient for sex was expected to be positive.

Analyses were performed in SPSS (v12) and the models were constructed in STATA (v6). Models were compared using the variance explained by the model (adj. R^2) and standard descriptive statistics (mean, sd, range) of the individual predicted values. The predictive ability of the model was assessed

using the mean error (ME), the mean absolute error (MAE), the root mean squared error (RMSE) and the proportion of values within the MID.[10] As we were interested in estimating mean cohort values to populate health states within a model as opposed to individual patient level values, the model was also assessed in terms of ability to predict mean values for sub-groups (age, history of CV condition(s) and time since event).

RESULTS

The mean age of all participants with EQ-5D data (n = 26,679) is 48 years (range 16-98) and 44% (11,837) are male. The mean age of respondents (n = 1,599) who report a doctor's diagnosis of CVD is 68 years (range 19-97) and 56% (897/1599) are male. The prevalence of CVD is low below the age of 50 years (<1%) compared to prevalence in the older group (14%), and is higher in males than females of the same age reflecting the increased risks in these cohorts. The mean duration of time since a doctor's diagnosis of CVD is 10 years (median: 10 years).

The data were sub-grouped according to type and history of CV conditions: just angina, just heart attack, just stroke, or any combination of these (Figure 1). Of the 1,599 with a doctor's diagnosis of CVD, 963 (57% male) have a history of angina, 652 (67% male) have a history of a heart attack and 522 have a history of a stroke (49% male). 63 (53% male) have a history of both angina and stroke, 323 (72% male) have a history of both angina and heart attack, 32 (59% male) have a history of both a heart attack and a stroke, and 60 (72% male) have a history of all three conditions. 643/1599 (56% male) of individuals with a history of CVD report they had at least one event in the previous 12 months. For angina, the majority (516/963) reported an event within the previous 12 months, but for heart attack and stroke this was 94/428 and 67/585 respectively.

INSERT Figure 1: Number of respondents with a doctor's diagnosis of CVD sub-grouped by history of condition and time since last event

Health state utility values: univariate results

The EQ-5D scores cover the full range (mean: 0.860; range: -0.59 to 1) and 58% (15409/26679) score the maximum value of 1. There is a significant difference (Table 1) in the mean EQ-5D scores for males compared with females (males EQ-5D = 0.87, females EQ-5D = 0.850; p <0.001). There is also a significant difference (p <0.001) in the mean EQ-5D scores for those with no history of CVD (EQ-5D = 0.870) compared with those with a history of CVD (EQ-5D = 0.650), and in those who reported an event within the previous 12 month period (EQ-5D = 0.589) compared with those who experienced an event prior to this (EQ-5D = 0.716; p <0.001). There is a trend in the data (Figure 2) suggesting CVD has a larger detriment on HSUVs for younger aged cohorts when compared to individuals with no history of CVD, particularly for individuals who reported an event within the previous 12 months.

INSERT Table 1: Mean EQ-5D scores sub-grouped by type and number of CV conditions

There is a significant difference in the mean HSUV for individuals with a history of one CV condition (N = 1,121; EQ-5D = 0.691) compared with those with a history of more than one CV condition (N = 478; EQ-5D = 0.604, p <0.001). The mean HSUVs for individuals with a history of just angina (n = 517), just heart attack (n = 237) or just stroke (n = 367) are 0.692, 0.740 and 0.660 respectively. For individuals with a history of more than one condition, the mean HSUVs for individuals with angina (n = 446), heart attack (n = 415) and stroke (n = 155) are 0.609, 0.605 and 0.562 respectively.

When sub-grouping according to time since the last CV event, there is a significant difference in the HSUVs for individuals who report at least one CV event in the previous 12 months (n = 643, mean EQ-5D = 0.590) compared to those who report a CV event prior to this (n=956, mean EQ-5D = 0.716; p <0.001). For individuals who reported just one event in the previous 12 months (N=610; EQ-5D = 0.597), there is a significant difference in the mean HSUVs for individuals with a history of just one CV condition (N = 378; EQ-5D = 0.626) compared with those with a history of more than one CV condition (N = 232; EQ-5D = 0.550, p <0.005).

INSERT Figure 2: Mean HSUVs sub-grouped by time since CV event

Exploring the relationship between HSUVs and clinical events

The results of the OLS multivariate regression between the EQ-5D preference-based index, history of CVD (either angina, heart attack or stroke given a history of just one CV condition; and either angina, heart attack or stroke given a history of more than one CV condition) and time since the most recent event (either within the previous 12 months or prior to the previous 12 months) is provided in Table 2.

INSERT Table 2: Results of the OLS multivariate regression showing the relationship between the EQ-5D preference-based index, patient characteristics, type and time of reported CV events

With regard to the effect of the clinical events, the coefficients are significant and negative for all events reported during the previous 12 months, illustrating the large detrimental effect on QoL during the first 12 months after an event. All coefficients for the health states describing no event reported within the previous 12 months are also significant and negative, showing there is a long term detrimental effect beyond the initial period after an event. The coefficients for the health states for individuals with greater than one CV condition are also larger in magnitude than the corresponding data for individuals with a history of just one CV condition demonstrating the additional detriment associated with a history of more than one CV condition. For individuals with a history of just one CV condition, angina has the largest detrimental effect during the first 12 months (-0.173), heart attack has the smallest effect (-0.018), and for individuals with a history of more than one CV condition, angina has the largest detriment on QoL (-0.308).

Looking at the predicted HSUVs for the full dataset, the scores (Table 2) range from 0.035 to 0.962 (mean = 0.873) compared to the observed range of -0.59 to 1.00 (mean = 0.860). With a MAE of 0.145

and RMSE of 0.215, just 31% of values are predicted within the MID. However, as the results are to be used to populate a cohort level model, we are more interested in the model's ability to predict mean health state values accurately. When sub-grouping by one year age bands (n = 901) and by 10 year age bands (Table 3) taking into account history of CVD disease (n = 48), the predicted values have a ME (MAE, RMSE) of 0.037 (0.151, 0.218) and 0.001 (0.057, 0.072) respectively with 41% and 67% of values correct to within the MID (|0.074|). Similarly, when predicting the mean EQ-5D scores for the sub-groups split by health condition and time since event (Table 4), the model predicts 12/13) of mean values within the MID.[10]

INSERT: Table 3: Observed and predicted mean EQ-5D scores for the 13 health states defined by type of CV history and time since event

INSERT: Table 4: Errors in predicted values for sub-groups of data

DISCUSSION

This study is the first to use a single data source (N = 26,679) in the UK to obtain HSUVs for health states most frequently used in CVD economic models, taking into account both the time since the most recent event and history of CV condition(s). Our results show there is a significant difference ($p < 0.05$) in the EQ-5D scores according to age, sex, CV history, time since CV event, and both the type and number of CV condition(s). The regression model will enable analysts to populate health states in economic models assessing primary prevention interventions using a baseline quality of life adjusted for age and sex from individuals with no history of CVD, and health states in economic models assessing secondary prevention interventions where individuals enter the model with a reduction in quality of life associated with the long term effects of CVD. We provide additional information to enable analysts to sample from these data in probabilistic analyses (Appendix 1).

There are, however, limitations with the dataset which may have implications with regard to the generalisability of the results. We use the self-reported responses to a doctor's diagnosis of CV disease, time of event (i.e. within the previous 12 months or prior to this), and the number and type of CV condition. This will inevitably introduce a degree of uncertainty in the results generated. In addition, HSE samples exclude individuals in nursing homes or hospitals. This may introduce a bias as individuals in private households are likely to be more independent, and the time since the last event is likely to be longer when compared to counterparts in residential homes or hospitals.

Our data show HSUVs for individuals with a history of angina or heart attack range from 0.56 to 0.77 or 0.53 to 0.74 respectively depending on the time since previous event and the history of other CV conditions. These data are comparable with values reported in the literature: EQ-5D = 0.50 for patients (n = 188) with refractory angina,[11] EQ-5D = 0.67 at baseline and 0.74 at 12 months for unstable angina/non ST-segment elevation myocardial infarction,[12] and EQ-5D = 0.683 and 0.718 respectively at six weeks and one year after discharge from hospital in patients experiencing a heart attack.[13] The existing evidence describing HSUVs for stroke are more diverse. One study reports values ranging from EQ-5D = 0.33 for patients (n=43) on discharge to a care home to EQ-5D = 0.60 for patients (n = 50) 12 months after discharge to their own home.[14] A second study reports mean values ranging from EQ-5D = 0.5907 at 6 weeks after stroke to EQ-5D = 0.6510 at 12 months after discharge (n = 153) for patients randomised to a stroke unit (n = 52), a stroke team (n = 152) or domiciliary care (n = 153).[15] However, as observed in our data (EQ-5D range: 0.417 (CI: 0.567, 0.715) to 0.668 (CI: 0.632, 0.704), there was a large variation (sd > 0.30) in the HSUVs in both studies.

The data were sub-grouped according to history of different CV conditions: just angina, just heart attack, just stroke, or a combination of these (Figure 2). While heart attacks and strokes are distinct time constrained medical events, angina is an ongoing condition characterised by periods of pain in the chest area. The condition encompasses a wide spectrum and severity ranges from mild discomfort on exercising to severe pain requiring urgent medical attention. As the majority of CV models do not define different health states to differentiate between the different classes of angina, for the purpose of this exercise, we identified individuals with a history of angina by using the positive response to a doctor's diagnosis of angina. While this ensures we cover the full spectrum of the condition weighted

by severity prevalence in the general population, this does introduce some ambiguity by what is meant by "experienced angina within the previous 12 months".

It is common for EQ-5D index scores to exhibit a ceiling effect, with a significant number of respondents rating themselves as being in full health, i.e. responses of 11111 on the original questionnaire give a preference-based tariff score of 1. To account for the non-linear distribution of the data, we explored Tobit and censored least absolute deviation (CLAD) models with upper censoring at 1.0 (results not shown). However, we found the OLS model we report was more accurate in predicting HSUVs than either the Tobit or CLAD models obtained.

CONCLUSION

While there are limitations with the sample used in the current study, the results show HSUVs differ by age, sex, type of CV condition, time since CV event and the number of concurrent CV conditions. The results of the regressions will enable analysts to populate the most frequently defined health states in CVD models.

ACKNOWLEDGEMENT

We are grateful to Health Survey for England for allowing us access to the data used in this study. The research was based on the Health Survey for England, 2003 and the Health Survey for England 2006, produced by the Joint Health Surveys Unit of Social and Community Planning and University College London, sponsored by the Department of Health, and supplied by the UK Data Archive. The data are Crown copyright.

REFERENCES

1. Ara R, Pandor A, Stevens J, Rees A, Rafia R. Early high-dose lipid-lowering therapy to avoid cardiac events: a systematic review and economic evaluation. Health Technol Assess. 2009 Jul;13(34):1-118.

2. Ara R, Pandor A, Tumur I, Paisley S, Duenas A, Williams R, Rees A, Wilkinson A, Durrington P, Chilcott J. Cost effectiveness of ezetimibe in patients with cardiovascular disease and statin intolerance or contraindications: a Markov model. Am J Cardiovasc Drugs. 2008;8(6):419-27.

3. Ward S, Lloyd Jones M, Pandor A, Holmes M, Ara R, Ryan A, Yeo W, Payne N. A systematic review and economic evaluation of statins for the prevention of coronary events. Health Technol Assess. 2007 Apr;11(14):1-160, iii-iv. Review.

4. National Institute of Health and Clinical Excellence. Guide to the methods of Technology Appraisal. 2008.

5. Sullivan PW, Ghushchyan V. Preference-based EQ-5D index scores for chronic conditions in the United States. Med Decis Making 2005;26:410-420.

6. Joint Health Surveys Unit of Social and Community Planning Research and University College London, Health Survey for England, 2003 [computer file]. 3rd Edition. Colchester, Essex: UK Data Archive [distributor], 2005. SN: 5098.

7. Joint Health Surveys Unit of Social and Community Planning Research and University College London, Health Survey for England, 2006 [computer file]. 3rd Edition. Colchester, Essex: UK Data Archive [distributor], 2008. SN: 5809.

8. EuroQol Group. EuroQol-a new facility for the measurement of health-related quality of life. Health Policy. 1990;16:199–208.

9. Dolan P, Gudex C, Kind P, Williams A. The time trade-off method: results from a general population study. Health Econ. 1996;5(2):141–54.

10. Walters SJ, Brazier JE. Comparison of the minimally important difference for two health state utility measures: EQ-5D and SF-6D Quality of Life Research (2005) 14:1523–1532.

11. Campbell HE, Tait S, Buxton MJ, Sharples LD, Cain N, Schofield PM, Wallwork J. A UK trial-based cost-utility analysis of transmyocardial laser revascularization compared to continued medical therapy for treatment of refractory angina pectoris European Journal of Cardio-thoracic Surgery 20 (2001) 312:318.

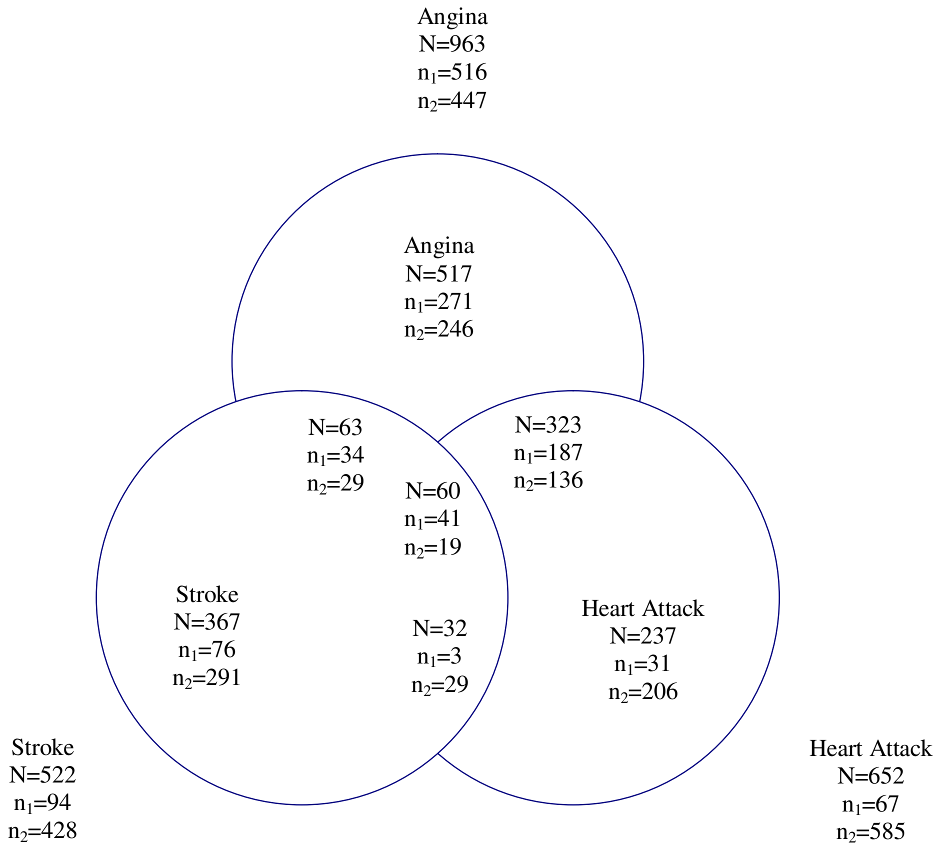
12. Kim J, Henderson RA, Pocock SJ, Clayton T, Sculpher MJ, Fox KAA and RITA-3 Trial Investigators. Health-related quality of life after interventional or conservative strategy in patients with unstable angina or non–ST-segment elevation myocardial infarction: One-year results of the third randomized intervention trial of unstable angina (RITA-3) J. Am. Coll. Cardiol. 2005;45;221-228.

13. Lacey EA, Walters SJ. Continuing inequality: gender and social class influences on self perceived health after a heart attack J. Epidemiol. Community Health 2003;57;622-627.

14. Leeds L, Meara J, Hobson P. The impact of discharge to a care home on longer term stroke outcomes. Clinical Rehabilitation 2004; 18: 924-928.

15. Patel A, Knapp M, Perez I, Evans A, Kalra L, Alternative Strategies for Stroke Care Cost-Effectiveness and Cost-Utility Analyses From a Prospective Randomized Controlled Trial Stroke. 2004;35:196-204.

Figure 1: Number of respondents with a doctor's diagnosis of CVD (N = 1,599) sub-grouped by history of condition and time since last event



N = number of individuals with a doctors diagnosis of the condition at any time
n_1 = number of individuals experiencing an event in the previous 12 months
n_2 = number of individuals not experiencing an event in the previous 12 months

Figure 2a: Mean EQ-5D scores sub-grouped by history of CVD and time since CV

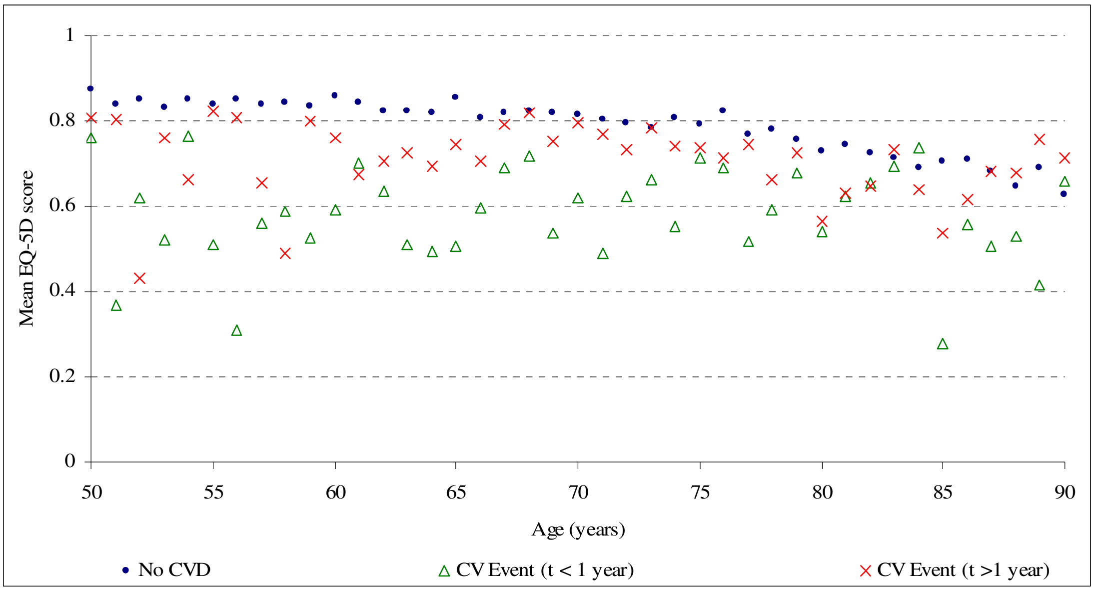


Figure 2b: Mean EQ-5D scores sub-grouped by history of CVD and number of CV conditions

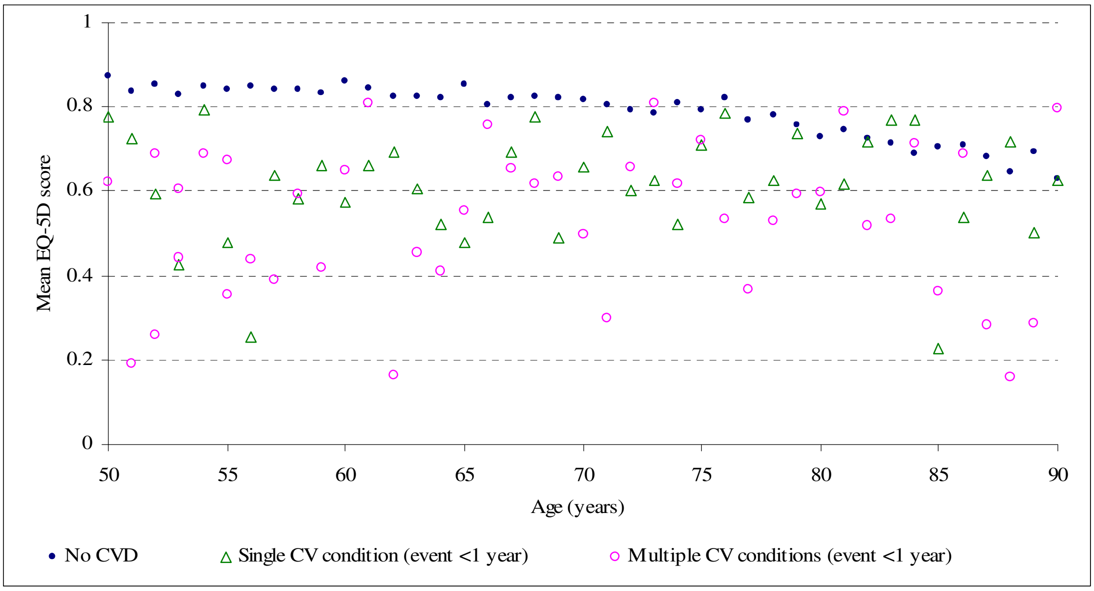


Table 1:Mean EQ-5D scores sub-grouped by type and number of CV conditions

Sub-group	N	EQ-5D mean	LCI	UCI	p-value
Male	11,837	0.8720	0.8680	0.8759	<0.001
Female	14,842	0.8496	0.8459	0.8534	
No history of CVD	25,080	0.8719	0.8692	0.8746	<0.001
History of any CVD (t = ever)	1,599	0.6653	0.6499	0.6806	
History of CVD and CV event < 12 months	640	0.5894	0.5641	0.6147	<0.001
History of CVD and no CV event < 12 months	956	0.7161	0.6975	0.7346	
Sub-grouped by the number of CV conditions and time since event					
History of just one CV condition	1,121	0.6909	0.6734	0.7083	<0.001
History of > one CV condition	478	0.6040	0.5737	0.6255	
History of just one CV condition, and a CV event < 12 months	378	0.6258	0.5941	0.6576	<0.005
History of > one CV condition, and a CV event < 12 months	232	0.5500	0.5081	0.5920	
Individuals with a history of just one CV condition, sub-grouped by condition (as defined by health states in a primary prevention model)					
History of just angina, angina < 12 months	271	0.6148	0.5770	0.6526	<0.001
History of just angina, no angina < 12 months	246	0.7748	0.7451	0.8046	
History of just heart attack, heart attack < 12 months	31	0.7213	0.6303	0.8123	0.700
History of just heart attack, no heart attack < 12 months	206	0.7418	0.7033	0.7803	
History of just stroke, stroke < 12 months	76	0.6262	0.5515	0.7010	0.301
History of just stroke, no stroke < 12 months	291	0.6684	0.6323	0.7044	
Individuals with a history of more than one CV condition, sub-grouped by condition (as defined by health states in a secondary prevention model)					
History of angina + other CV condition(s), angina < 12 months	213	0.5563	0.5127	0.5999	<0.001
History of angina + other condition(s), angina < 12 months, no event < 12 months	184	0.7149	0.6710	0.7589	

History of heart attack + other condition(s), heart attack < 12 months	11	0.5250	0.3038	0.7462	0.113
History of heart attack + other condition(s), no event < 12 months	184	0.6847	0.6378	0.7316	
History of stroke + other condition(s), stroke < 12 months	8	0.4170	0.5668	0.7146	0.072
History of stroke + other condition(s), no event < 12 months	77	0.6407	0.1032	0.7308	
Comparing the effect on HSUVs for events within the last 12 months, sub-grouped by history of number of CV conditions					
History of just angina, angina < 12 months	213	0.5563	0.5127	0.5999	<0.05
History of angina + other CV condition(s), angina < 12 months	271	0.6148	0.5770	0.6526	
History just heart attack, heart attack < 12 months	11	0.5250	0.3038	0.7462	<0.005
History heart attack + other CV condition(s), heart attack < 12 months	237	0.7391	0.7038	0.7744	
History just stroke, stroke < 12 months	76	0.6262	0.5515	0.7010	0.170
History stroke + other CV condition(s), stroke < 12 months	155	0.5618	0.5082	0.6155	

Table 2: Results of the models exploring the relationship between the EQ-5D preference-based index, patient characteristics, type and time of reported CV events

	OLS		
	Beta	se	Sig
Male	0.0246479	0.0027	**
Age	-0.0008459	0.0004	*
Age^2	-0.0000224	0.0000	**
Age*CVD	-0.0001961	0.0003	[a]
History of just angina, angina < 12 months	-0.1726541	0.0268	**
History of just angina, no angina < 12 months	-0.0184099	0.0271	[b]
History of just heart attack, heart attack < 12 months	-0.0864901	0.0446	*
History of just heart attack, no heart attack < 12 months	-0.0595563	0.0274	*
History of just stroke, stroke < 12 months	-0.1609510	0.0336	**
History of just stroke, no stroke < 12 months	-0.1255921	0.0262	**
History of angina + other CV condition(s), angina < 12 months	-0.2370623	0.0278	**
History of angina + other condition(s), no event < 12 months	-0.0801248	0.0300	**
History of heart attack + other condition(s), heart attack < 12 months	-0.2560437	0.0689	**
History of heart attack + other condition(s), no event < 12 months~			
History of stroke + other condition(s), stroke < 12 months	-0.3324484	0.0805	**
History of stroke + other condition(s), no event < 12 months	-0.0634942	0.0306	*
Constant	0.9569784	0.0089	**
min	0.0353		
mean	0.8727		
max	0.9624		
Adj. R^2	0.2138		
Errors in predicted values for individual level patient (n = 26,679) responses			
ME	0.0131		
MAE	0.1446		
RMSE	0.2151		
$\|0.074\|^{\#}$	31%		

|0.05|	15%

Significance: * p <0.05; ** p<0.01, [a] p = 0.574, [b] p = 0.497, [c]p = 0.639; [#] = MID, ~ as history of angina + other condition(s), no event < 12 months. See Appendix 1 for variance covariance matrix.

Table 3: Errors in predicted values for sub-groups of data

	1 year age bands (n = 901)	10 year age bands and history of CV condition (s) (n = 48)
ME	0.0274	0.0014
MAE	0.1508	0.0571
RMSE	0.2184	0.0722
|0.074|#	41%	67%
|0.05|	32%	46%

= MID

Table 4: Observed and predicted mean EQ-5D scores for the 13 health states defined by type of CV history and time since event

	n	Observed	Predicted	Error
No history of CVD	25,080	0.872	0.878	0.007
history of just angina, angina < 12 months	271	0.615	0.621	0.006
history of just angina, no angina < 12 months	246	0.775	0.778	0.003
history of just heart attack, heart attack < 12 months	31	0.721	0.724	0.003
history of just heart attack, no heart attack < 12 months	206	0.742	0.745	0.004
history of just stroke, stroke < 12 months	76	0.626	0.632	0.006
history of just stroke, no stroke < 12 months	291	0.668	0.673	0.005
history of angina + other CV condition(s), angina < 12 months	213	0.556	0.559	0.003
history of angina + other condition(s), angina < 12 months, no event < 12 months	184	0.715	0.714	-0.001
history of heart attack + other condition(s), heart attack < 12 months	11	0.525	0.529	0.004
history of heart attack + other condition(s), no event < 12 months	184	0.685	0.715	0.031
history of stroke + other condition(s), stroke < 12 months	8	0.417	0.419	0.002
history of stroke + other condition(s), no event < 12 months	77	0.641	0.723	0.082
MAE				0.012
RMSE				0.025
<|0.074|			12/13	92%
<|0.05|			12/13	92%

[#] = MID

Appendix: Var-Covar Matrix used for generating samples from the regression

	sex	age	age2	agecv	rjang	nrjang	rjhrt	nrjhrt	rjstr	nrjstr	rmang	cnrmamh
Sex	0.0000070											
Age	0.0000000	0.0000002										
Age^2	0.0000000	0.0000000	0.0000000									
Age*CVD	0.0000000	0.0000000	0.0000000	0.0000001								
The next six rows relate to health states with a history of just one CV condition												
rjang	0.0000001	-0.0000014	0.0000000	-0.0000081	0.0007190							
nrjang	-0.0000008	-0.0000014	0.0000000	-0.0000081	0.0005480	0.0007340						
rjhrt	-0.0000018	-0.0000014	0.0000000	-0.0000078	0.0005290	0.0005280	0.0019920					
nrjhrt	-0.0000017	-0.0000014	0.0000000	-0.0000080	0.0005390	0.0005380	0.0005190	0.0007520				
rjstr	0.0000003	-0.0000012	0.0000000	-0.0000080	0.0005370	0.0005360	0.0005170	0.0005270	0.0011300			
nrjstr	0.0000001	-0.0000013	0.0000000	-0.0000080	0.0005380	0.0005370	0.0005180	0.0005280	0.0005260	0.0006850		
The next five rows relate to health states with a history of > one CV condition												
rmang	-0.0000012	-0.0000014	0.0000000	-0.0000082	0.0005520	0.0005510	0.0005320	0.0005420	0.0005400	0.0005410	0.0007700	
nrmang	-0.0000021	-0.0000014	0.0000000	-0.0000082	0.0005550	0.0005540	0.0005340	0.0005440	0.0005420	0.0005430	0.0005570	0.0008980
rmhrt	0.0000006	-0.0000013	0.0000000	-0.0000083	0.0005600	0.0005590	0.0005390	0.0005490	0.0005480	0.0005490	0.0005630	0.0005650
rmstr	-0.0000023	-0.0000010	0.0000000	-0.0000093	0.0006330	0.0006310	0.0006090	0.0006210	0.0006190	0.0006200	0.0006360	0.0006390
nrmstr	0.0000012	0.0000000	0.0000000	-0.0000002	0.0000130	0.0000120	0.0000120	0.0000120	0.0000120	0.0000120	0.0000120	-0.0003260
Constant	-0.0000025	-0.0000032	0.0000000	-0.0000004	0.0000240	0.0000240	0.0000260	0.0000250	0.0000200	0.0000230	0.0000250	0.0000260

History of just one CV condition: Rjang = history of just angina, angina < 12 months, nrjang = history of just angina, no angina < 12 months, rjhrt = history of just heart attack, heart attack < 12 months, nrjhrt = history of just heart attack, no heart attack < 12 months, rjstr = history of just stroke, stroke < 12 months, nrjstr = history of just stroke, no stroke < 12 months

History of > one CV condition: rmang = history of angina + other CV condition(s), angina < 12 months, nrmang = history of angina + other condition(s), angina < 12 months, no event < 12 months, rmhrt = history of heart attack + other condition(s), heart attack < 12 months, rmstr = history of stroke + other condition(s), stroke < 12 months, nrmstr = history of stroke + other condition(s), no event < 12 months