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Using electronic health records to predict costs and outcomes in stable coronary artery disease

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Statistical package: R (V.3.1.0) and the R package flexsurv (V.0.3) were used to conduct the statistical analysis in the paper.

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ABSTRACT

Objectives To use electronic health records (EHR) to predict lifetime costs and health outcomes of patients with stable coronary artery disease (stable-CAD) stratified by their risk of future cardiovascular events, and to evaluate the cost-effectiveness of treatments targeted at these populations.

Methods The analysis was based on 94 966 patients with stable-CAD in England between 2001 and 2010, identified in four prospectively collected, linked EHR sources. Markov modelling was used to estimate lifetime costs and quality-adjusted life years (QALYs) stratified by baseline cardiovascular risk.

Results For the lowest risk tenth of patients with stable-CAD, predicted discounted remaining lifetime healthcare costs and QALYs were £62 210 (95% CI £33 724 to £90 043) and 12.0 (95% CI 11.5 to 12.5) years, respectively. For the highest risk tenth of the population, the equivalent costs and QALYs were £35 549 (95% CI £31 679 to £39 615) and 2.9 (95% CI 2.6 to 3.1) years, respectively. A new treatment with a hazard reduction of 20% for myocardial infarction, stroke and cardiovascular disease death and no side-effects would be cost-effective if priced below £72 per year for the lowest risk patients and £646 per year for the highest risk patients.

Conclusions Existing EHRs may be used to estimate lifetime healthcare costs and outcomes of patients with stable-CAD. The stable-CAD model developed in this study lends itself to informing decisions about commissioning, pricing and reimbursement. At current prices, to be cost-effective some established as well as future stable-CAD treatments may require stratification by patient risk.

INTRODUCTION

Cardiovascular disease (CVD) is a leading cause of mortality in England with approximately a third of all deaths attributed to it.[1] The combination of an ageing population and improvements in survival after acute coronary syndrome[2] has resulted in a large and growing number of patients with stable coronary artery disease (stable-CAD). CVD has, therefore, also become a major source of morbidity and healthcare resource use: there are >5 million people living with CVD in England costing the National Health Service (NHS) more than £30 billion per year.[3 4] The stable-CAD population serves as an important example of a patient population suffering from a long-term condition. With such conditions becoming increasingly prevalent, questions regarding their prognosis have become increasingly important.[5 6] The prognosis for patients with stable-CAD is particularly topical with new treatments,[7] and new applications of existing treatments,[8] currently undergoing phase III trials in this patient population.

Thus far, the majority of models to estimate the costs and health effects of CVD have focused on primary prevention,[9 10] have made predictions only over relatively short time horizons (up to 10 years)[11] so are unable to estimate lifetime costs and health effects, are based on selected samples[12] potentially biasing baseline risk and cost estimates hence limiting their generalisability or fail to model all relevant endpoints and their interdependence.[13] The use of linked electronic health records (EHR) can help to address many of these limitations in modelling the costs and outcomes in chronic diseases providing a source of long-term data, capturing a wide range of clinical endpoints and recording resource use in a real-world setting. As far as we are aware, there has been limited use of EHR in decision modelling.

The availability of primary care data linked with hospitalisation data, disease-specific registries and mortality data makes the English NHS an attractive setting in which to develop and demonstrate our approach for modelling the long-term costs and outcomes of chronic disease. The CALIBER (CArdiovascular disease research using Linked BEspoke studies and Electronic Health Records) data platform[14] used in this study combines these key datasets and has been shown to be a valuable resource for cardiovascular epidemiology.[12 15–17] This paper reports on the use of CALIBER to model prognosis in patients with stable-CAD, estimating their baseline risk of experiencing further CVD events and then predicting both costs and key health outcomes over the lifetime of these patients stratified by their baseline CVD risk. In doing so, the model provides a better understanding of the implications of this growing population under current standards of care as well as a framework for the evaluation of the cost-effectiveness of new treatment strategies, potentially differentiated by risk group.

METHODS

Patient population

The model was based on the analysis of 94 966 patients with stable-CAD from the CALIBER

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collaboration. CALIBER links primary care data from the Clinical Practice Research Datalink with EHR from the Myocardial Ischaemia National Audit Project Registry, hospital inpatient records from Hospital Episode Statistics and cause-specific mortality from the Office for National Statistics. The CALIBER dataset has been described in detail by Denaxas *et al*.[14] Patients with stable-CAD were defined as those patients in the CALIBER dataset who were event free for at least 6 months after having had unstable angina, ST elevation myocardial infarction (STEMI) or non-STEMI (NSTEMI) or those patients with stable angina or other coronary heart disease (CHD) diagnoses. The median follow-up of these patients was 4.2 (IQR 1.9–6.9) years, during which 16 783 patients died and 8203 patients experienced one or more non-fatal coronary outcomes.

Endpoints

The primary clinical endpoints were first occurrences of non-fatal myocardial infarction (MI), ischaemic stroke and haemorrhagic stroke, as well as CVD and non-CVD mortality. Other clinical endpoints were CVD and non-CVD mortality following a non-fatal event. These were combined to produce the primary economic outputs from the model which were quality-adjusted life years (QALYs) as well as total and CVD-specific costs, each predicted over the remaining lifetime of the patient. The model was also used to produce estimates of event rates and disease progression over time stratified by baseline CVD risk.

Model

A state transition model (shown in figure 1) was developed to capture the natural history of patients with stable-CAD. The structure of the model was determined with reference to both previous models in CVD[13] and expert clinical advice. All patients entered the model in the stable-CAD state and progressed through the model until they experienced either CVD or non-CVD mortality. The time horizon of the model was, therefore, the patient's remaining lifetime. The model captured time varying and age-dependent risks, costs and health-related quality of life (HRQoL) in 90-day segments. Costs and HRQoL were attached to model states and, in order to stratify by patients' baseline risk, adjusted for patient covariates at baseline as well as for age and for time elapsed following non-fatal events. Model predicted costs, life years and QALYs were discounted at 3.5% per annum in keeping with the guidelines in England.[18] While only first occurrences of non-fatal CVD events were explicitly modelled, further non-fatal events were implicitly captured in the time varying risk, cost and HRQoL estimates.

Statistical modelling of risk equations

Rapsomaniki *et al*[19] developed, tested and validated a range of prognostic models for patients with stable-CAD using the CALIBER dataset. We built on their recommended prognostic model, using it as the basis for the risk equations underpinning the prediction of the five primary clinical endpoints. Using the prognostic factors and missing data imputation algorithm of Rapsomaniki *et al*[19] we estimated various parametric survival models (generalised gamma, lognormal, Weibull, exponential) for each of the five endpoints. For each endpoint the best fitting parametric model was selected as determined by the Akaike information criteria. Predictions resulting from the selected models were assessed for plausibility by clinical experts (AT, CPG, ADS, HH). Key prognostic factors included in the models were demographic measures (age, sex, social deprivation), stable-CAD subtype (stable angina, unstable angina, STEMI, NSTEMI and other CHD), use of long-acting nitrates, whether coronary artery bypass graft or percutaneous coronary intervention (PCI) had been performed in the 6 months following CAD diagnosis, previous MI, smoking, blood pressure, diagnosis of hypertension, diabetes, lipids,

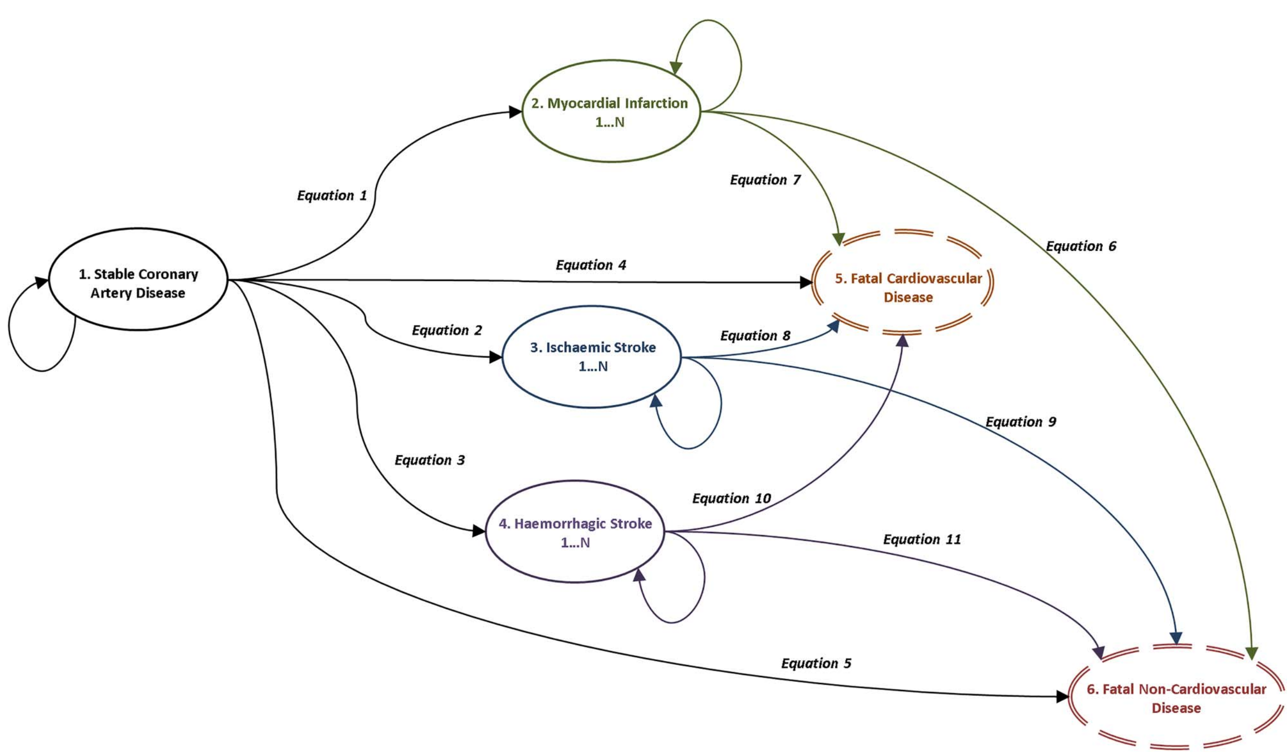

Figure 1 Structure of the Markov model and the role played by the 11 risk equations that we use to model disease progression.

Table 1 Patient characteristics by risk group

Risk group	Lowest risk	2	3	4	5	6	7	8	9	Highest risk	Overall
Patient average covariate profiles based on tenths of patient population grouped by 5-year risk of composite CVD event estimated at baseline											
Number of patients in dataset	10 035	9903	9797	9626	9516	9455	9382	9335	9249	8668	94 966
5-year risk (%; average across patients)	3.69	5.70	7.37	9.15	11.20	13.71	17.14	22.14	30.42	52.37	16.68
5-year risk (%; at average covariate values)	3.46	5.43	6.95	8.53	10.36	12.57	15.64	20.07	27.23	44.18	11.64
Sociodemographic characteristics											
Sex (% female)	64	48	42	39	37	37	38	42	44	46	44
Age (years if male)	49	55	59	62	65	67	71	74	77	81	67
Age (years if female)	53	62	67	70	73	75	78	80	83	87	72
Age (weighted average)	52	59	62	65	68	70	73	76	80	84	69
Most deprived quintile (%)	15	17	18	19	20	21	21	22	22	24	20
Stable-CAD diagnosis (%)											
NSTEMI	0	1	3	5	8	10	12	17	23	43	10
STEMI	1	4	8	12	13	14	13	9	6	4	7
Unstable angina	10	13	12	12	12	12	13	15	17	15	14
Stable angina	78	65	56	49	43	39	37	34	29	18	47
Non-specific CHD	11	17	20	22	24	24	25	26	25	20	23
Stable-CAD severity (%)											
PCI in past 6 months	9	12	13	14	13	13	11	9	6	4	9
CABG in past 6 months	9	7	6	5	5	4	4	3	2	1	4
Previous/recurrent MI	2	6	10	14	18	23	26	29	32	43	18
Use of nitrates	10	16	19	21	24	28	33	37	43	56	28
CVD risk factors											
Smoking status (%)											
Current smoker	31	35	36	37	38	38	37	35	32	30	35
Ex-smoker	27	30	31	32	32	33	34	34	34	34	32
Never smoked	41	35	33	31	30	29	29	31	33	36	33
Hypertension (%)	69	70	71	71	72	74	76	79	83	87	76
Diabetes (%)	4	8	10	12	14	16	18	21	24	32	16
Total cholesterol (mmol/L)	4.95	4.91	4.84	4.79	4.74	4.74	4.70	4.68	4.64	4.54	4.79
HDL (mmol/L)	1.41	1.37	1.35	1.35	1.35	1.35	1.36	1.37	1.37	1.35	1.37
CVD comorbidities (%)											
Heart failure	5	7	9	12	15	19	27	37	52	73	26
Peripheral arterial disease	1	2	3	4	6	8	10	13	16	25	8
Atrial fibrillation	3	5	7	9	10	13	16	21	29	43	15
Stroke	0	1	1	2	3	5	8	14	22	39	9
Non-CVD comorbidities (%)											
Chronic kidney disease	2	2	3	4	4	5	7	9	12	20	7
Chronic obstructive pulmonary disease	20	20	20	21	22	23	25	27	28	30	23
Cancer	4	5	6	7	8	9	11	13	14	12	9
Chronic liver disease	0	1	1	1	1	1	1	1	1	1	1
Psychosocial characteristics											
Depression at diagnosis (%)	20	17	15	15	14	14	15	17	18	21	17
Anxiety at diagnosis (%)	7	6	6	7	7	7	8	8	10	12	8
Biomarkers											
Heart rate (bpm)	72	71	71	71	71	71	72	73	74	76	72
Creatinine (mmol/L)	88	92	95	96	98	100	101	104	109	125	100
White cell count (10^9/L)	6.81	7.05	7.19	7.31	7.44	7.54	7.62	7.76	7.88	8.22	7.46
Haemoglobin (g/100 mL)	1.43	1.43	1.42	1.41	1.39	1.37	1.35	1.32	1.28	1.22	1.36

Deprivation measured by index of multiple deprivation, 2010. All values in table are means. Percentage of missing data imputed: smoking status 32%, total cholesterol 54%, HDL 55%, heart rate 78%, creatinine 38%, white cell count 56% and haemoglobin 53%.
CABG, coronary artery bypass graft; CAD, coronary artery disease; CHD, coronary heart disease; CVD, cardiovascular disease; HDL, high-density lipoprotein; MI, myocardial infarction; NSTEMI, non-ST segment elevation myocardial infarction; PCI, percutaneous coronary intervention; stable-CAD, stable coronary artery disease; STEMI, ST segment elevation myocardial infarction.

CVD comorbidities (heart failure, peripheral arterial disease, atrial fibrillation, stroke), non-CVD comorbidities (chronic renal disease, chronic obstructive pulmonary disease, cancer, chronic liver disease), psychosocial factors (depression, anxiety) and clinically assessed biomarkers (heart rate, white cell count, haemoglobin, creatinine).

Risk equations for the six subsequent events, namely, CVD and non-CVD mortality following non-fatal MI, ischaemic stroke and haemorrhagic stroke, were estimated in a similar way. However, due to the greatly reduced numbers of events observed, these use only sex and age at time of non-fatal event as covariates. Non-CVD mortality beyond the maximum

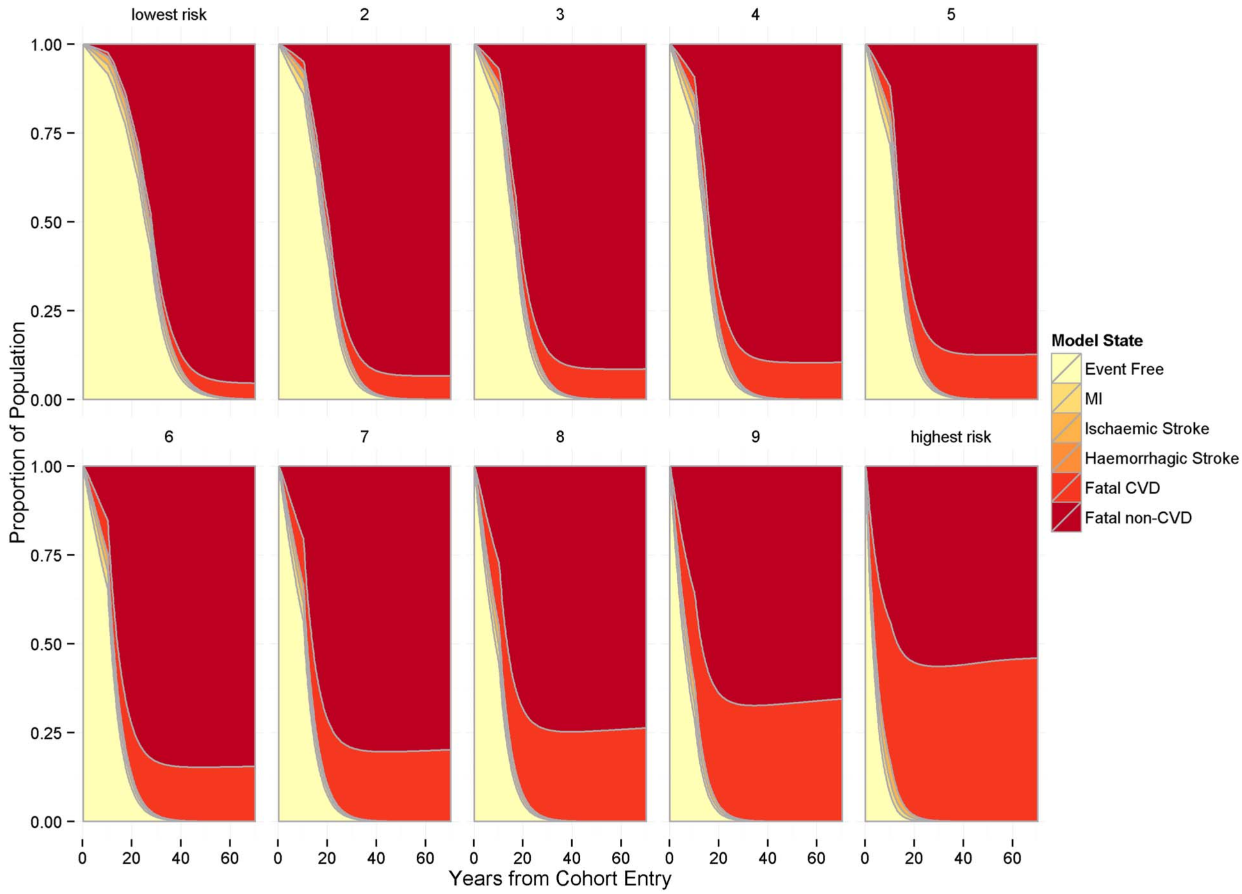

Figure 2 Proportion of patients in each of the six model states over time as predicted by the Markov model used in this study. Each plot within the panel represents a risk decile as categorised by the baseline 5-year CVD event risk ranging from the lowest risk decile (1) to the highest risk decile (10). As can be seen in the plots the model is run until all the patients in the cohort have experienced either a fatal CVD or a fatal non-CVD event. CVD, cardiovascular disease; MI, myocardial infarction.

follow-up in the CALIBER dataset (10 years) was based on age/sex-specific non-CVD mortality from national life tables.[20]

These risk equations were developed into cumulative incidence functions which were then combined using a competing risks framework to account for the interdependence of the outcomes. We used methods outlined by Putter *et al*[21] that acknowledge state transition probabilities are affected by the event being modelled and also by the other events that could occur from a given health state. Survival models were estimated using R (V.3.1.0) and the R package flexsurv (V.0.3).

Resource use and costs

Healthcare resource use was estimated directly from the CALIBER dataset. A panel was constructed using a 90-day cycle length for patients with stable-CAD in CALIBER capturing resource use in terms of hospital episodes, use of drugs, diagnostic tests and primary care consultations. Costs were attached to this resource use using the NHS reference costs,[22] NHS prescription cost analysis[23] and Personal Social Services Research Unit (PSSRU) unit costs for primary care[24] datasets. All costs were calculated from a health systems perspective and based on the price year 2011/2012. Panel data models were used to estimate patient costs adjusted for the prognostic factors used in the model, as well as for the key CVD events in the model. This allowed us to attach costs to model states adjusted for baseline patient characteristics and event history.

Health-related quality of life

HRQoL estimates were not available from the CALIBER dataset. Instead a catalogue of EQ-5D scores for the UK[25] was used to calculate age-specific, condition-specific and event-specific HRQoL. These were attached to states in the model to calculate patient-specific estimates of remaining lifetime QALYs.

Analysis

Given that the model was designed to be used with a heterogeneous population, results were produced stratified by risk group. The 5 year baseline risk of experiencing at least one CVD event for each patients with stable-CAD in the CALIBER dataset was predicted based on the estimated risk equations given the patient's baseline covariate values as input parameters. The baseline values were those from the prognostic factors used in the risk equations measured at the point that the patient entered into the stable-CAD cohort. Patients were ranked by risk predictions and grouped into 10 equally sized risk groups. Model results were calculated at the mean baseline covariate value across patients within each risk group. In addition, estimates were predicted for a representative patient within each of the 10 risk groups demonstrating both the population-level and patient-level results produced by the model. The model was evaluated probabilistically by means of a Monte Carlo simulation run for 1000 iterations in order to incorporate and characterise the uncertainty in the model inputs.[26]

The model was used to calculate life expectancy, QALYs, total healthcare costs and CVD-specific healthcare costs for standard care, as well as for indicative new treatments assumed to reduce CVD risks by 10%, 20%, 30% and 40%. The indicative treatments were assumed to have constant costs and treatment effects, no direct effect on the risk of non-CVD mortality and no side-effects. When interpreting the results of this analysis it should be recognised that these assumptions may not hold in practice. The results were used to estimate the maximum price that could be charged for the new treatments in each of the risk groups assuming a range of cost-effectiveness thresholds between £10 000 and £40 000 per QALY. National Institute for Health and Care Excellence (NICE) employ a threshold ranging between £20 000 and £30 000 per QALY[18] for considering an intervention cost-effective in England, and recent empirical evidence provides a central estimate of the threshold in England of approximately £13 000 per QALY.[27]

Further details about the (a) patients with stable-CAD in the CALIBER dataset, (b) the economic model, (c) the estimation of costs and transition probabilities for use in the model, (d) the risk equations used to estimate model transition probabilities, (e) patient profiles for the 10 representative patients and (f) extended tables of results can be found in the accompanying online supplementary material appendices. The full model source code detailing all calculations performed in the model, including the model input parameters for the 10 risk groups and 10 representative patients as well as detailed instructions on how to run the model, are available from: https://github.com/miqdadasaria/caliber-scad-model.

RESULTS

The average baseline patient covariates by risk group are shown in table 1. For the cohort, the mean age at cohort entry was 67 years for males and 72 years for females. Stable angina (47%) was the most frequent stable-CAD subgroup and STEMI (7%) the least. One in 10 patients had received PCI within the previous 6 months, over a quarter had heart failure, nearly one in five had depression at the time of stable-CAD diagnosis and one in six had atrial fibrillation.

There was large variation in CVD risk between the lowest and highest risk groups, with an absolute difference in 5-year risk between the lowest and highest risk group of 40.7%. The risk of clinical events positively correlated with age, higher levels of CVD risk factors (such as hypertension and diabetes) and higher prevalence of CVD comorbidities. There were no obvious trends in the key modifiable CVD risk factors such as the lipid profile.

The modelled progression of CVD over time by risk group is shown in figure 2. Higher risk groups were predicted to have much higher levels of CVD mortality compared with lower risk groups, whereas the latter were predicted to remain event free for a much longer period and were more likely to die of non-CVD-related causes.

Summary model results by risk group are shown in table 2. The risk of all non-fatal events increased with overall CVD risk, and the risk of non-CVD mortality declined with overall CVD risk. Lower risk patients were estimated to have greater remaining life expectancy, QALYs and healthcare costs. For low risk patients (5-year CVD risk 3.5%), the remaining expected discounted lifetime healthcare costs were £62 210, and patients had 12.0 expected discounted QALYs remaining. For the highest risk group (5-year CVD risk 44.2%), the remaining expected discounted lifetime healthcare costs were £35 549, and patients had 2.8 remaining expected discounted QALYs.

Figure 3 shows the maximum price that the health system should be willing to pay for new treatments targeted at each risk

Table 2 Model results by risk group

Risk group (95% CI)	Lowest risk	2	3	4	5	6	7	8	9	Highest risk
Model results split by 5-year risk of composite CVD event										
Life years	26.81 (26.63 to 26.98)	19.62 (19.48 to 19.80)	17.34 (17.18 to 17.53)	15.63 (15.47 to 15.84)	14.26 (14.08 to 14.49)	13.03 (12.83 to 13.28)	11.92 (11.69 to 12.21)	10.48 (10.21 to 10.84)	8.52 (8.19 to 8.94)	5.51 (5.09 to 6.02)
Discounted life years*	16.77 (16.69 to 16.85)	13.66 (13.58 to 13.75)	12.5 (12.41 to 12.61)	11.56 (11.46 to 11.68)	10.76 (10.65 to 10.89)	9.99 (9.87 to 10.15)	9.26 (9.11 to 9.44)	8.27 (8.10 to 8.50)	6.90 (6.67 to 7.17)	4.67 (4.38 to 5.01)
QALYs	19.11 (18.06 to 19.93)	13.97 (13.26 to 14.54)	12.29 (11.66 to 12.80)	11.01 (10.45 to 11.48)	9.97 (9.44 to 10.41)	9.03 (8.53 to 9.45)	8.13 (7.65 to 8.53)	6.99 (6.54 to 7.40)	5.50 (5.09 to 5.89)	3.34 (3.01 to 3.72)
Discounted QALYs*	12.04 (11.45 to 12.53)	9.77 (9.31 to 10.17)	8.9 (8.47 to 9.25)	8.18 (7.78 to 8.51)	7.55 (7.17 to 7.87)	6.95 (6.58 to 7.25)	6.34 (5.98 to 6.63)	5.55 (5.21 to 5.84)	4.47 (4.16 to 4.76)	2.85 (2.60 to 3.13)
Total costs (£,1000s)	117 (65 to 168)	81 (55 to 108)	73 (54 to 92)	68 (54 to 83)	65 (53 to 76)	62 (54 to 71)	61 (55 to 69)	59 (54 to 65)	54 (49 to 60)	43 (38 to 49)
Discounted total costs (£,1000s)*	62 (34 to 90)	51 (34 to 67)	48 (36 to 60)	47 (37 to 56)	45 (38 to 53)	45 (39 to 51)	45 (41 to 50)	45 (41 to 49)	42 (39 to 46)	36 (32 to 40)
CVD costs (£,1000s)	72 (29 to 114)	52 (30 to 74)	48 (31 to 64)	45 (33 to 58)	43 (34 to 53)	42 (35 to 50)	42 (36 to 48)	41 (37 to 46)	38 (34 to 43)	31 (27 to 35)
Discounted CVD costs (£,1000s)*	38 (15 to 60)	32 (19 to 46)	31 (21 to 41)	31 (23 to 39)	31 (24 to 37)	31 (26 to 36)	31 (27 to 35)	31 (28 to 34)	30 (27 to 33)	26 (23 to 29)
Time to first event (years)	24.55 (24.31 to 24.76)	17.80 (17.64 to 17.95)	15.62 (15.47 to 15.75)	13.98 (13.85 to 14.11)	12.67 (12.54 to 12.8)	11.49 (11.36 to 11.62)	10.43 (10.29 to 10.57)	9.00 (8.85 to 9.15)	7.06 (6.91 to 7.22)	4.07 (3.90 to 4.23)
MI as primary endpoint (%)	6.00 (5.55 to 6.49)	7.11 (6.73 to 7.49)	8.06 (7.72 to 8.43)	8.94 (8.61 to 9.29)	9.84 (9.50 to 10.15)	10.70 (10.39 to 11.01)	11.59 (11.28 to 11.90)	12.33 (12.01 to 12.64)	12.89 (12.57 to 13.22)	14.3 (13.87 to 14.73)
Ischaemic stroke as primary endpoint (%)	5.51 (5.01 to 6.06)	5.70 (5.34 to 6.11)	6.06 (5.73 to 6.43)	6.39 (6.07 to 6.74)	6.80 (6.48 to 7.11)	7.37 (7.05 to 7.68)	8.29 (7.95 to 8.63)	9.31 (8.96 to 9.68)	10.07 (9.72 to 10.43)	9.97 (9.58 to 10.38)
Haemorrhagic stroke as primary endpoint (%)	0.67 (0.48 to 0.89)	0.67 (0.54 to 0.81)	0.71 (0.59 to 0.82)	0.72 (0.62 to 0.84)	0.74 (0.65 to 0.84)	0.76 (0.67 to 0.86)	0.79 (0.70 to 0.89)	0.78 (0.69 to 0.88)	0.7 (0.61 to 0.81)	0.48 (0.40 to 0.57)
CVD mortality (%)	4.48 (3.45 to 5.55)	6.60 (5.45 to 7.51)	8.52 (7.22 to 9.47)	10.39 (8.97 to 11.44)	12.63 (11.07 to 13.85)	15.48 (13.78 to 17.07)	20.17 (18.17 to 22.63)	26.29 (23.61 to 30.18)	34.46 (30.65 to 39.32)	45.95 (41.34 to 50.07)
Non-CVD mortality (%)	95.46 (94.40 to 96.49)	93.40 (92.49 to 94.55)	91.48 (90.53 to 92.78)	89.60 (88.56 to 91.03)	87.37 (86.15 to 88.93)	84.52 (82.93 to 86.22)	79.83 (77.37 to 81.83)	73.71 (69.82 to 76.39)	65.54 (60.68 to 69.35)	54.05 (49.93 to 58.66)

*Discounted figures presented in this table are discounted at 3.5% per annum.
CVD, cardiovascular disease; MI, myocardial infarction; QALYs, quality-adjusted life years.

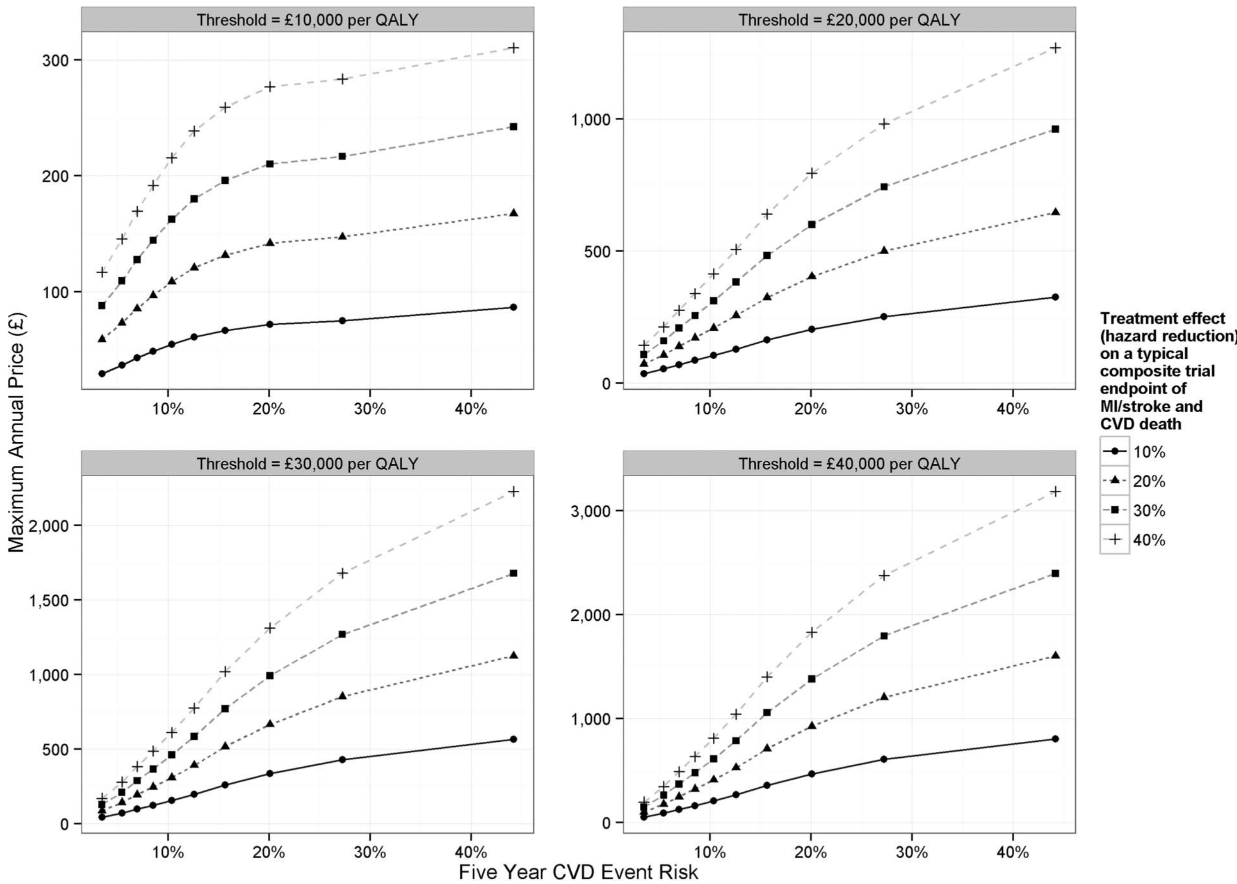

Figure 3 Maximum annual price for therapies as a function of baseline 5-year CVD event risk. Each plot within the panel shows the results at a given cost-effectiveness threshold ranging from £10 000 to £40 000 per QALY. The lines within the plots represent the different efficacies of our modelled treatments having hazard reductions on CVD endpoints associated with them ranging from 10% to 40%. CVD, cardiovascular disease; MI, myocardial infarction; QALYs, quality-adjusted life years.

group that reduce CVD hazards by between 10% and 40%. This maximum price increased with both increasing baseline risk and with larger treatment effects in terms of proportionate risk reduction.

More detailed breakdowns of these results as well as results presented for the representative patients drawn from each risk group can be found in online supplementary appendix (f).

DISCUSSION

We report the first comprehensive lifetime model of stable-CAD based on long-term EHR data. The model encompasses a full range of CVD endpoints and accounts for the interdependence of CVD risks among patients with stable-CAD. The sample sizes, duration of follow-up and the large number of endpoints and risk factors captured by the multisource EHR dataset (CALIBER) provided the opportunity to build a model which more fully and accurately captured the biological and medical nuances of such a condition. In quantifying the expected costs, life expectancy and quality-adjusted life expectancy of patients with stable-CAD, this analysis provides a means to plan budgets and services for such patients in the NHS in particular, and in health systems in developed countries more generally.

We found that at NICE's lower bound cost-effectiveness threshold (£20 000 per QALY), a treatment aimed at the lowest risk patients (5-year risk of 3.5%), would be cost-effective with annual prices up to £36, £72, £108 or £143 if the treatment was able to reduce CVD risk by 10%, 20%, 30% and 40%, respectively. For the highest risk patients (5-year risk of 44.2%), the respective maximum prices would be £325, £645, £961 or £1269. For comparison, statins commonly used by these patients reduce CVD risk by approximately a third[28] and cost £16 per patient per year,[29] whereas the annual cost of new anti-platelet agents can be up to £712 per patient per year.[29] These estimates provide a basis for developers of new medications and health technologies for stable-CAD to define necessary effect sizes that they will need to demonstrate to be considered value for money by health systems.

In this study it has been shown that using EHR data, in combination with an analytical model such as that used by NICE in the English NHS, provides a powerful framework within which to assess the cost-effectiveness of new technologies. In the many healthcare systems with constrained budgets, cost-effectiveness analysis provides a means of comparing the additional health benefits from a new intervention with the health other patients forgo because expenditure on other types of treatments is necessarily curtailed in order to finance the new intervention (opportunity costs).[30] The current analysis uses this approach as a basis for identifying the minimum treatment effect a new intervention for stable-CAD will have to achieve at a given price (or the maximum price for a given treatment effect) and cost-effectiveness threshold. These necessary treatment effects and prices will inevitably vary according to patients' underlying risk of CVD events.

There are very few comparable studies that focus on modelling the costs and health effects over the lifetime of patients with stable-CAD. Studies that we are aware of in this area[13] are typically based on short-term trial data, model only a subset of the relevant CVD endpoints and make predictions over short time horizons. Models suitable for the economic evaluation of health technologies in disease areas such as CVD where there are substantial mortality impacts need to estimate all relevant healthcare costs and health outcomes over the remaining lifetimes of patients. This is why in our study, despite having 10 years of follow-up data, we still required a model to extrapolate up to a maximum of 60 years beyond our data to estimate total lifetime costs and consequences for the full cohort of modelled patients. Limitations of our study are that HRQoL data were not recorded in the CALIBER dataset and so had to be drawn from external studies; that changes in prognostic risk factors over time were not explicitly modelled; instead the equations underpinning our model were informed by the baseline values of these risk factors; the dataset we used did not contain left ventricular ejection fraction which is an important prognostic factor in this patient population; and that the long follow-up period of our dataset may mean that the modelled risk equations may not fully reflect contemporary risk levels in the population. Additionally a number of structural assumptions had to be made for modelling purposes and these are detailed in online supplementary appendix (b).

The model we have produced allows policy makers to quantify and understand both the health and the cost burden of stable-CAD and serves as a basis for evaluating the cost-effectiveness of new treatments targeted at reducing CVD risk in this population. Our results suggest that, for the vast majority of patients with stable-CAD, it is likely that low cost interventions to improve adherence to existing secondary prevention drugs should be prioritised over high cost new treatments. It is also notable from our results that, even among the groups with the highest CVD risk, more patients are predicted to die of non-CVD-related causes than of CVD-related causes. This highlights the vital role of primary care in the holistic management of both CVD and non-CVD risk for these patients.

Key messages

What is already known on this subject?

- Electronic health records have been shown to be useful in prognosis, but thus far their use in decision analytic models and cost-effectiveness analysis has been limited.
- The recent improvement in acute coronary syndrome survivorship means that a growing number of people are living with cardiovascular disease.

What might this study add?

- This study provides the first lifetime model of the costs and health effects of patients with stable coronary artery disease based on long-term linked electronic health records, predicting key cardiovascular endpoints for these patients and capturing the interdependence of these endpoints.

How might this impact on clinical practice?

- This model can be used to evaluate and to target appropriately new treatments as they emerge for this patient population as well as to inform commissioning, pricing and reimbursement decisions.

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Contributors MA conducted the main data analysis and drafted and revised the paper and is the guarantor of the study. SW, SP and MS advised on health economic issues and helped to design the model. ADS, CPG, AT and HH advised on clinical issues. KRA, MC and AM advised on statistical issues. AT and HH were responsible for the overall grant from the NIHR. All authors commented on drafts of the paper. All authors, external and internal, had full access to all of the data (including statistical reports and tables) in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. MA affirms that the manuscript is an honest, accurate and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

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Competing interests All authors have completed the Unified Competing Interests form at http://www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare that MA, SW, SP, CPG, ADS, MC and HH have nothing to disclose. AM reports and currently sits on one of the NICE Technology Appraisal Committees. MS received grant funding for the work reported in this paper from the National Institute for Health Research. Outside of the published work, he has received personal fees from various pharmaceutical and medical device companies some of which have products used in cardiovascular disease. AT reports personal fees from Menarini Pharmaceuticals, other from Servier, outside the submitted work. KRA reports personal fees from ABPI, Roche, Novo Nordisk, AstraZeneca, Janssen, Allergan, outside the submitted work.

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Data sharing statement An extensive supplementary appendix with additional analyses has been submitted alongside the paper and the model source code and instructions on how to use it to reproduce the results in the paper are available at https://github.com/miqdadasaria/caliber-scad-model.

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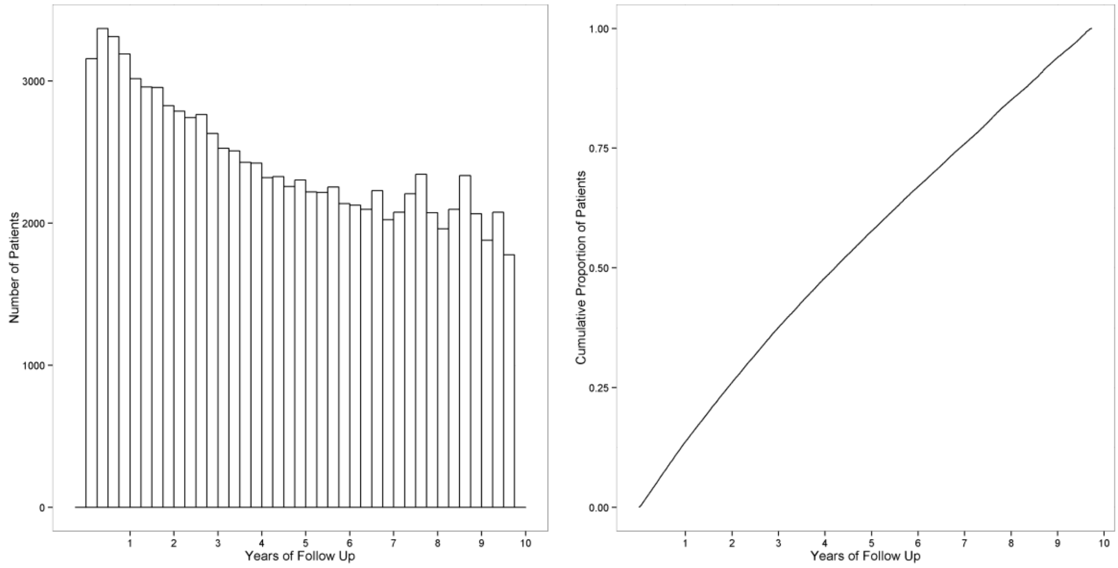
Modelling lifetime costs and health outcomes for patients with stable coronary artery disease

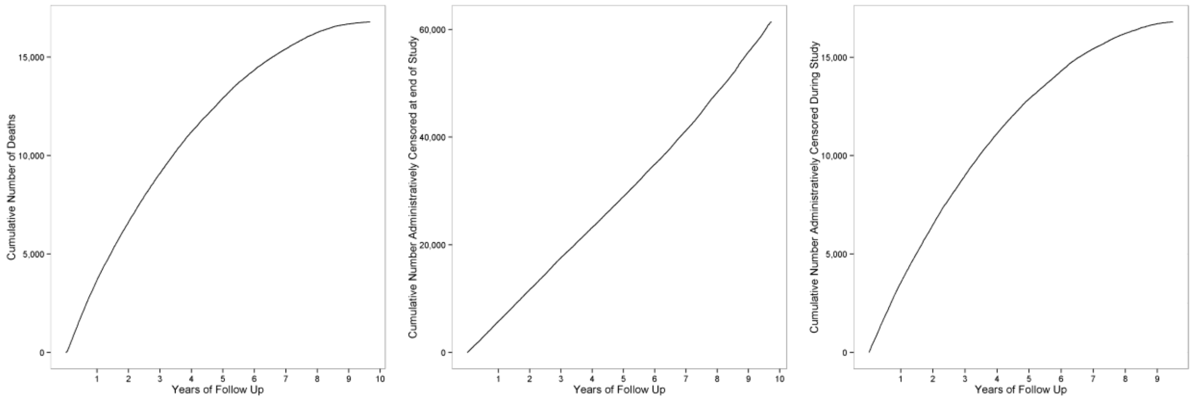
Appendix A: CALIBER dataset

Patient population consists of patients with stable coronary artery disease (SCAD) in our linked dataset who have had no event in the 180 days post SCAD diagnosis. This is a total of 94,966 patients observed between January 2001 and March 2010. This comprises 12,839 patients with unstable angina as their index event, 6,276 patients with STEMI as their index event, 9,304 patients with NSTEMI as their index event, 45,038 patients with stable angina and 21,509 patients with other CHD diagnoses. Median follow up for these patients was 4.2 (IQR 1.9 to 6.9) years though patients were censored from the dataset throughout the 10 year follow up period as described in the figure.



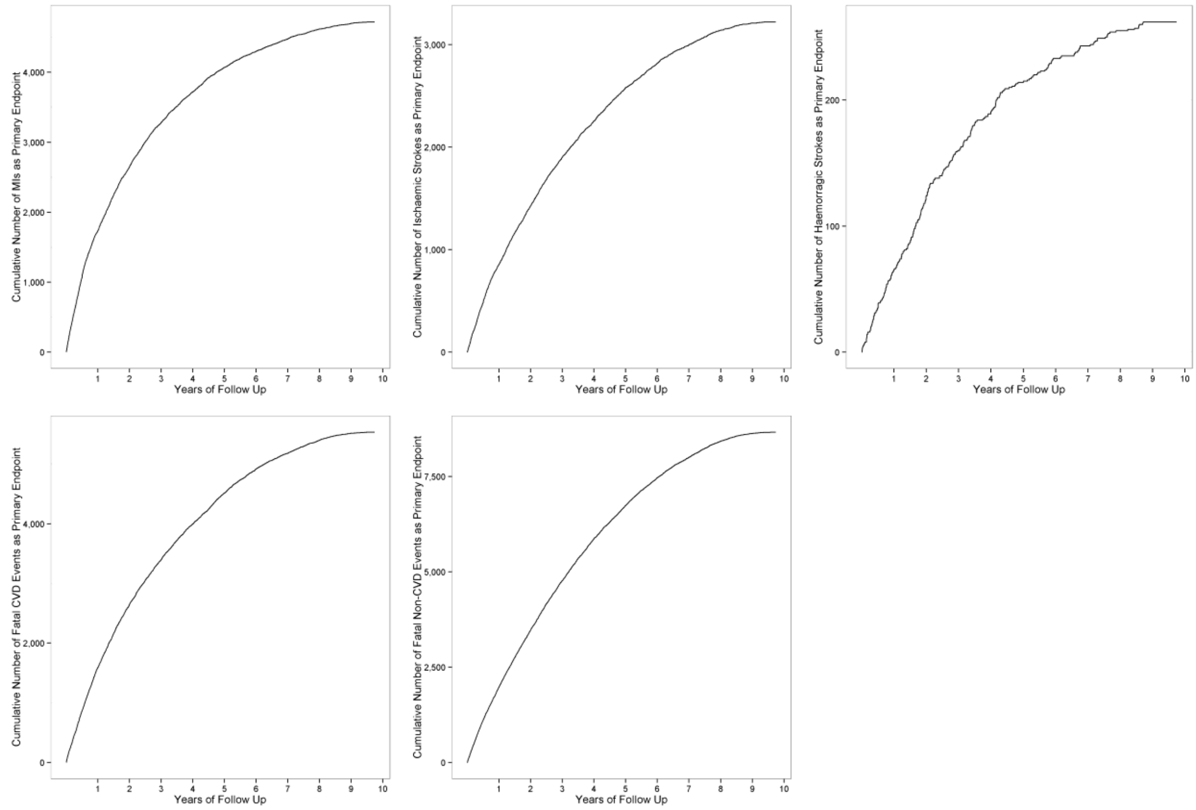
Reasons for leaving the dataset were either death (16,783 of which 6,800 were from cardiovascular causes) or administrative censoring both during (16,790) and at the end of (61,393) the period of observation. Administrative censoring during the period of observation was due to patients moving away from a primary care practice that contribute data to the CPRD dataset.

Not all patients entered the cohort at the start of the study in 2001, rather patients entered the cohort once they had experienced a qualifying event during the study period. We counted events and the time from cohort entry to experience each event at the patient level. Where multiple records for a death were recorded in the datasets constituting CALIBER the earliest date attributed to the death was attributed as the patient's date of death. For other events repeated recordings of the same event within a 30 day window were considered to be records for the same event and the earliest recorded event date was attributed to that event for the patient.



We looked at primary endpoints of type myocardial infarction (4,719), ischaemic stroke (3,222), haemorrhagic stroke (262), death from cardiovascular causes (5,536) and death from non-cardiovascular causes (8,663) as first events experienced subsequent to cohort entry. The validation study by Herrett E, Shah A. D, Boggon R, et al. (Completeness and diagnostic validity of recording acute myocardial infarction events in primary care, hospital care, disease registry, and national mortality records: cohort study. BMJ 2013 http://www.ncbi.nlm.nih.gov/pubmed/23692896) demonstrates the importance of using information from the multiple sources across the linked EHR datasets to determine the occurrence of events, we follow this recommendation with our events being defined using the CPRD, HES, ONS and MINAP codes described on the CALIBER data portal: https://www.caliberresearch.org/portal.

The distributions of times to primary endpoints measured in the time from entry into the cohort are shown in the figures below.



We also looked at deaths from CVD and non-CVD causes following a non-fatal primary endpoint. After an MI we observe 813 CVD deaths and 760 non-CVD deaths, after ischaemic stroke we observe 410 CVD deaths and 525 non-CVD deaths and after haemorrhagic stroke we observe 41 CVD deaths and 35 non-CVD deaths in the CALIBER dataset.

Multiple imputation was used to handle missing covariate values in the CALIBER dataset that was used in estimating the models. Full details about the imputation model used can be found in this technical appendix:
http://eurheartj.oxfordjournals.org/content/ehj/suppl/2013/12/01/eht533.DC1/eht533supp1.pdf

Our study protocol was submitted to CPRD and approved by the Independent Scientific Advisory Committee (ISAC) on the 4th December 2012. Protocol title “Cost effectiveness analyses of treatments for patients with chronic stable angina”, protocol number 12_132R.

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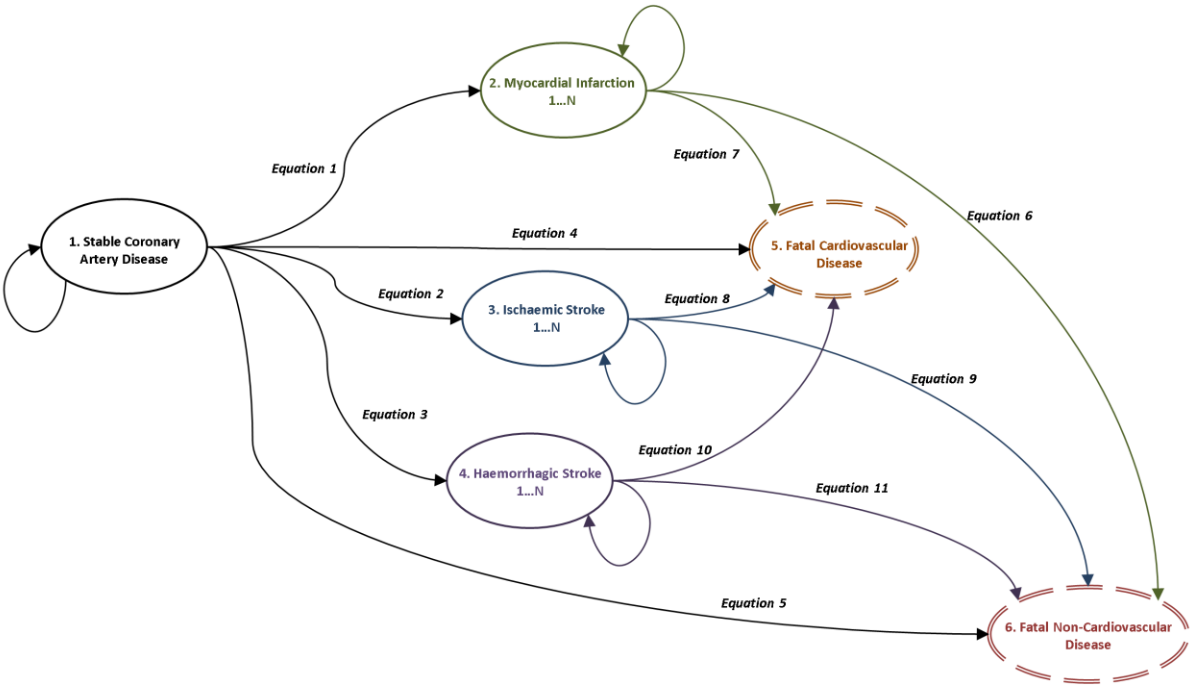
Appendix B: CALIBER economic model

A Markov state transition model was constructed to model the pathway of stable coronary artery disease (SCAD) patients. The model captured the primary endpoints of first MI, ischaemic stroke, haemorragic stroke. fatal CVD event and non-fatal CVD events after the cohort entry date as well as any subsequent CVD or non-CVD mortality. All patients start the model in the SCAD state and progress through the model until they die of either CVD related or non-CVD related causes. While only first occurrences of non-fatal CVD events are explicitly modelled, further non-fatal events are implicitly captured in the time varying risk, cost and HRQoL estimates used in the model.



The eleven risk equations corresponding to the model transitions were estimated using flexible parametric survival models. The detail of these estimated risk equations is provided in supplementary appendix (d). These risk equations were combined in a competing risks framework to account for the interdependence of the modelled events following the methods outlined in Putter et al (2007) [Tutorial in biostatistics: Competing risks and multi-state model in Statistics in Medicine 26:2389-2430]. This was used to estimate cumulative incidences of the transitions modelled which in turn was used to compute the transition probabilities in the Markov model.

Given that the risk equations for these events captured the time varying nature of the hazards (i.e. did not display constant hazards) we modelled the non-fatal primary endpoints as tunnel states. We implemented our model with a 90 day cycle length and attached costs and utilities to the states in the model. The 90 day cycle length we felt gave a good trade-off between capturing the time varying hazards and the granularity of resource use captured.

The non-linear nature of our model meant that we needed to run it probabilistically and average over the results to capture the uncertainty in the model input parameters appropriately. We ran the model for 1,000 iterations for each patient profile and treatment scenario combination. For each simulation of the model the coefficients in the risk-equations, cost equations and HRQL equations were resampled and model results were computed. The average across these simulated results comprise the central estimate for each patient profile and treatment combination with the variance in these simulated results providing the confidence intervals around these results.

A number of assumptions were made in the modelling process these include:

(a) Only first events were explicitly modelled with recurrent event implicitly captured in the time varying nature of costs and risks following events
(b) We assume current estimates of event rates are valid as predictions of future event rates
(c) For simulation in the PSA we assign a multivariate normal distribution to the costs and beta and gamma distributions to the constant level and event specific decrements in HRQL respectively.
(d) The following parametric models were assigned to the risk equations to extrapolate them and multivariate normal distributions were used to simulate the coefficients from these equations in the PSA

Risk Equation	**Parametric Model**
Equation 1: Stable-CAD to MI	Weibull
Equation 2: Stable-CAD to Stroke I	Weibull
Equation 3: Stable-CAD to Stroke H	Exponential
Equation 4: Stable-CAD to Fatal CVD	Weibull
Equation 5: Stable-CAD to Fatal non-CVD	Weibull
Equation 6: MI to Fatal CVD	Log Normal
Equation 7: MI to Fatal non-CVD	Generalised Gamma
Equation 8: Stroke I to Fatal CVD	Generalised Gamma
Equation 9: Stroke I to Fatal non-CVD	Generalised Gamma
Equation 10: Stroke H to Fatal CVD	Log Normal
Equation 11: Stroke H to Fatal non-CVD	Weibull

The model was run for a range of different patient and population profiles and a range of indicative treatment effects. To handle the computational burden involved the N8 supercomputer was used to run all iterations and scenarios in parallel.

The full model code in R along with UNIX shell scripts to run the model in parallel on a sun grid engine supercomputer is available at: https://github.com/miqdadasaria/caliber-scad-model

To run the model for a new patient / population profile the following patient characteristics must be defined in a csv file, with one patient per row and headings following the variable name column:

Variable Name	**Variable Description**	**Example Value Individual**	**Example Value Population**
Sex	Female=1, Male=0	1	0.398146
IMD5	Whether person lives in most deprived fifth of LSOAs	TRUE	0.190781
dx7CHD	SCAD index event other CHD	FALSE	0
dx7NSTEMI	SCAD index event NSTEMI	TRUE	0.641551
dx7STEMI	SCAD index event STEMI	FALSE	0.358449
dx7UA	SCAD index event Unstable Angina	FALSE	0
earlyPCI	PCI in last 6 months	TRUE	0.231131
earlyCABG	CABG in last 6 months	FALSE	0.064769
recurrent_mi	Previous/recurrent MI	TRUE	0.267824
nitrates_long	Use of Nitrates		0.270175
Smcatcurrent	Current Smoker	FALSE	0.279943
Smcatex	Ex-Smoker	FALSE	0.354583
Hypertension	Hypertension	TRUE	0.680935
Diabetes	Diabetes	TRUE	0.220554
hist_hf	History of Heart failure	FALSE	0.279316
hist_pad	History of Peripheral arterial disease	TRUE	0.107208
hist_af	History of Atrial fibrillation	FALSE	0.196657
hist_stroke	History of Stroke	FALSE	0
hist_renal	History of Chronic kidney disease	FALSE	0.10982
hist_copd	History of Chronic obstructive pulmonary disease	FALSE	0.235962
hist_cancer	History of Cancer	TRUE	0.112562

hist_liver	History of Chronic liver disease	FALSE	0.010969
Depression	Depression at diagnosis	TRUE	0.141029
hist_anxiety	Anxiety at diagnosis	FALSE	0.073257
age0_ori	Age	70	75.1106
pulse_rate_ori	Heart rate (b.p.m.)	75	70.00349
HDL_ori	HDL (mmol/L)	1.4	1.32259
TCHOL_ori	Total cholesterol (mmol/L)	4.8	4.218232
CREAT_ori	Creatinine (mmol/L)	90	105.7011
WCC_ori	White cell count (10^9/L)	7	7.638091
HGB_ori	Haemoglobin (g/100ml)	14	13.27026
sex:age0	Average age difference between men and women in population	NA	3.239488

Where all the SCAD index events are set to false the index event is taken to be stable angina, where all the smoking status variables are set to false the smoking status is taken to be never smoked. Population level values for these sets of grouped variables including the excluded category must sum to 1.

The model is then run by calling: *"RScript run_model.R <patient> <iteration> manual <path to csv file>"* from the command line.

Where <patient> indicates the patient profile to select from the csv file starting from 1, <iteration> represents the PSA iteration that you want the model to run for ranging between 1 and 10,000 (this will reference pre-computed realisations from the underlying input parameter distributions), manual indicates that you want to provide patient information using a csv file other options here are deciles and clinical to load up the patient profiles used to generate the results in the paper, finally <path to csv file> indicates the path from the working directory to the file where the patient profiles have been saved.

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Appendix C: Cost and Health Related Quality of Life Input Parameters

Panel data methods with time invariant covariates were used to estimate patient costs over each 90 day period. The costs for each individual in the CALIBER data set were calculated and partitioned into equal time periods, with the length of each period matching the 90 days cycle length of the model, to create a longitudinal data set of costs. Panel data estimates based on linear regression were then applied to estimate the costs for use in the model. Using these methods both an underlying background cost as well as an event specific cost for the events (captured using a dummy variable in the time period in which the event occurred) were calculated. Costs were adjusted based on important patient risk factors and co-morbidities to allow for the appropriate capturing of heterogeneity within the model. Aggregate costs were also estimated using the generalised linear model using a log link function to compare with the results generated from the linear model. Both methods gave similar results reassuring us that the linear model was appropriate to use for estimating costs for use in the model.

Mean costs were used in the model along with the cholesky decomposition of the estimated variance covariance matrix from the regression for use in the probabilistic sensitivity analysis.

Costs were assumed to follow a beta distribution.Costs were allocated to states in the model and adjusted for baseline co-variates as well as for patient age and time elapsed since previous non-fatal CVD event.

HRQL estimates were taken from the Sullivan et al (2011) catalogue. The uncertainty around the HRQL was inferred from the standard errors reported in the catalogue and was assumed to follow a gamma distribution.

As with costs the HRQL values were attached to model states and adjusted for baseline patient covariates and updated for patient age as patients progressed through the model.

Total Costs Mean Estimates

fatalCVD	fatalNONCVD	firsteventMI	MIdiabetes	firsteventMI2	MIdiabetes2	firsteventMI3	MIdiabetes3	firsteventMI4
2008	2240	5028	776	1282	1100	675	785	692

MIdiabetes4	feMI	feMIdiabetes	firsteventStroke_I	firsteventStroke_I2	firsteventStroke_I3	firsteventStroke_I4	feSTROKE_I	firsteventStroke_H
550	521	369	6215	1239	795	654	564	7011

firsteventStroke_H2	firsteventStroke_H3	firsteventStroke_H4	feSTROKE_H	age0	timeperiod	diabetes	hist_liver	hist_hf
1767	947	751	927	7	10	338	530	364

hist_af	hist_pad	hist_copd	hist_cancer	hist_renal	sex	CHD	NSTEMI	STEMI
186	327	231	331	756	-7	-20	157	-26

UA	_cons
153	341

Total Costs Cholesky Decomposition of Variance Covariance Matrix

	fatalCVD	fatalNONCVD	firsteventMI	MIdiabetes	firsteventMI2	MIdiabetes2	firsteventMI3	MIdiabetes3	firsteventMI4
fatalCVD	24.878								
fatalNONCVD	0.158	20.161							
firsteventMI	0.128	0.106	34.413						
MIdiabetes	0.019	0.045	-34.375	67.544					
firsteventMI2	-0.598	-0.417	3.408	0.020	36.673				
MIdiabetes2	-0.164	-0.051	-3.367	7.123	-36.638	72.441			
firsteventMI3	-0.276	-0.154	3.406	0.021	3.299	0.018	38.865		
MIdiabetes3	-0.099	-0.337	-3.361	7.102	-3.259	6.874	-38.830	77.096	
firsteventMI4	-0.245	-0.136	3.433	0.023	3.325	0.020	3.230	0.018	40.428
MIdiabetes4	-0.335	-0.057	-3.384	7.049	-3.281	6.823	-3.191	6.622	-40.392
feMI	-0.255	-0.194	3.554	0.040	3.443	0.037	3.345	0.035	3.214
feMIdiabetes	-0.131	-0.124	-3.471	7.076	-3.365	6.845	-3.273	6.641	-3.145
firsteventStroke_I	0.130	0.146	0.062	0.038	0.057	0.034	0.052	0.031	0.050
firsteventStroke_I2	-0.430	-0.498	0.066	0.040	0.061	0.036	0.057	0.033	0.055
firsteventStroke_I3	-0.279	-0.224	0.071	0.042	0.065	0.038	0.061	0.035	0.059
firsteventStroke_I4	-0.222	-0.239	0.075	0.044	0.070	0.040	0.066	0.037	0.064
feSTROKE_I	-0.277	-0.200	0.111	0.061	0.106	0.057	0.101	0.054	0.099
firsteventStroke_H	0.121	0.127	0.060	0.033	0.055	0.030	0.051	0.027	0.048
firsteventStroke_H2	-0.501	-0.572	0.061	0.034	0.056	0.031	0.053	0.029	0.051
firsteventStroke_H3	-0.703	-0.189	0.065	0.035	0.061	0.032	0.057	0.030	0.055
firsteventStroke_H4	0.003	-0.088	0.069	0.034	0.065	0.032	0.062	0.030	0.060
feSTROKE_H	-0.314	-0.153	0.106	0.050	0.101	0.048	0.097	0.046	0.095
age0	-0.012	-0.013	-0.003	-0.001	-0.002	-0.001	-0.001	-0.001	-0.001
timeperiod	-0.006	-0.008	-0.005	-0.002	-0.005	-0.002	-0.005	-0.002	-0.005
diabetes	-0.066	-0.025	0.196	-0.551	0.164	-0.468	0.141	-0.406	0.125
hist_liver	-0.087	-0.328	-0.026	-0.051	0.004	-0.023	-0.006	-0.013	-0.010
hist_hf	-0.271	-0.193	-0.035	-0.035	-0.023	-0.023	-0.017	-0.013	-0.012
hist_af	-0.098	-0.068	0.006	0.015	0.003	0.008	0.009	0.009	0.008
hist_pad	-0.146	-0.097	-0.077	-0.063	-0.063	-0.043	-0.052	-0.042	-0.046
hist_copd	0.003	-0.113	-0.023	-0.008	-0.020	-0.008	-0.013	-0.005	-0.013
hist_cancer	0.011	-0.470	-0.014	0.004	-0.011	0.005	-0.004	0.004	-0.002
hist_renal	-0.078	-0.066	-0.007	-0.046	-0.002	-0.018	0.002	-0.003	0.001
sex	0.071	0.063	0.040	0.016	0.034	0.011	0.030	0.011	0.026
CHD	-0.036	0.043	-0.047	-0.013	-0.040	-0.012	-0.038	-0.011	-0.035
NSTEMI	-0.220	-0.045	-0.240	-0.195	-0.219	-0.160	-0.191	-0.136	-0.170
STEMI	-0.025	-0.001	-0.171	-0.053	-0.157	-0.049	-0.145	-0.046	-0.131
UA	-0.048	-0.002	-0.083	-0.034	-0.068	-0.033	-0.063	-0.029	-0.057
_cons	-0.075	-0.075	-0.084	0.056	-0.061	0.051	-0.049	0.044	-0.038

	MIdiabetes4	feMI	feMIdiabetes	firsteventStroke_I	firsteventStroke_I2	firsteventStroke_I3	firsteventStroke_I4	feSTROKE_I	firsteventStroke_H
MIdiabetes4	80.331								
feMI	0.034	17.361							
feMIdiabetes	6.365	-17.053	35.516						
firsteventStroke_I	0.029	0.201	0.104	36.008					
firsteventStroke_I2	0.031	0.225	0.114	3.121	37.899				
firsteventStroke_I3	0.033	0.247	0.124	3.103	3.004	40.821			
firsteventStroke_I4	0.035	0.268	0.133	3.115	3.017	3.007	42.796		
feSTROKE_I	0.053	0.435	0.208	3.303	3.199	3.188	3.113	18.906	
firsteventStroke_H	0.026	0.192	0.093	0.062	0.058	0.053	0.051	0.177	125.411
firsteventStroke_H2	0.027	0.210	0.102	0.066	0.062	0.058	0.055	0.196	11.091
firsteventStroke_H3	0.029	0.232	0.111	0.070	0.066	0.062	0.060	0.216	10.719
firsteventStroke_H4	0.029	0.255	0.116	0.074	0.071	0.066	0.064	0.236	10.546
feSTROKE_H	0.046	0.420	0.188	0.114	0.111	0.105	0.102	0.385	11.324
age0	0.000	-0.002	-0.001	-0.004	-0.004	-0.003	-0.002	-0.006	-0.001
timeperiod	-0.002	-0.024	-0.011	-0.005	-0.006	-0.005	-0.005	-0.022	-0.001
diabetes	-0.359	0.309	-0.955	-0.040	-0.032	-0.029	-0.026	-0.061	-0.003
hist_liver	0.001	-0.001	-0.065	-0.032	-0.032	-0.030	-0.015	0.014	0.022
hist_hf	-0.009	-0.031	-0.039	-0.034	-0.025	-0.018	-0.017	-0.043	0.004
hist_af	0.009	0.018	0.031	-0.072	-0.057	-0.042	-0.035	-0.094	-0.034
hist_pad	-0.035	-0.099	-0.065	-0.045	-0.043	-0.034	-0.034	-0.089	0.006
hist_copd	-0.004	-0.035	0.003	0.003	0.005	0.001	-0.001	-0.007	0.003
hist_cancer	0.007	-0.006	0.024	0.016	0.006	0.004	0.006	0.004	0.013
hist_renal	-0.007	0.001	-0.004	0.025	0.018	0.023	0.023	0.030	-0.019
sex	0.008	0.079	0.032	0.009	0.007	0.007	0.005	0.017	0.015
CHD	-0.011	-0.079	-0.026	-0.002	-0.005	-0.004	-0.004	-0.016	0.000
NSTEMI	-0.128	-0.423	-0.352	-0.002	-0.008	-0.013	-0.012	-0.053	0.006
STEMI	-0.038	-0.314	-0.115	0.009	0.009	0.010	0.008	0.028	0.019
UA	-0.022	-0.142	-0.057	-0.021	-0.022	-0.021	-0.021	-0.065	-0.010
_cons	0.042	0.005	0.154	-0.049	-0.032	-0.022	-0.012	0.061	-0.027

	firsteventStroke_H2	firsteventStroke_H3	firsteventStroke_H4	feSTROKE_H	age0	timeperiod	diabetes	hist_liver	hist_hf
firsteventStroke_H2	138.357								
firsteventStroke_H3	10.863	154.464							
firsteventStroke_H4	10.687	11.061	164.086						
feSTROKE_H	11.475	11.876	11.772	70.462					
age0	-0.001	0.000	0.000	-0.001	0.418				
timeperiod	-0.001	-0.001	-0.001	-0.006	0.004	0.175			
diabetes	-0.006	-0.005	0.000	0.004	0.367	0.125	13.630		
hist_liver	0.028	0.022	0.018	0.043	1.366	0.231	-1.452	50.663	
hist_hf	0.002	0.001	0.005	0.018	-2.542	0.185	-0.901	-0.245	11.922
hist_af	-0.022	-0.021	-0.021	-0.072	-2.216	0.204	0.257	-0.073	-3.140
hist_pad	0.003	0.000	0.001	0.007	-1.075	0.107	-1.100	-0.095	-1.207
hist_copd	0.001	0.002	-0.001	-0.006	0.234	0.084	-0.165	-0.193	-1.349
hist_cancer	0.008	0.005	0.006	0.006	-2.419	0.237	0.058	-0.107	-0.673
hist_renal	-0.012	0.004	-0.002	0.001	-1.286	0.678	-2.117	-0.234	-2.576
sex	0.012	0.011	0.005	0.006	-1.768	0.003	0.346	0.137	-1.153
CHD	0.002	0.002	-0.003	-0.013	-0.929	-0.174	-0.194	0.167	-0.857
NSTEMI	0.023	0.017	0.014	0.014	-1.753	0.294	-0.696	-0.080	-0.939
STEMI	0.020	0.016	0.012	0.010	1.323	0.220	0.291	-0.058	1.167
UA	-0.005	0.001	0.004	-0.007	0.133	0.002	-0.156	-0.140	-0.694
_cons	-0.022	-0.017	-0.010	0.008	2.819	-2.025	-1.669	-0.386	-1.049

	hist_af	hist_pad	hist_copd	hist_cancer	hist_renal	sex	CHD	NSTEMI	STEMI
hist_af	13.788								
hist_pad	-0.637	17.674							
hist_copd	-0.360	-0.480	11.483						
hist_cancer	-0.760	-0.318	-0.311	17.301					
hist_renal	-1.453	-1.342	-0.619	-1.008	20.482				
sex	0.004	0.322	-0.511	-0.085	-0.128	9.839			
CHD	0.050	-0.637	0.255	-0.096	0.085	1.467	12.227		
NSTEMI	-1.260	-1.190	-0.180	-0.509	-1.422	1.143	3.999	17.602	
STEMI	0.910	0.342	0.640	0.515	0.185	2.672	3.999	-0.043	20.809
UA	-0.357	-0.569	-0.364	-0.098	-0.192	0.553	3.999	1.869	1.585
_cons	-1.637	-1.070	-2.398	-1.330	-1.035	-5.049	-3.999	-1.869	-1.584

	UA	_cons
UA	14.113	
_cons	-1.906	4.823

CVD Specific Costs Mean Estimates

fatalCVD	fatalNONCVD	firsteventMI	MIdiabetes	firsteventMI2	MIdiabetes2	firsteventMI3	MIdiabetes3
2071	1737	4854	674	1209	1042	640	660

firsteventMI4	MIdiabetes4	feMI	feMIdiabetes	firsteventStroke_I	firsteventStroke_I2	firsteventStroke_I3	firsteventStroke_I4
675	403	481	280	5957	1151	675	539

feSTROKE_I	firsteventStroke_H	firsteventStroke_H2	firsteventStroke_H3	firsteventStroke_H4	feSTROKE_H	age0	timeperiod
448	6836	1517	585	393	670	6	7

diabetes	hist_liver	hist_hf	hist_af	hist_pad	hist_copd	hist_cancer	hist_renal
194	279	248	221	242	142	154	418

sex	CHD	NSTEMI	STEMI	UA	_cons
-23	2	145	29	125	224

CVD Specific Costs Cholesky Decomposition of Variance Covariance Matrix

	fatalCVD	fatalNONCVD	firsteventMI	MIdiabetes	firsteventMI2	MIdiabetes2	firsteventMI3	MIdiabetes3
fatalCVD	21.298							
fatalNONCVD	0.142	17.279						
firsteventMI	0.110	0.097	29.547					
MIdiabetes	0.020	0.039	-29.515	57.965				
firsteventMI2	-0.513	-0.353	2.720	0.016	31.513			
MIdiabetes2	-0.138	-0.044	-2.686	5.659	-31.484	62.225		
firsteventMI3	-0.231	-0.125	2.722	0.017	2.654	0.015	33.415	
MIdiabetes3	-0.081	-0.288	-2.685	5.648	-2.621	5.508	-33.386	66.266
firsteventMI4	-0.204	-0.109	2.743	0.019	2.675	0.016	2.613	0.015
MIdiabetes4	-0.283	-0.045	-2.703	5.611	-2.639	5.472	-2.581	5.343
feMI	-0.210	-0.158	2.817	0.032	2.748	0.030	2.685	0.028
feMIdiabetes	-0.110	-0.100	-2.751	5.577	-2.686	5.434	-2.626	5.304
firsteventStroke_I	0.114	0.127	0.055	0.035	0.050	0.031	0.046	0.028
firsteventStroke_I2	-0.367	-0.425	0.059	0.036	0.054	0.033	0.050	0.030
firsteventStroke_I3	-0.235	-0.188	0.062	0.038	0.057	0.034	0.053	0.031
firsteventStroke_I4	-0.184	-0.199	0.065	0.039	0.061	0.036	0.057	0.033
feSTROKE_I	-0.230	-0.163	0.094	0.053	0.090	0.050	0.086	0.047
firsteventStroke_H	0.106	0.112	0.054	0.030	0.049	0.027	0.045	0.024
firsteventStroke_H2	-0.429	-0.488	0.054	0.030	0.049	0.028	0.046	0.025
firsteventStroke_H3	-0.600	-0.156	0.057	0.031	0.053	0.028	0.049	0.027
firsteventStroke_H4	0.009	-0.070	0.060	0.029	0.056	0.028	0.053	0.026
feSTROKE_H	-0.261	-0.126	0.090	0.042	0.086	0.041	0.082	0.039
age0	-0.010	-0.011	-0.002	-0.001	-0.002	-0.001	-0.001	-0.001
timeperiod	-0.004	-0.007	-0.004	-0.002	-0.004	-0.002	-0.004	-0.002
diabetes	-0.053	-0.021	0.162	-0.454	0.137	-0.389	0.118	-0.340
hist_liver	-0.067	-0.261	-0.020	-0.043	0.003	-0.020	-0.005	-0.011
hist_hf	-0.216	-0.155	-0.029	-0.028	-0.019	-0.019	-0.014	-0.011
hist_af	-0.079	-0.054	0.005	0.012	0.003	0.006	0.008	0.007
hist_pad	-0.116	-0.078	-0.065	-0.053	-0.053	-0.037	-0.044	-0.036
hist_copd	0.002	-0.091	-0.019	-0.007	-0.017	-0.007	-0.011	-0.004
hist_cancer	0.010	-0.369	-0.012	0.003	-0.009	0.003	-0.003	0.002
hist_renal	-0.066	-0.056	-0.007	-0.040	-0.003	-0.016	0.001	-0.003
sex	0.057	0.051	0.033	0.013	0.028	0.009	0.025	0.009
CHD	-0.029	0.034	-0.039	-0.011	-0.034	-0.010	-0.032	-0.009
NSTEMI	-0.173	-0.038	-0.198	-0.154	-0.182	-0.127	-0.160	-0.109
STEMI	-0.025	-0.001	-0.143	-0.051	-0.133	-0.046	-0.122	-0.043
UA	-0.038	-0.002	-0.068	-0.028	-0.057	-0.027	-0.052	-0.024
_cons	-0.060	-0.061	-0.071	0.045	-0.052	0.042	-0.042	0.036

	firsteventMI4	MIdiabetes4	feMI	feMIdiabetes	firsteventStroke_I	firsteventStroke_I2	firsteventStroke_I3	firsteventStroke_I4
firsteventMI4	34.772							
MIdiabetes4	-34.742	69.080						
feMI	2.592	0.028	14.664					
feMIdiabetes	-2.535	5.109	-14.406	29.956				
firsteventStroke_I	0.044	0.027	0.174	0.093	30.944			
firsteventStroke_I2	0.048	0.028	0.194	0.101	2.515	32.590		
firsteventStroke_I3	0.052	0.030	0.213	0.109	2.504	2.438	35.117	
firsteventStroke_I4	0.055	0.032	0.230	0.117	2.516	2.449	2.451	36.826
feSTROKE_I	0.084	0.046	0.371	0.180	2.652	2.583	2.585	2.534
firsteventStroke_H	0.043	0.023	0.166	0.082	0.056	0.052	0.047	0.045
firsteventStroke_H2	0.044	0.024	0.181	0.089	0.059	0.055	0.051	0.048
firsteventStroke_H3	0.048	0.025	0.200	0.096	0.061	0.058	0.054	0.052
firsteventStroke_H4	0.052	0.025	0.219	0.099	0.065	0.062	0.058	0.056
feSTROKE_H	0.081	0.039	0.358	0.160	0.097	0.094	0.089	0.087
age0	-0.001	0.000	-0.002	-0.001	-0.004	-0.003	-0.002	-0.002
timeperiod	-0.004	-0.002	-0.020	-0.009	-0.004	-0.005	-0.005	-0.005
diabetes	0.105	-0.302	0.264	-0.812	-0.034	-0.027	-0.025	-0.022
hist_liver	-0.008	0.001	0.001	-0.055	-0.028	-0.027	-0.026	-0.013
hist_hf	-0.010	-0.007	-0.026	-0.033	-0.029	-0.021	-0.015	-0.015
hist_af	0.007	0.007	0.015	0.026	-0.061	-0.048	-0.036	-0.030
hist_pad	-0.039	-0.030	-0.085	-0.056	-0.037	-0.036	-0.029	-0.028
hist_copd	-0.011	-0.004	-0.030	0.002	0.003	0.004	0.000	-0.001
hist_cancer	-0.002	0.006	-0.006	0.019	0.012	0.004	0.004	0.004
hist_renal	0.000	-0.007	-0.001	-0.002	0.020	0.015	0.019	0.019
sex	0.022	0.007	0.068	0.028	0.007	0.005	0.005	0.004
CHD	-0.029	-0.009	-0.068	-0.022	-0.002	-0.004	-0.003	-0.003
NSTEMI	-0.143	-0.103	-0.359	-0.289	-0.003	-0.007	-0.011	-0.010
STEMI	-0.111	-0.036	-0.270	-0.107	0.008	0.008	0.009	0.007
UA	-0.048	-0.019	-0.121	-0.047	-0.018	-0.019	-0.018	-0.018
_cons	-0.032	0.035	0.005	0.131	-0.042	-0.028	-0.019	-0.011

	feSTROKE_I	firsteventStroke_H	firsteventStroke_H2	firsteventStroke_H3	firsteventStroke_H4	feSTROKE_H	age0	timeperiod
feSTROKE_I	16.041							
firsteventStroke_H	0.154	107.730						
firsteventStroke_H2	0.170	8.894	118.948					
firsteventStroke_H3	0.186	8.635	8.806	132.879				
firsteventStroke_H4	0.203	8.510	8.677	9.024	141.206			
feSTROKE_H	0.329	9.080	9.259	9.628	9.580	59.812		
age0	-0.005	-0.001	-0.001	0.000	0.000	-0.001	0.318	
timeperiod	-0.019	-0.001	-0.001	-0.001	-0.001	-0.005	0.004	0.150
diabetes	-0.053	-0.003	-0.005	-0.004	0.000	0.003	0.270	0.108
hist_liver	0.012	0.018	0.023	0.019	0.015	0.037	1.037	0.196
hist_hf	-0.037	0.003	0.001	0.000	0.004	0.015	-1.926	0.157
hist_af	-0.080	-0.029	-0.018	-0.018	-0.018	-0.062	-1.686	0.174
hist_pad	-0.076	0.005	0.003	0.000	0.001	0.007	-0.824	0.092
hist_copd	-0.006	0.002	0.001	0.002	-0.001	-0.005	0.174	0.071
hist_cancer	0.003	0.010	0.007	0.004	0.005	0.006	-1.840	0.201
hist_renal	0.025	-0.016	-0.010	0.003	-0.002	0.001	-0.966	0.586
sex	0.014	0.012	0.010	0.010	0.004	0.005	-1.343	0.004
CHD	-0.014	0.000	0.002	0.002	-0.002	-0.011	-0.704	-0.148
NSTEMI	-0.043	0.006	0.019	0.013	0.011	0.010	-1.207	0.246
STEMI	0.021	0.016	0.018	0.015	0.011	0.011	0.844	0.195
UA	-0.056	-0.009	-0.004	0.001	0.003	-0.006	0.104	0.002
_cons	0.053	-0.023	-0.019	-0.014	-0.009	0.007	2.143	-1.759

	diabetes	hist_liver	hist_hf	hist_af	hist_pad	hist_copd	hist_cancer	hist_renal
diabetes	10.359							
hist_liver	-1.090	38.645						
hist_hf	-0.685	-0.185	9.058					
hist_af	0.194	-0.055	-2.389	10.493				
hist_pad	-0.834	-0.072	-0.921	-0.487	13.439			
hist_copd	-0.127	-0.146	-1.022	-0.271	-0.363	8.719		
hist_cancer	0.043	-0.078	-0.512	-0.576	-0.243	-0.236	13.180	
hist_renal	-1.617	-0.174	-1.970	-1.103	-1.024	-0.476	-0.766	15.727
sex	0.260	0.102	-0.878	0.003	0.238	-0.391	-0.072	-0.096
CHD	-0.147	0.127	-0.651	0.038	-0.484	0.195	-0.074	0.065
NSTEMI	-0.501	-0.071	-0.633	-0.883	-0.841	-0.107	-0.341	-1.003
STEMI	0.187	-0.033	0.781	0.595	0.179	0.455	0.336	0.058
UA	-0.118	-0.105	-0.529	-0.270	-0.434	-0.275	-0.074	-0.145
_cons	-1.263	-0.292	-0.786	-1.236	-0.807	-1.815	-1.001	-0.774

	sex	CHD	NSTEMI	STEMI	UA	_cons
sex	7.461					
CHD	1.116	9.259				
NSTEMI	0.936	3.035	13.090			
STEMI	1.947	3.035	0.842	15.259		
UA	0.423	3.035	1.443	1.158	10.706	
_cons	-3.830	-3.035	-1.443	-1.158	-1.445	3.658

CHD Specific Costs Mean Estimates

fatalCVD	fatalNONCVD	firsteventMI	MIdiabetes	firsteventMI2	MIdiabetes2	firsteventMI3	MIdiabetes3
1407	1068	4658	643	1166	792	590	701

firsteventMI4	MIdiabetes4	feMI	feMIdiabetes	firsteventStroke_I	firsteventStroke_I2	firsteventStroke_I3	firsteventStroke_I4
642	330	475	269	3029	620	415	262

feSTROKE_I	firsteventStroke_H	firsteventStroke_H2	firsteventStroke_H3	firsteventStroke_H4	feSTROKE_H	age0	timeperiod
256	2874	790	218	301	251	4	4

diabetes	hist_liver	hist_hf	hist_af	hist_pad	hist_copd	hist_cancer	hist_renal
144	198	143	84	161	117	107	201

sex	CHD	NSTEMI	STEMI	UA	_cons
-23	82	219	111	163	179

CHD Specific Costs Cholesky Decomposition of Variance Covariance Matrix

	fatalCVD	fatalNONCVD	firsteventMI	MIdiabetes	firsteventMI2	MIdiabetes2	firsteventMI3	MIdiabetes3
fatalCVD	17.056							
fatalNONCVD	0.116	13.843						
firsteventMI	0.088	0.079	23.686					
MIdiabetes	0.017	0.031	-23.661	46.458				
firsteventMI2	-0.411	-0.281	2.109	0.013	25.271			
MIdiabetes2	-0.109	-0.035	-2.082	4.379	-25.247	49.891		
firsteventMI3	-0.184	-0.098	2.111	0.014	2.064	0.012	26.802	
MIdiabetes3	-0.064	-0.230	-2.082	4.373	-2.039	4.278	-26.779	53.145
firsteventMI4	-0.161	-0.085	2.128	0.015	2.081	0.013	2.038	0.012
MIdiabetes4	-0.225	-0.035	-2.096	4.346	-2.053	4.251	-2.012	4.162
feMI	-0.165	-0.124	2.177	0.025	2.130	0.023	2.086	0.022
feMIdiabetes	-0.088	-0.079	-2.126	4.300	-2.081	4.203	-2.040	4.112
firsteventStroke_I	0.092	0.103	0.045	0.029	0.041	0.026	0.038	0.023
firsteventStroke_I2	-0.294	-0.340	0.048	0.030	0.044	0.027	0.040	0.024
firsteventStroke_I3	-0.187	-0.149	0.050	0.031	0.046	0.028	0.043	0.026
firsteventStroke_I4	-0.146	-0.158	0.053	0.032	0.049	0.029	0.046	0.027
feSTROKE_I	-0.181	-0.128	0.075	0.043	0.072	0.040	0.068	0.038
firsteventStroke_H	0.085	0.091	0.044	0.024	0.040	0.022	0.036	0.020
firsteventStroke_H2	-0.343	-0.391	0.044	0.025	0.040	0.022	0.037	0.021
firsteventStroke_H3	-0.480	-0.123	0.046	0.025	0.042	0.023	0.040	0.021
firsteventStroke_H4	0.009	-0.055	0.048	0.024	0.045	0.022	0.043	0.021
feSTROKE_H	-0.207	-0.099	0.071	0.033	0.068	0.032	0.065	0.031
age0	-0.008	-0.009	-0.002	-0.001	-0.001	-0.001	-0.001	0.000
timeperiod	-0.003	-0.005	-0.003	-0.001	-0.003	-0.001	-0.003	-0.001
diabetes	-0.042	-0.016	0.128	-0.357	0.108	-0.307	0.094	-0.269
hist_liver	-0.051	-0.203	-0.015	-0.034	0.003	-0.016	-0.004	-0.009
hist_hf	-0.168	-0.121	-0.023	-0.022	-0.015	-0.015	-0.011	-0.008
hist_af	-0.062	-0.042	0.004	0.009	0.002	0.005	0.006	0.005
hist_pad	-0.090	-0.061	-0.051	-0.042	-0.042	-0.030	-0.035	-0.029
hist_copd	0.001	-0.071	-0.015	-0.005	-0.013	-0.006	-0.009	-0.004
hist_cancer	0.008	-0.285	-0.009	0.002	-0.007	0.002	-0.003	0.002
hist_renal	-0.053	-0.044	-0.006	-0.032	-0.002	-0.013	0.001	-0.003
sex	0.044	0.040	0.026	0.010	0.022	0.007	0.020	0.007
CHD	-0.023	0.027	-0.031	-0.009	-0.027	-0.008	-0.025	-0.007
NSTEMI	-0.136	-0.031	-0.157	-0.120	-0.145	-0.100	-0.128	-0.086
STEMI	-0.018	0.001	-0.112	-0.041	-0.104	-0.038	-0.097	-0.035
UA	-0.030	-0.002	-0.054	-0.022	-0.045	-0.022	-0.042	-0.019
_cons	-0.047	-0.048	-0.056	0.035	-0.042	0.033	-0.034	0.029

	firsteventMI4	MIdiabetes4	feMI	feMIdiabetes	firsteventStroke_I	firsteventStroke_I2	firsteventStroke_I3	firsteventStroke_I4
firsteventMI4	27.894							
MIdiabetes4	-27.871	55.414						
feMI	2.018	0.022	11.667					
feMIdiabetes	-1.974	3.970	-11.462	23.821				
firsteventStroke_I	0.036	0.022	0.140	0.076	24.816			
firsteventStroke_I2	0.039	0.023	0.156	0.082	1.958	26.142		
firsteventStroke_I3	0.042	0.024	0.171	0.089	1.951	1.903	28.173	
firsteventStroke_I4	0.044	0.026	0.185	0.095	1.960	1.912	1.918	29.548
feSTROKE_I	0.067	0.037	0.297	0.145	2.061	2.012	2.018	1.981
firsteventStroke_H	0.035	0.019	0.134	0.066	0.046	0.042	0.038	0.036
firsteventStroke_H2	0.036	0.020	0.145	0.072	0.048	0.045	0.041	0.039
firsteventStroke_H3	0.039	0.021	0.160	0.078	0.050	0.047	0.044	0.042
firsteventStroke_H4	0.041	0.020	0.175	0.080	0.052	0.050	0.046	0.045
feSTROKE_H	0.065	0.031	0.286	0.127	0.078	0.075	0.071	0.069
age0	-0.001	0.000	-0.001	-0.001	-0.003	-0.002	-0.002	-0.002
timeperiod	-0.003	-0.002	-0.016	-0.007	-0.003	-0.004	-0.004	-0.004
diabetes	0.084	-0.240	0.212	-0.649	-0.027	-0.022	-0.020	-0.018
hist_liver	-0.006	0.001	0.002	-0.044	-0.022	-0.022	-0.021	-0.010
hist_hf	-0.008	-0.006	-0.020	-0.026	-0.022	-0.016	-0.012	-0.012
hist_af	0.005	0.006	0.013	0.021	-0.048	-0.038	-0.028	-0.024
hist_pad	-0.031	-0.024	-0.068	-0.045	-0.029	-0.028	-0.023	-0.023
hist_copd	-0.009	-0.003	-0.023	0.001	0.002	0.003	0.000	-0.001
hist_cancer	-0.002	0.004	-0.005	0.015	0.009	0.003	0.003	0.004
hist_renal	0.000	-0.005	-0.001	-0.001	0.016	0.011	0.015	0.015
sex	0.017	0.005	0.054	0.022	0.005	0.004	0.004	0.003
CHD	-0.023	-0.007	-0.054	-0.018	-0.002	-0.003	-0.002	-0.002
NSTEMI	-0.114	-0.081	-0.291	-0.227	-0.004	-0.007	-0.010	-0.009
STEMI	-0.089	-0.030	-0.215	-0.089	0.009	0.008	0.009	0.007
UA	-0.038	-0.015	-0.097	-0.037	-0.014	-0.015	-0.014	-0.014
_cons	-0.026	0.028	0.004	0.105	-0.033	-0.022	-0.015	-0.009

	feSTROKE_I	firsteventStroke_H	firsteventStroke_H2	firsteventStroke_H3	firsteventStroke_H4	feSTROKE_H	age0	timeperiod
feSTROKE_I	12.788							
firsteventStroke_H	0.124	86.379						
firsteventStroke_H2	0.137	6.909	95.405					
firsteventStroke_H3	0.149	6.721	6.872	106.606				
firsteventStroke_H4	0.162	6.627	6.776	7.062	113.304			
feSTROKE_H	0.263	7.052	7.210	7.513	7.489	47.692		
age0	-0.004	-0.001	-0.001	0.000	0.000	-0.001	0.243	
timeperiod	-0.015	-0.001	-0.001	-0.001	-0.001	-0.004	0.003	0.120
diabetes	-0.042	-0.002	-0.004	-0.003	0.000	0.002	0.206	0.086
hist_liver	0.010	0.014	0.018	0.015	0.012	0.030	0.791	0.157
hist_hf	-0.029	0.003	0.001	0.000	0.003	0.012	-1.467	0.124
hist_af	-0.064	-0.023	-0.014	-0.014	-0.015	-0.050	-1.285	0.139
hist_pad	-0.060	0.003	0.002	0.000	0.001	0.006	-0.630	0.073
hist_copd	-0.005	0.002	0.001	0.001	-0.001	-0.005	0.134	0.057
hist_cancer	0.002	0.008	0.005	0.003	0.004	0.005	-1.405	0.159
hist_renal	0.020	-0.013	-0.008	0.002	-0.002	0.001	-0.731	0.470
sex	0.011	0.010	0.008	0.008	0.004	0.004	-1.024	0.003
CHD	-0.011	0.000	0.002	0.002	-0.002	-0.009	-0.538	-0.119
NSTEMI	-0.037	0.005	0.015	0.011	0.010	0.014	-0.935	0.203
STEMI	0.019	0.012	0.014	0.011	0.008	0.002	0.653	0.150
UA	-0.045	-0.007	-0.003	0.001	0.003	-0.005	0.080	0.001
_cons	0.043	-0.018	-0.015	-0.012	-0.007	0.006	1.635	-1.416

	diabetes	hist_liver	hist_hf	hist_af	hist_pad	hist_copd	hist_cancer	hist_renal
sex	5.701							
CHD	0.854	7.068						
NSTEMI	0.708	2.320	10.054					
STEMI	1.499	2.320	0.626	11.643				
UA	0.324	2.320	1.096	0.887	8.179			
_cons	-2.927	-2.320	-1.096	-0.887	-1.104	2.795		

Health Related Quality of Life

	_cons	age	male	acute_mi	old_mi	angina	hf	stroke
mean	0.8280	-0.0003	0.0010	-0.0626	-0.0368	-0.0854	-0.1167	-0.1171
standard error	0.0015	0.0002	0.0006	0.0132	0.0257	0.0134	0.0144	0.0121

Variable names and defiitions

Event costs

fatalCVD	Cost of a fatal cardiovascular event
fatalNONCVD	Cost of a fatal noncardiovascular event
firsteventMI	Cost of myocardial infarction in first quarter following event
MIdiabetes	Additional cost of myocardial infarction in first quarter for patients with diabetes
firsteventMI2	Cost of myocardial infarction in second quarter following event
MIdiabetes2	Additional cost of myocardial infarction in second quarter for patients with diabetes
firsteventMI3	Cost of myocardial infarction in third quarter following event
MIdiabetes3	Additional cost of myocardial infarction in second quarter for patients with diabetes
firsteventMI4	Cost of myocardial infarction in fourth quarter following event
MIdiabetes4	Additional cost of myocardial infarction in fourth quarter for patients with diabetes
feMI	Cost of myocardial infarction in all subsequent quarters following event
feMIdiabetes	Additional cost of myocardial infarction in all subsequent for patients with diabetes
firsteventStroke_I	Cost of ischemic stroke in first quarter following event
firsteventStroke_I2	Cost of ischemic stroke in second quarter following event
firsteventStroke_I3	Cost of ischemic stroke in third quarter following event
firsteventStroke_I4	Cost of ischemic stroke in fourth quarter following event
feSTROKE_I	Cost of ischemic stroke in all subsequent quarters following event
firsteventStroke_H	Cost of hemorrhagic stroke in first quarter following event
firsteventStroke_H2	Cost of hemorrhagic stroke in second quarter following event
firsteventStroke_H3	Cost of hemorrhagic stroke in third quarter following event
firsteventStroke_H4	Cost of hemorrhagic stroke in fourth quarter following event
feSTROKE_H	Cost of hemorrhagic stroke in all subsequent quarters following event

Background cost coefficients for quarter costs

age0	Baseline age
timeperiod	Model cycle number
diabetes	History of diabetes
hist_liver	History of liver disease
hist_hf	History of heart failure
hist_af	History of atrial fibrillation
hist_pad	History of peripheral artery disease
hist_copd	History of chronic obstructive pulmonary disease
hist_cancer	History of cancer
hist_renal	History of renal disease
sex	Female
CHD	Other CHD
NSTEMI	NSTEMI
STEMI	STEMI
UA	Unstable Angina
_cons	Constant

Modelling lifetime costs and health outcomes for patients with stable coronary artery disease

Appendix D: Modelling and Selection of Risk Equations

The prognostic factors used in the risk equations as covariates were taken from the work of Rapsomaniki, Eleni, et al. "Prognostic models for stable coronary artery disease based on electronic health record cohort of 102 023 patients." European heart journal 35.13 (2014): 844-852. This study compares different prognostic models using the CALIBER dataset and develops a model to best exploit the unique properties of this dataset. We also follow this study in terms of the imputation model used to impute missing covariate values as detailed in the technical appendix to that study:
http://eurheartj.oxfordjournals.org/content/ehj/suppl/2013/12/01/eht533.DC1/eht533supp1.pdf

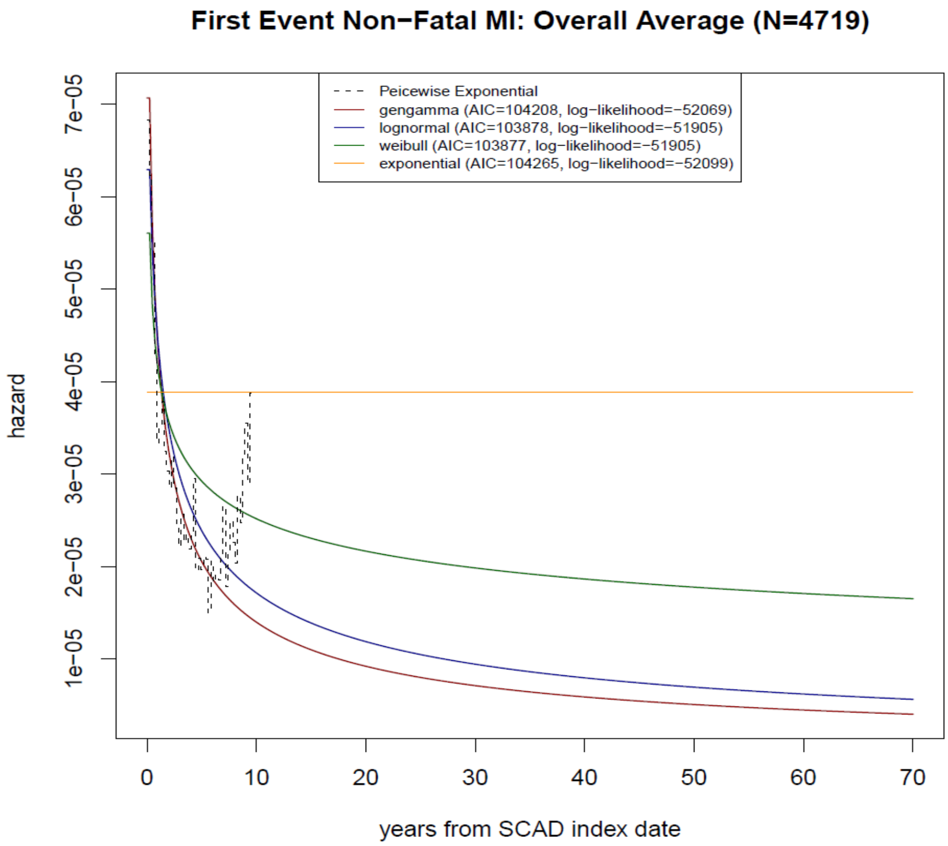
In this study we use these prognostic factors to fit a range of parametric survival models to each of the 11 risk equations in our model. We calculate hazards and survival over the time period we need to extrapolate our model over for every patient in the dataset and plot average values of these for each parametric model. These average predictions were used to assess clinical plausibility of the extrapolation made. The plots also contain piecewise exponentials for the hazards and Kaplan Meir estimates for survival to allow us to visually compare observed event rates to those predicted by averaging our parametric equations.

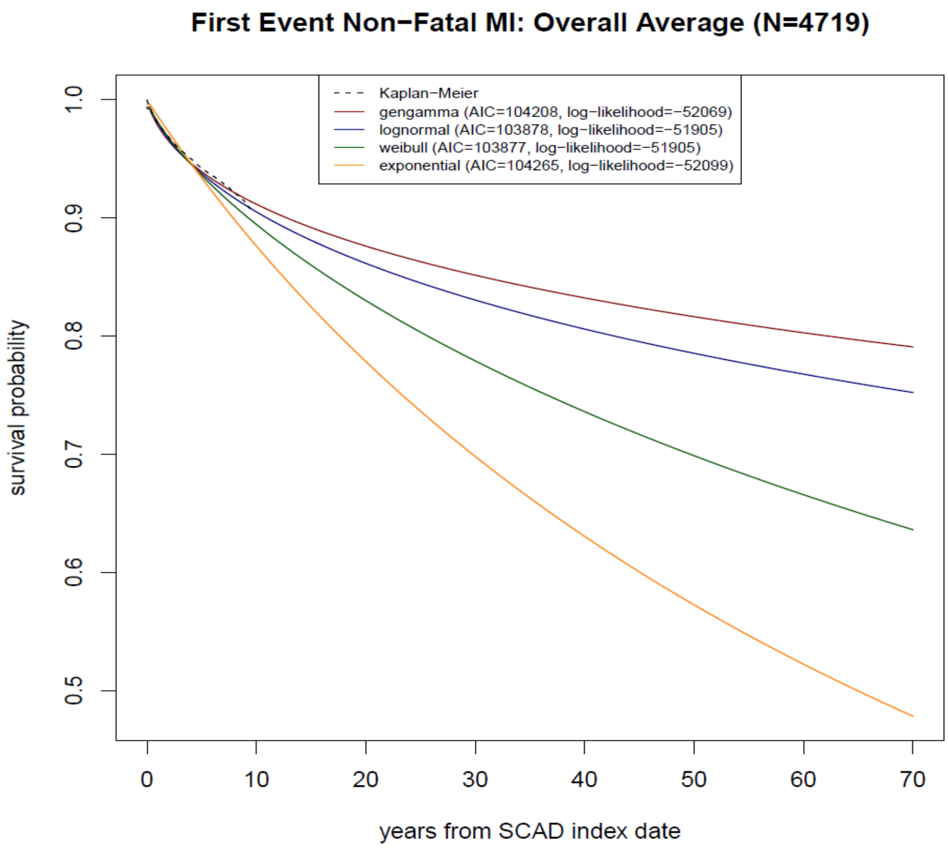
We also use the Akaike information criteria (AIC) to assess the goodness of fit of the various different parametric survival models to the observed data. The parametric model which has the best performance on the AIC is highlighted in red for each equation. These "best" performing models across the 11 equations were all deemed to be plausible extrapolations by our clinical experts and were combined in a competing risks framework using the methods proposed by Putter, H., M. Fiocco, and R. B. Geskus. "Tutorial in biostatistics: competing risks and multi-state models." Statistics in medicine 26.11 (2007): 2389.

The competing risks model was used to estimate patient specific time dependent transition probabilities for the Markov model described in appendix (b) by using the patient specific prognostic factors as covariates in the 11 risk equations to generate appropriate cumulative incidence functions from which transition probabilities could be derived.

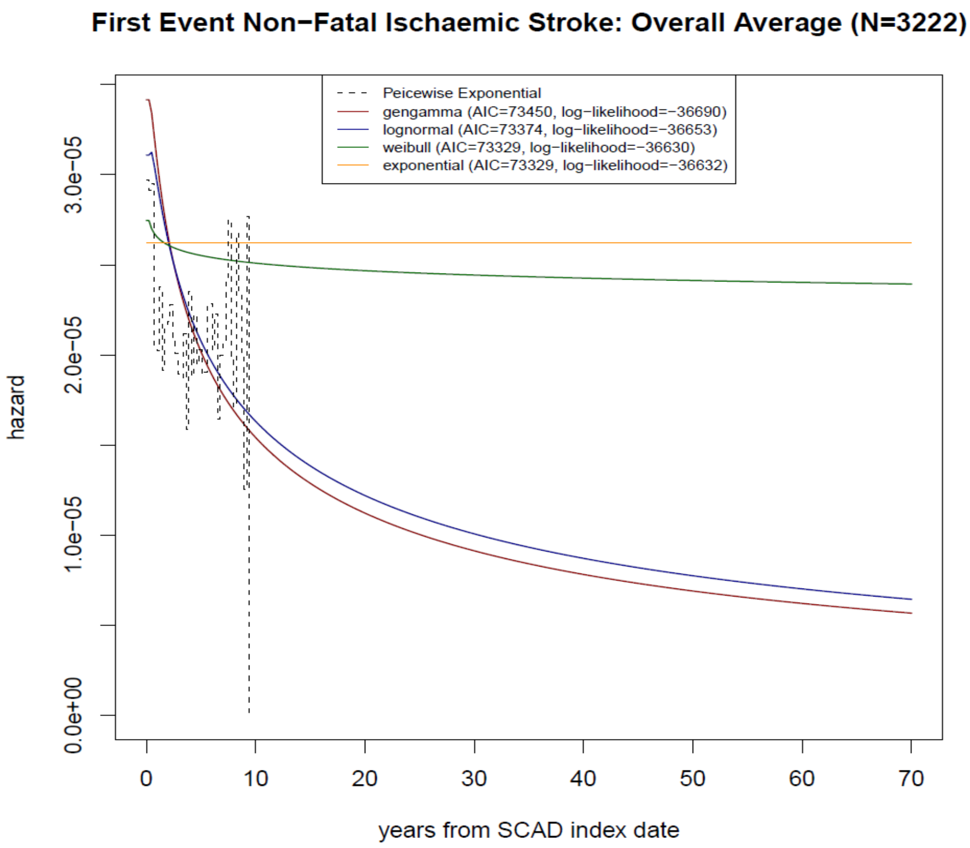
The variance covariances matrices from the estimated models for the risk equations were used in the probabilistic sensitvity analysis of the model to account for the non-linearities in the model and characterise the uncertainty around the model estimates.

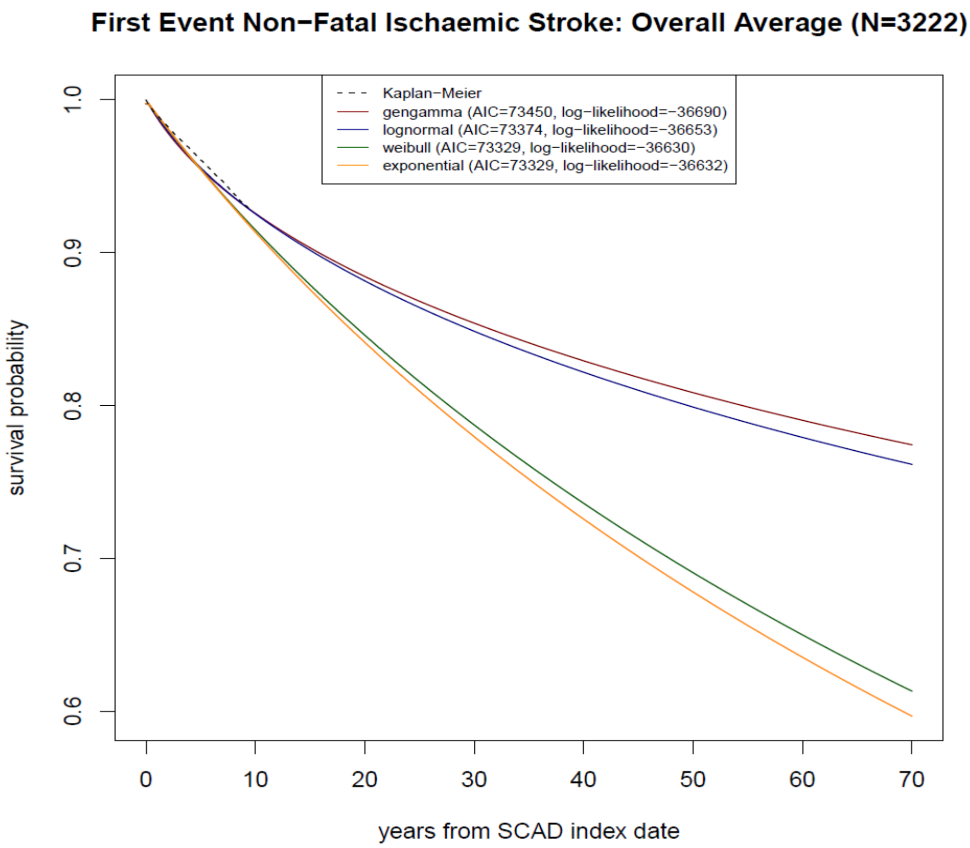
Equation 1: FE MI	GenGamma	LogNormal	Weibull	Exponential
Sociodemographic characteristics				
Age in men	0.98 (0.96-0.99)	0.98 (0.98-0.99)	0.98 (0.98-0.98)	0.98 (0.98-0.99)
Age in women	0.98 (0.97-1.00)	0.98 (0.98-0.99)	0.98 (0.98-0.99)	0.99 (0.98-0.99)
Women vs men	1.59 (1.19-2.14)	1.49 (1.32-1.68)	1.44 (1.29-1.59)	1.35 (1.24-1.46)
Most deprived quintile, yes vs. no	0.89 (0.62-1.27)	0.81 (0.73-0.89)	0.85 (0.78-0.93)	0.88 (0.82-0.94)
SCAD diagnosis and severity				
Other CHD vs. stable angina	0.89 (0.69-1.13)	0.85 (0.75-0.96)	0.79 (0.71-0.89)	0.84 (0.77-0.92)
NSTEMI vs. stable angina	0.19 (0.14-0.26)	0.19 (0.17-0.22)	0.23 (0.20-0.26)	0.31 (0.28-0.34)
STEMI vs stable angina	0.26 (0.19-0.36)	0.26 (0.22-0.32)	0.29 (0.25-0.35)	0.37 (0.33-0.43)
Unstable angina vs. stable angina	0.58 (0.47-0.71)	0.57 (0.50-0.65)	0.56 (0.50-0.63)	0.64 (0.58-0.70)
PCI in last 6 months	1.20 (0.77-1.87)	1.13 (0.97-1.32)	1.11 (0.97-1.27)	1.05 (0.95-1.17)
CABG in last 6 months	3.81 (1.90-7.62)	3.05 (2.39-3.91)	2.88 (2.28-3.65)	2.37 (1.97-2.85)
Previous/recurrent MI	0.53 (0.46-0.62)	0.57 (0.51-0.63)	0.62 (0.56-0.68)	0.69 (0.64-0.74)
Use of nitrates	0.62 (0.52-0.73)	0.64 (0.59-0.71)	0.69 (0.64-0.75)	0.75 (0.70-0.80)
CVD risk factors				
Current smoker vs. never	0.85 (0.65-1.10)	0.80 (0.69-0.92)	0.85 (0.75-0.97)	0.91 (0.83-1.01)
Ex-smoker vs. never	0.91 (0.68-1.21)	0.91 (0.79-1.05)	0.92 (0.81-1.05)	0.94 (0.85-1.04)
Hypertension	1.34 (0.85-2.10)	1.19 (1.07-1.32)	1.15 (1.05-1.27)	1.12 (1.04-1.21)
Diabetes mellitus	0.63 (0.44-0.91)	0.60 (0.54-0.67)	0.63 (0.57-0.70)	0.69 (0.64-0.75)
Total cholesterol, per 1 mmol/L increase	0.88 (0.76-1.03)	0.91 (0.86-0.96)	0.92 (0.87-0.97)	0.94 (0.90-0.98)
HDL, per 0.5 mmol/L increase	1.20 (0.98-1.47)	1.11 (1.04-1.18)	1.10 (1.04-1.17)	1.08 (1.03-1.13)
CVD co-morbidities				
Heart failure	0.86 (0.70-1.05)	0.86 (0.77-0.95)	0.86 (0.79-0.95)	0.88 (0.82-0.94)
Peripheral arterial disease	0.72 (0.41-1.28)	0.62 (0.54-0.71)	0.64 (0.57-0.71)	0.69 (0.63-0.75)
Atrial fibrillation	1.13 (0.84-1.51)	1.03 (0.92-1.17)	1.00 (0.90-1.11)	0.98 (0.90-1.06)
Stroke	0.77 (0.60-0.99)	0.79 (0.69-0.90)	0.80 (0.71-0.90)	0.82 (0.75-0.90)
Non-CVD co-morbidities				
Chornic kidney disease	0.84 (0.41-1.70)	0.97 (0.81-1.16)	0.90 (0.77-1.05)	0.84 (0.74-0.94)
Chronic obstructive pulmonary disease	0.91 (0.73-1.13)	0.85 (0.77-0.94)	0.86 (0.78-0.94)	0.88 (0.82-0.94)
Cancer	0.93 (0.70-1.25)	0.96 (0.83-1.11)	0.96 (0.84-1.09)	0.95 (0.86-1.05)
Chronic liver disease	0.83 (0.26-2.59)	0.77 (0.51-1.15)	0.75 (0.53-1.07)	0.78 (0.59-1.02)
Psychosocial characteristics				
Depression at diagnosis	1.16 (1.00-1.35)	1.15 (1.02-1.29)	1.11 (0.99-1.24)	1.06 (0.97-1.15)
Anxiety at diagnosis	1.11 (0.79-1.58)	1.04 (0.88-1.22)	1.04 (0.90-1.21)	1.02 (0.91-1.15)
Biomarkers				
Heart rate, per 10 b.p.m. increase	1.02 (0.96-1.08)	1.00 (0.95-1.05)	0.99 (0.95-1.04)	0.99 (0.95-1.03)
Creatinine, per 30 micromol/L increase	0.88 (0.77-1.00)	0.89 (0.85-0.94)	0.91 (0.87-0.95)	0.93 (0.90-0.96)
White cell count, per 1.5 10^9/L increase	0.89 (0.82-0.97)	0.89 (0.85-0.93)	0.90 (0.87-0.93)	0.92 (0.89-0.94)
Haemoglobin, per 1.5 g/dL increase	1.21 (1.09-1.34)	1.17 (1.10-1.25)	1.15 (1.08-1.21)	1.12 (1.07-1.17)
Generalised gamma model parameters				
mu	13.24 (12.32-14.16)	12.79 (12.59-12.99)	11.83 (11.65-12.00)	10.90 (10.80-11.00)
sigma	3.67 (2.27-5.95)	2.91 (2.84-2.97)	1.28 (1.24-1.31)	1
Q	-0.23 (-0.77-0.31)	0	1	1
Model Fit				
Log-likelihood	-52068.90	-51904.95	-51904.60	-52099.34
AIC	104207.81	103877.90	103877.20	104264.68


First Event Non−Fatal MI: Overall Average (N=4719)
Peicewise Exponential
gengamma (AIC=104208, log−likelihood=−52069)
lognormal (AIC=103878, log−likelihood=−51905)
weibull (AIC=103877, log−likelihood=−51905)
exponential (AIC=104265, log−likelihood=−52099)
hazard
1e−05
2e−05
3e−05
4e−05
5e−05
6e−05
7e−05
0
10
20
30
40
50
60
70
years from SCAD index date

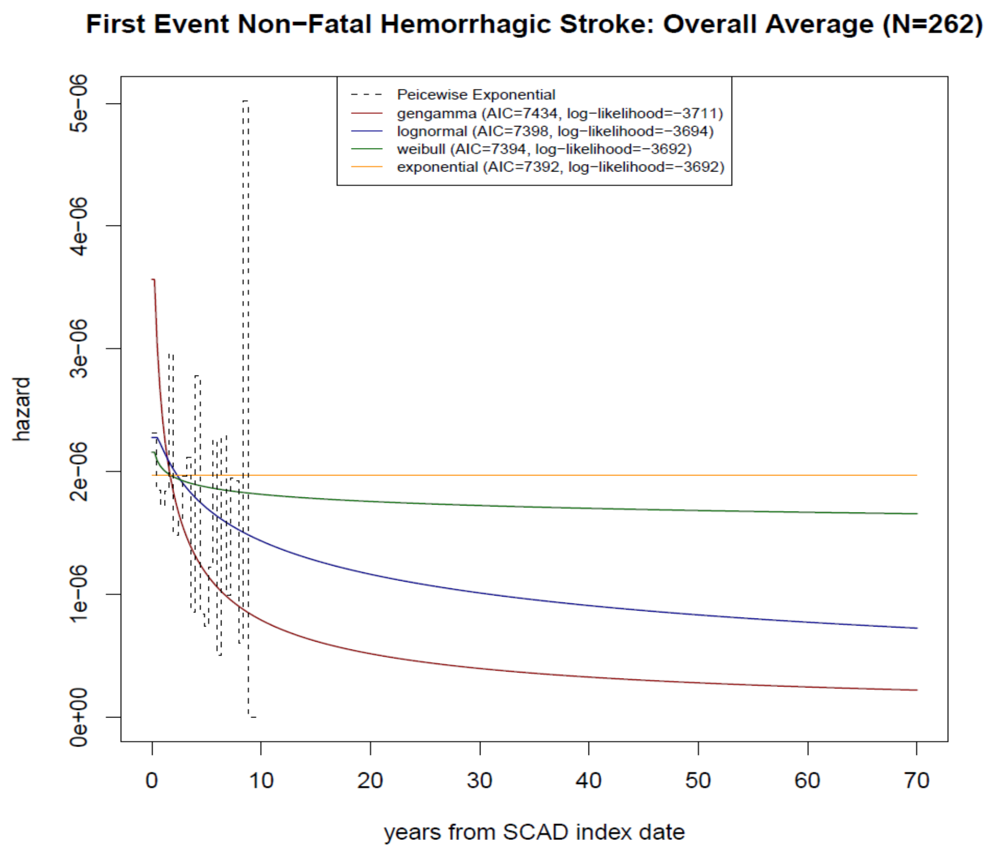

First Event Non−Fatal MI: Overall Average (N=4719)
Kaplan−Meier
gengamma (AIC=104208, log−likelihood=−52069)
lognormal (AIC=103878, log−likelihood=−51905)
weibull (AIC=103877, log−likelihood=−51905)
exponential (AIC=104265, log−likelihood=−52099)
survival probability
0.5
0.6
0.7
0.8
0.9
1.0
0
10
20
30
40
50
60
70
years from SCAD index date

Equation 2: FE Stroke I	GenGamma	LogNormal	Weibull	Exponential
Sociodemographic characteristics				
Age in men	0.95 (0.95-0.96)	0.95 (0.95-0.96)	0.96 (0.95-0.96)	0.96 (0.95-0.96)
Age in women	1.01 (1.00-1.02)	1.01 (1.00-1.01)	1.00 (1.00-1.01)	1.00 (1.00-1.01)
Women vs men	1.12 (0.98-1.28)	1.13 (1.02-1.25)	1.12 (1.02-1.23)	1.12 (1.02-1.23)
Most deprived quintile, yes vs. no	0.77 (0.68-0.87)	0.78 (0.71-0.86)	0.81 (0.74-0.88)	0.81 (0.75-0.88)
SCAD diagnosis and severity				
Other CHD vs. stable angina	0.99 (0.86-1.14)	1.01 (0.90-1.14)	1.00 (0.90-1.11)	1.00 (0.91-1.11)
NSTEMI vs. stable angina	1.00 (0.84-1.18)	0.92 (0.78-1.08)	0.93 (0.81-1.08)	0.93 (0.81-1.07)
STEMI vs stable angina	1.22 (0.68-2.18)	1.06 (0.84-1.34)	1.05 (0.84-1.31)	1.04 (0.84-1.30)
Unstable angina vs. stable angina	0.91 (0.75-1.11)	0.88 (0.77-0.99)	0.88 (0.79-0.98)	0.88 (0.79-0.98)
PCI in last 6 months	1.09 (0.80-1.49)	1.13 (0.94-1.37)	1.14 (0.95-1.36)	1.13 (0.95-1.35)
CABG in last 6 months	1.21 (0.96-1.52)	1.19 (0.95-1.48)	1.15 (0.94-1.41)	1.15 (0.95-1.40)
Previous/recurrent MI	0.87 (0.69-1.08)	0.88 (0.78-0.99)	0.90 (0.81-1.00)	0.90 (0.82-1.00)
Use of nitrates	0.97 (0.84-1.14)	0.96 (0.88-1.05)	0.97 (0.89-1.05)	0.97 (0.89-1.04)
CVD risk factors				
Current smoker vs. never	0.74 (0.59-0.92)	0.74 (0.65-0.84)	0.79 (0.71-0.88)	0.80 (0.72-0.89)
Ex-smoker vs. never	0.99 (0.81-1.21)	1.01 (0.89-1.14)	1.01 (0.90-1.14)	1.01 (0.91-1.13)
Hypertension	1.02 (0.85-1.22)	1.04 (0.93-1.15)	1.02 (0.93-1.13)	1.02 (0.93-1.12)
Diabetes mellitus	0.69 (0.60-0.80)	0.72 (0.64-0.80)	0.74 (0.67-0.82)	0.75 (0.68-0.82)
Total cholesterol, per 1 mmol/L increase	0.94 (0.86-1.02)	0.93 (0.89-0.99)	0.95 (0.90-1.00)	0.95 (0.91-1.00)
HDL, per 0.5 mmol/L increase	1.00 (0.90-1.11)	1.00 (0.91-1.10)	0.99 (0.91-1.07)	0.99 (0.91-1.07)
CVD co-morbidities				
Heart failure	0.85 (0.75-0.96)	0.86 (0.78-0.95)	0.90 (0.83-0.98)	0.90 (0.83-0.98)
Peripheral arterial disease	0.80 (0.67-0.96)	0.84 (0.73-0.96)	0.87 (0.78-0.98)	0.87 (0.78-0.98)
Atrial fibrillation	0.59 (0.51-0.68)	0.62 (0.56-0.69)	0.66 (0.60-0.72)	0.67 (0.61-0.73)
Stroke	0.23 (0.19-0.28)	0.22 (0.20-0.25)	0.30 (0.27-0.33)	0.31 (0.28-0.33)
Non-CVD co-morbidities				
Chornic kidney disease	1.23 (0.96-1.57)	1.11 (0.92-1.34)	1.05 (0.88-1.25)	1.03 (0.87-1.23)
Chronic obstructive pulmonary disease	1.07 (0.96-1.20)	1.08 (0.98-1.19)	1.07 (0.98-1.16)	1.06 (0.98-1.16)
Cancer	1.08 (0.89-1.31)	1.03 (0.90-1.19)	1.04 (0.92-1.17)	1.03 (0.92-1.17)
Chronic liver disease	0.72 (0.41-1.24)	0.79 (0.52-1.19)	0.78 (0.55-1.12)	0.79 (0.55-1.12)
Psychosocial characteristics				
Depression at diagnosis	0.90 (0.76-1.06)	0.90 (0.81-1.01)	0.89 (0.81-0.98)	0.89 (0.81-0.98)
Anxiety at diagnosis	0.96 (0.80-1.16)	0.94 (0.81-1.09)	0.94 (0.82-1.07)	0.94 (0.83-1.07)
Biomarkers				
Heart rate, per 10 b.p.m. increase	1.00 (0.93-1.07)	0.99 (0.94-1.04)	0.99 (0.95-1.03)	0.99 (0.95-1.03)
Creatinine, per 30 micromol/L increase	0.97 (0.90-1.03)	0.96 (0.90-1.02)	0.97 (0.92-1.02)	0.97 (0.92-1.02)
White cell count, per 1.5 10^9/L increase	0.92 (0.88-0.97)	0.93 (0.90-0.97)	0.94 (0.91-0.97)	0.94 (0.91-0.97)
Haemoglobin, per 1.5 g/dL increase	1.04 (0.99-1.09)	1.04 (0.98-1.09)	1.03 (0.99-1.08)	1.03 (0.99-1.08)
Generalised gamma model parameters				
mu	12.56 (12.32-12.8)	12.37 (12.17-12.57)	11.28 (11.11-11.45)	11.19 (11.07-11.31)
sigma	2.72 (2.29-3.23)	2.47 (2.40-2.54)	1.02 (0.99-1.06)	1
Q	-0.09 (-0.36-0.17)	0	1	1
Model Fit				
Log-likelihood	-36689.77	-36652.82	-36630.25	-36631.56
AIC	73449.54	73373.64	73328.51	73329.11

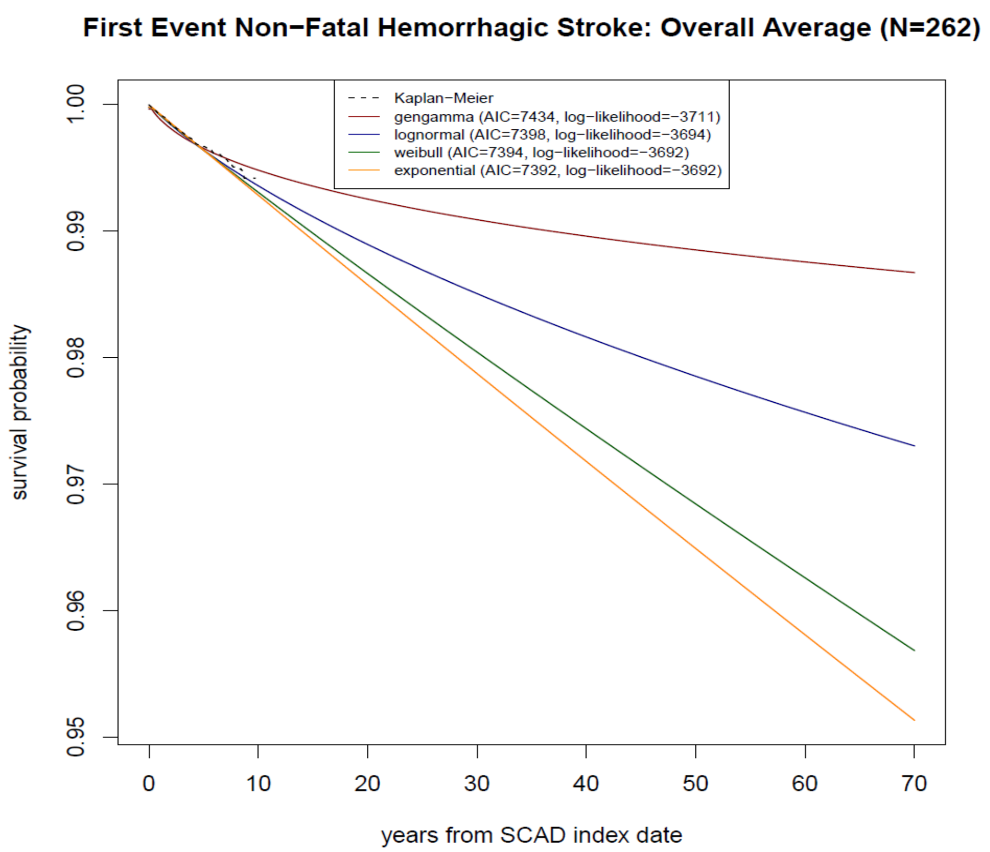

First Event Non−Fatal Ischaemic Stroke: Overall Average (N=3222)
Peicewise Exponential
gengamma (AIC=73450, log−likelihood=−36690)
lognormal (AIC=73374, log−likelihood=−36653)
weibull (AIC=73329, log−likelihood=−36630)
exponential (AIC=73329, log−likelihood=−36632)
hazard
0.0e+00
1.0e−05
2.0e−05
3.0e−05
0
10
20
30
40
50
60
70
years from SCAD index date


First Event Non−Fatal Ischaemic Stroke: Overall Average (N=3222)
Kaplan−Meier
gengamma (AIC=73450, log−likelihood=−36690)
lognormal (AIC=73374, log−likelihood=−36653)
weibull (AIC=73329, log−likelihood=−36630)
exponential (AIC=73329, log−likelihood=−36632)
survival probability
0.6
0.7
0.8
0.9
1.0
0
10
20
30
40
50
60
70
years from SCAD index date

Equation 3: FE Stroke H	GenGamma	LogNormal	Weibull	Exponential
Sociodemographic characteristics				
Age in men	0.94 (0.92-0.96)	0.95 (0.93-0.97)	0.95 (0.94-0.97)	0.95 (0.94-0.97)
Age in women	1.02 (0.98-1.05)	1.01 (0.98-1.03)	1.01 (0.99-1.03)	1.01 (0.99-1.03)
Women vs men	1.83 (1.24-2.70)	1.49 (1.11-2.00)	1.41 (1.07-1.86)	1.39 (1.07-1.81)
Most deprived quintile, yes vs. no				
SCAD diagnosis and severity				
Other CHD vs. stable angina				
NSTEMI vs. stable angina				
STEMI vs stable angina				
Unstable angina vs. stable angina				
PCI in last 6 months				
CABG in last 6 months				
Previous/recurrent MI				
Use of nitrates				
CVD risk factors				
Current smoker vs. never				
Ex-smoker vs. never				
Hypertension				
Diabetes mellitus				
Total cholesterol, per 1 mmol/L increase				
HDL, per 0.5 mmol/L increase				
CVD co-morbidities				
Heart failure				
Peripheral arterial disease				
Atrial fibrillation				
Stroke				
Non-CVD co-morbidities				
Chornic kidney disease				
Chronic obstructive pulmonary disease				
Cancer				
Chronic liver disease				
Psychosocial characteristics				
Depression at diagnosis				
Anxiety at diagnosis				
Biomarkers				
Heart rate, per 10 b.p.m. increase				
Creatinine, per 30 micromol/L increase				
White cell count, per 1.5 10^9/L increase				
Haemoglobin, per 1.5 g/dL increase				
Generalised gamma model parameters				
mu	23.07 (21.60-24.54)	16.59 (15.65-17.53)	13.36 (12.73-13.99)	13.09 (12.93-13.25)
sigma	14.52 (12.56-16.78)	3.41 (3.09-3.77)	1.05 (0.94-1.17)	1
Q	-2.76 (-3.32--2.19)	0	1	1
Model Fit				
Log-likelihood	-3711.20	-3694.11	-3691.75	-3692.16
AIC	7434.41	7398.23	7393.50	7392.32

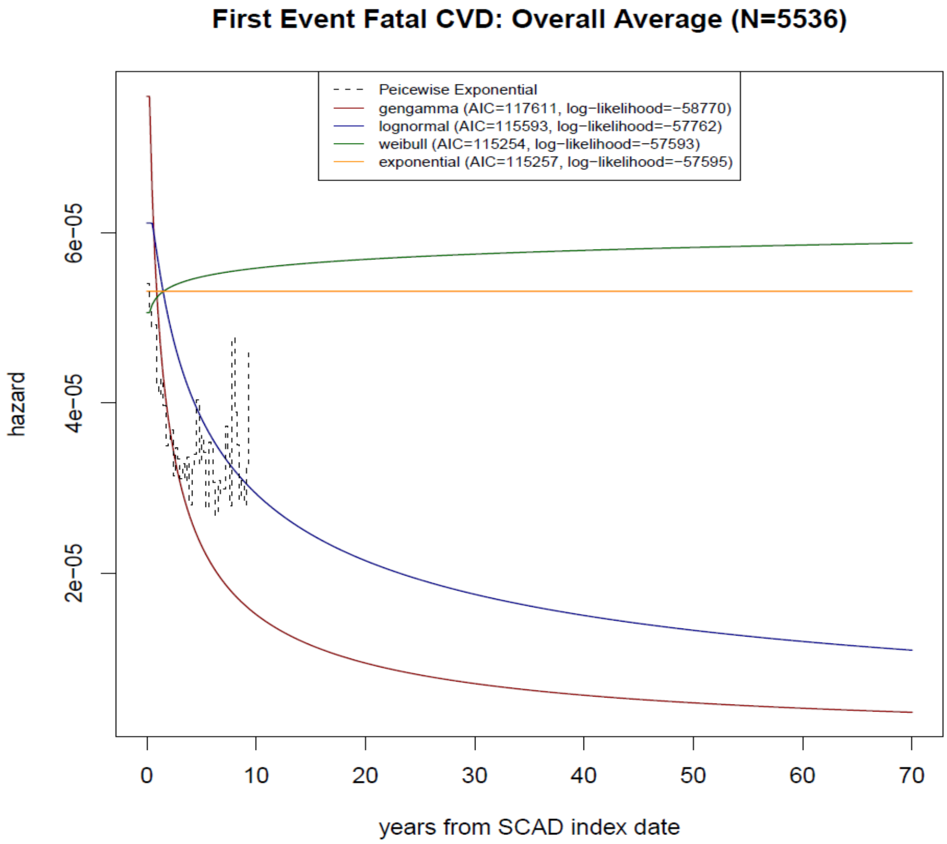


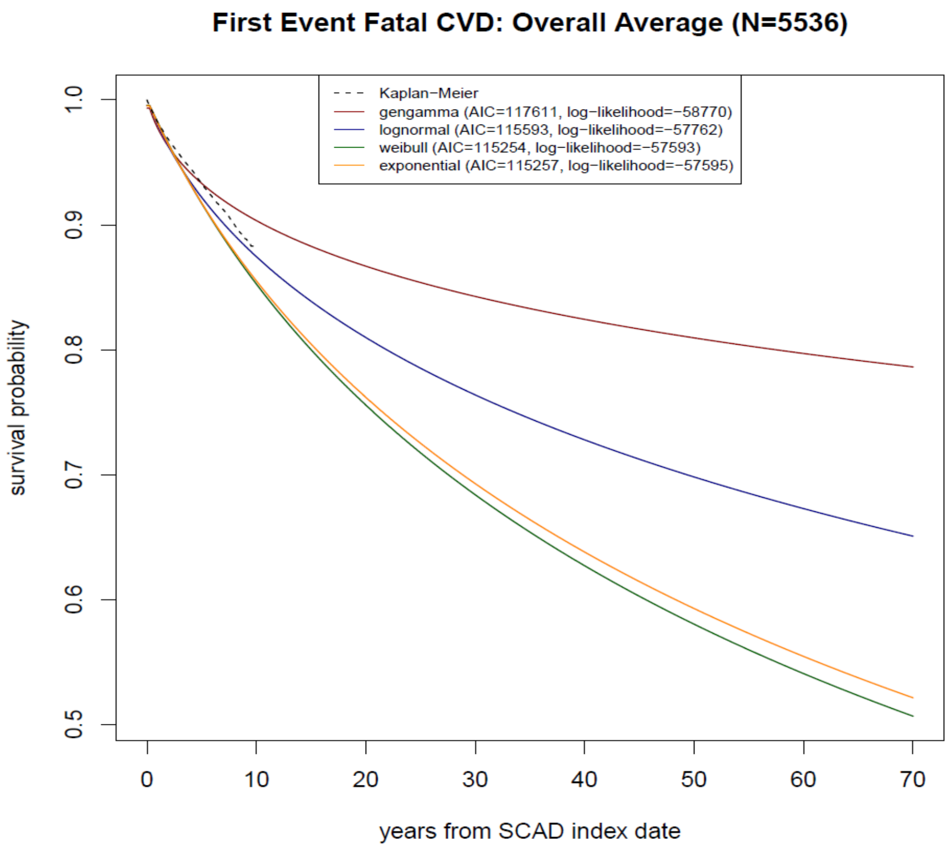
First Event Non−Fatal Hemorrhagic Stroke: Overall Average (N=262)
Peicewise Exponential
gengamma (AIC=7434, log−likelihood=−3711)
lognormal (AIC=7398, log−likelihood=−3694)
weibull (AIC=7394, log−likelihood=−3692)
exponential (AIC=7392, log−likelihood=−3692)
hazard
0e+00
1e−06
2e−06
3e−06
4e−06
5e−06
0
10
20
30
40
50
60
70
years from SCAD index date



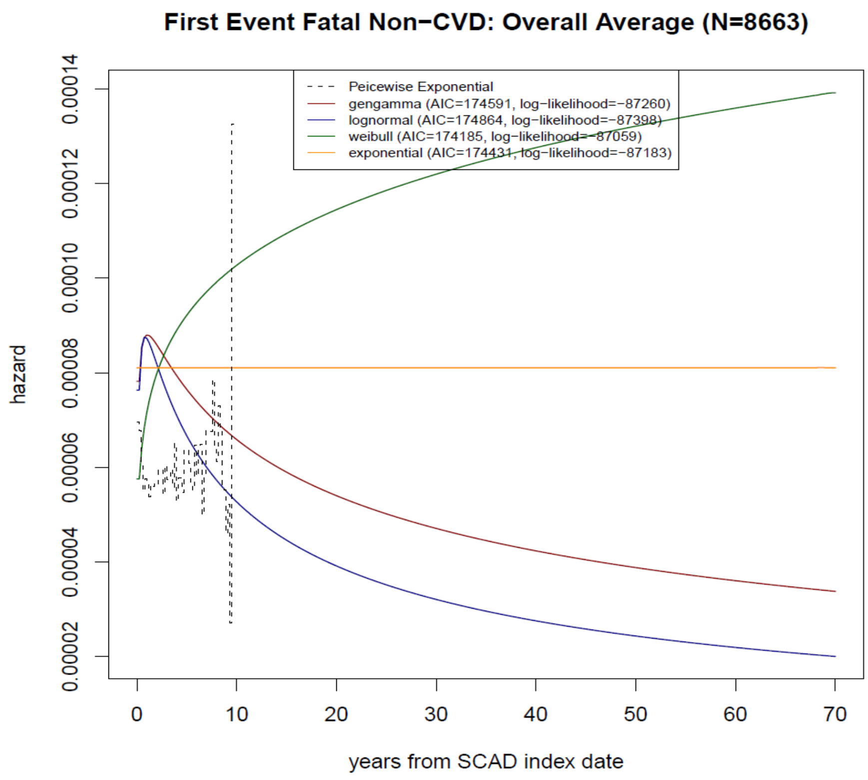
First Event Non−Fatal Hemorrhagic Stroke: Overall Average (N=262)
Kaplan−Meier
gengamma (AIC=7434, log−likelihood=−3711)
lognormal (AIC=7398, log−likelihood=−3694)
weibull (AIC=7394, log−likelihood=−3692)
exponential (AIC=7392, log−likelihood=−3692)
survival probability
0.95
0.96
0.97
0.98
0.99
1.00
0
10
20
30
40
50
60
70
years from SCAD index date

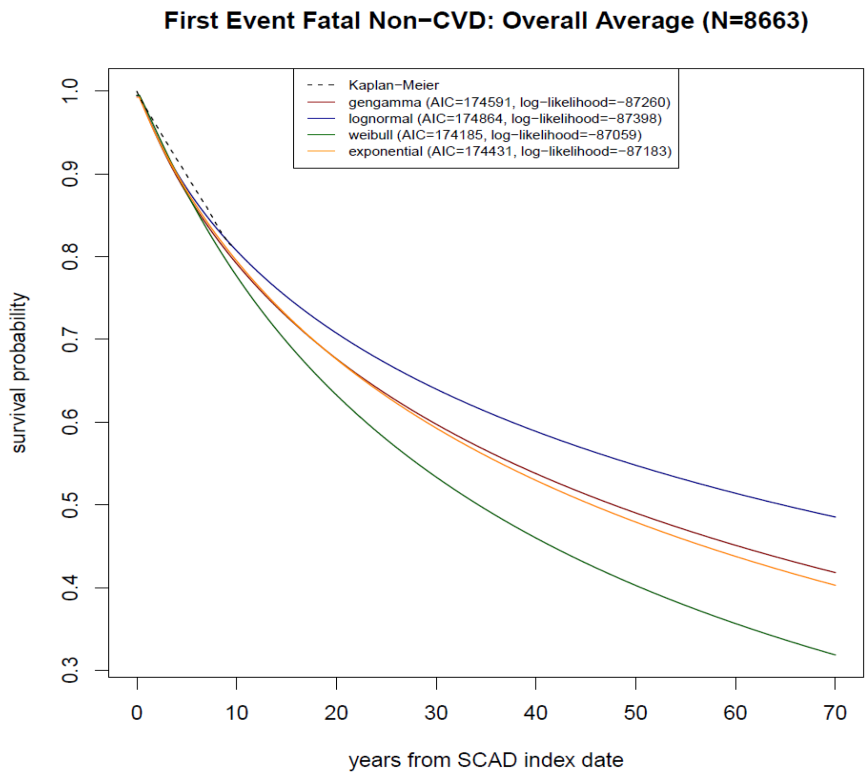
Equation 4: FE Fatal CVD	GenGamma	LogNormal	Weibull	Exponential
Sociodemographic characteristics				
Age in men	0.94 (0.92-0.96)	0.94 (0.93-0.94)	0.94 (0.94-0.94)	0.94 (0.94-0.94)
Age in women	0.97 (0.95-1.00)	0.97 (0.97-0.98)	0.97 (0.97-0.98)	0.97 (0.97-0.98)
Women vs men	1.82 (0.95-3.46)	2.04 (1.86-2.24)	1.97 (1.81-2.16)	2.00 (1.83-2.19)
Most deprived quintile, yes vs. no	0.90 (0.51-1.58)	0.85 (0.79-0.92)	0.90 (0.84-0.96)	0.90 (0.84-0.96)
SCAD diagnosis and severity				
Other CHD vs. stable angina	0.84 (0.57-1.24)	0.85 (0.78-0.93)	0.85 (0.79-0.92)	0.85 (0.78-0.91)
NSTEMI vs. stable angina	0.54 (0.33-0.88)	0.54 (0.48-0.60)	0.57 (0.53-0.63)	0.57 (0.52-0.62)
STEMI vs stable angina	0.73 (0.29-1.84)	0.74 (0.62-0.87)	0.77 (0.65-0.90)	0.77 (0.65-0.90)
Unstable angina vs. stable angina	0.91 (0.61-1.34)	0.90 (0.82-1.00)	0.89 (0.81-0.97)	0.89 (0.81-0.97)
PCI in last 6 months	1.42 (0.56-3.56)	1.71 (1.46-2.00)	1.82 (1.55-2.13)	1.85 (1.58-2.18)
CABG in last 6 months	1.58 (0.46-5.46)	2.09 (1.73-2.51)	1.98 (1.65-2.36)	2.00 (1.67-2.41)
Previous/recurrent MI	0.68 (0.52-0.90)	0.72 (0.66-0.78)	0.76 (0.72-0.82)	0.76 (0.71-0.81)
Use of nitrates	0.71 (0.59-0.85)	0.70 (0.65-0.74)	0.75 (0.71-0.79)	0.74 (0.70-0.79)
CVD risk factors				
Current smoker vs. never	0.60 (0.34-1.04)	0.76 (0.68-0.84)	0.80 (0.73-0.87)	0.79 (0.72-0.86)
Ex-smoker vs. never	0.77 (0.51-1.17)	0.95 (0.86-1.05)	0.96 (0.87-1.05)	0.96 (0.87-1.05)
Hypertension	0.93 (0.71-1.22)	0.98 (0.90-1.06)	0.98 (0.91-1.06)	0.98 (0.91-1.06)
Diabetes mellitus	0.79 (0.57-1.11)	0.73 (0.68-0.80)	0.75 (0.70-0.80)	0.75 (0.70-0.80)
Total cholesterol, per 1 mmol/L increase	0.97 (0.84-1.13)	0.96 (0.91-1.00)	0.97 (0.93-1.01)	0.97 (0.92-1.01)
HDL, per 0.5 mmol/L increase	1.05 (0.81-1.36)	1.05 (0.99-1.12)	1.03 (0.98-1.08)	1.03 (0.98-1.09)
CVD co-morbidities				
Heart failure	0.47 (0.38-0.59)	0.52 (0.48-0.55)	0.58 (0.54-0.61)	0.57 (0.53-0.60)
Peripheral arterial disease	0.70 (0.44-1.12)	0.72 (0.66-0.79)	0.75 (0.70-0.81)	0.75 (0.69-0.81)
Atrial fibrillation	0.69 (0.59-0.82)	0.73 (0.68-0.79)	0.76 (0.72-0.81)	0.76 (0.71-0.81)
Stroke	0.63 (0.35-1.14)	0.66 (0.60-0.71)	0.72 (0.67-0.77)	0.71 (0.66-0.77)
Non-CVD co-morbidities				
Chornic kidney disease	1.04 (0.33-3.33)	0.98 (0.86-1.11)	0.94 (0.84-1.04)	0.95 (0.85-1.05)
Chronic obstructive pulmonary disease	1.22 (0.78-1.91)	1.05 (0.98-1.13)	1.03 (0.97-1.10)	1.04 (0.97-1.10)
Cancer	1.29 (0.83-2.00)	1.10 (1.00-1.22)	1.12 (1.03-1.22)	1.12 (1.03-1.23)
Chronic liver disease	0.44 (0.09-2.09)	0.64 (0.48-0.85)	0.76 (0.59-0.99)	0.76 (0.59-0.99)
Psychosocial characteristics				
Depression at diagnosis	0.89 (0.58-1.37)	0.90 (0.83-0.98)	0.89 (0.83-0.96)	0.89 (0.83-0.96)
Anxiety at diagnosis	0.71 (0.39-1.28)	0.85 (0.77-0.95)	0.88 (0.80-0.97)	0.88 (0.80-0.97)
Biomarkers				
Heart rate, per 10 b.p.m. increase	0.89 (0.81-0.98)	0.90 (0.87-0.93)	0.92 (0.89-0.95)	0.92 (0.89-0.94)
Creatinine, per 30 micromol/L increase	0.89 (0.81-0.97)	0.89 (0.86-0.92)	0.91 (0.89-0.93)	0.90 (0.88-0.93)
White cell count, per 1.5 10^9/L increase	0.85 (0.77-0.95)	0.89 (0.86-0.93)	0.91 (0.88-0.94)	0.91 (0.88-0.94)
Haemoglobin, per 1.5 g/dL increase	1.30 (1.12-1.50)	1.28 (1.23-1.32)	1.23 (1.19-1.26)	1.23 (1.19-1.27)
Generalised gamma model parameters				
mu	12.33 (11.37-13.29)	11.49 (11.35-11.63)	10.9 (10.77-11.02)	10.98 (10.88-11.09)
sigma	4.24 (3.86-4.66)	2.09 (2.05-2.14)	0.97 (0.95-1.00)	1
Q	-1.30 (-1.78--0.81)	0	1	1
Model Fit				
Log-likelihood	-58770.27	-57762.41	-57592.89	-57595.48
AIC	117610.54	115592.82	115253.77	115256.97


First Event Fatal CVD: Overall Average (N=5536)
Peicewise Exponential
gengamma (AIC=117611, log−likelihood=−58770)
lognormal (AIC=115593, log−likelihood=−57762)
weibull (AIC=115254, log−likelihood=−57593)
exponential (AIC=115257, log−likelihood=−57595)
hazard
6e−05
4e−05
2e−05
0
10
20
30
40
50
60
70
years from SCAD index date

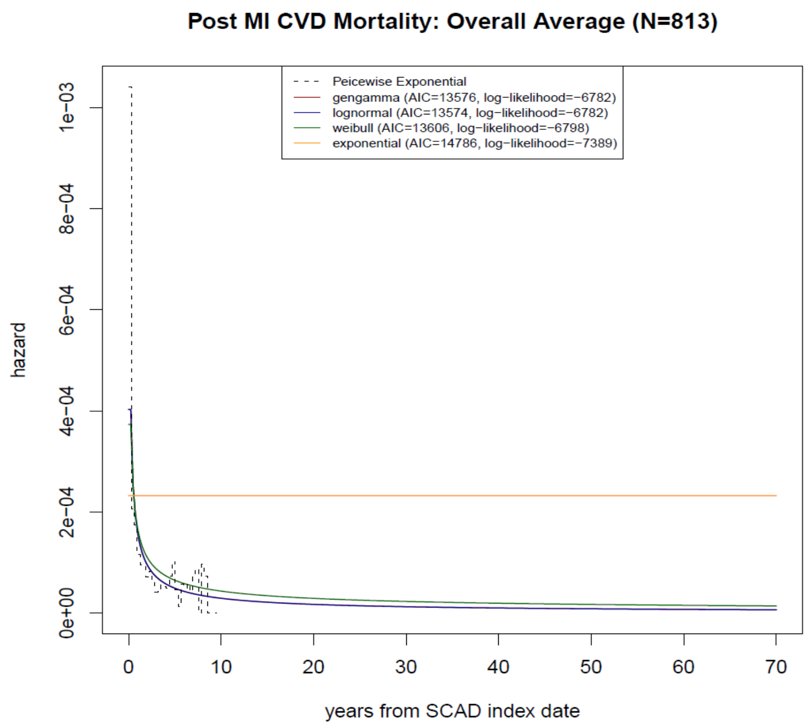

First Event Fatal CVD: Overall Average (N=5536)
Kaplan−Meier
gengamma (AIC=117611, log−likelihood=−58770)
lognormal (AIC=115593, log−likelihood=−57762)
weibull (AIC=115254, log−likelihood=−57593)
exponential (AIC=115257, log−likelihood=−57595)
survival probability
1.0
0.9
0.8
0.7
0.6
0.5
0
10
20
30
40
50
60
70
years from SCAD index date

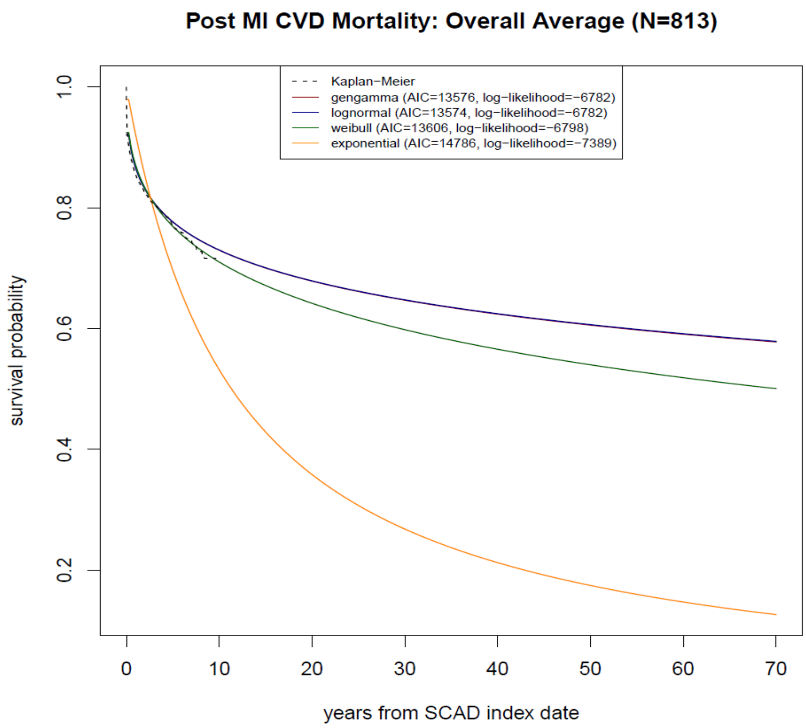
Equation 5: FE Fatal non-CVD	GenGamma	LogNormal	Weibull	Exponential
Sociodemographic characteristics				
Age in men	0.94 (0.94-0.95)	0.94 (0.94-0.95)	0.94 (0.94-0.95)	0.94 (0.93-0.94)
Age in women	0.99 (0.98-0.99)	0.99 (0.98-0.99)	0.99 (0.98-0.99)	0.99 (0.98-0.99)
Women vs men	1.71 (1.60-1.84)	1.75 (1.65-1.86)	1.65 (1.56-1.74)	1.75 (1.64-1.87)
Most deprived quintile, yes vs. no	0.90 (0.74-1.08)	0.84 (0.79-0.88)	0.86 (0.82-0.90)	0.85 (0.80-0.89)
SCAD diagnosis and severity				
Other CHD vs. stable angina	1.03 (0.90-1.18)	1.04 (0.98-1.11)	1.02 (0.97-1.08)	1.02 (0.96-1.08)
NSTEMI vs. stable angina	0.91 (0.70-1.19)	0.89 (0.82-0.96)	0.90 (0.84-0.96)	0.90 (0.84-0.98)
STEMI vs stable angina	1.05 (0.62-1.77)	0.93 (0.83-1.04)	0.90 (0.81-1.00)	0.91 (0.80-1.02)
Unstable angina vs. stable angina	1.07 (0.91-1.26)	1.03 (0.96-1.10)	1.02 (0.96-1.09)	1.02 (0.95-1.10)
PCI in last 6 months	1.31 (1.07-1.59)	1.34 (1.21-1.50)	1.32 (1.19-1.47)	1.40 (1.24-1.58)
CABG in last 6 months	1.75 (1.23-2.50)	1.85 (1.62-2.12)	1.74 (1.53-1.99)	1.86 (1.60-2.17)
Previous/recurrent MI	1.02 (0.90-1.16)	1.01 (0.95-1.08)	1.00 (0.95-1.06)	1.00 (0.94-1.07)
Use of nitrates	0.90 (0.85-0.96)	0.89 (0.85-0.93)	0.92 (0.88-0.96)	0.91 (0.87-0.95)
CVD risk factors				
Current smoker vs. never	0.73 (0.65-0.81)	0.70 (0.65-0.76)	0.74 (0.69-0.80)	0.69 (0.64-0.75)
Ex-smoker vs. never	0.86 (0.79-0.94)	0.84 (0.78-0.91)	0.85 (0.80-0.91)	0.83 (0.77-0.89)
Hypertension	1.15 (1.08-1.22)	1.11 (1.05-1.18)	1.11 (1.06-1.17)	1.13 (1.07-1.19)
Diabetes mellitus	0.90 (0.81-1.00)	0.91 (0.86-0.97)	0.91 (0.86-0.95)	0.90 (0.85-0.95)
Total cholesterol, per 1 mmol/L increase	1.00 (0.96-1.04)	1.01 (0.98-1.04)	1.01 (0.98-1.04)	1.00 (0.97-1.04)
HDL, per 0.5 mmol/L increase	0.97 (0.94-1.00)	0.98 (0.95-1.01)	0.98 (0.95-1.01)	0.98 (0.95-1.01)
CVD co-morbidities				
Heart failure	0.72 (0.68-0.77)	0.71 (0.67-0.74)	0.76 (0.73-0.80)	0.74 (0.70-0.77)
Peripheral arterial disease	0.84 (0.76-0.93)	0.81 (0.75-0.86)	0.83 (0.78-0.87)	0.81 (0.76-0.87)
Atrial fibrillation	0.88 (0.75-1.03)	0.84 (0.80-0.90)	0.88 (0.84-0.93)	0.88 (0.83-0.93)
Stroke	0.86 (0.75-0.98)	0.84 (0.79-0.90)	0.87 (0.82-0.92)	0.86 (0.81-0.92)
Non-CVD co-morbidities				
Chornic kidney disease	0.92 (0.81-1.05)	0.91 (0.83-0.99)	0.89 (0.82-0.96)	0.93 (0.85-1.02)
Chronic obstructive pulmonary disease	0.74 (0.63-0.86)	0.73 (0.70-0.77)	0.76 (0.73-0.79)	0.74 (0.70-0.77)
Cancer	0.49 (0.42-0.57)	0.41 (0.39-0.44)	0.56 (0.53-0.58)	0.51 (0.49-0.54)
Chronic liver disease	0.44 (0.27-0.72)	0.43 (0.36-0.52)	0.53 (0.46-0.62)	0.50 (0.42-0.59)
Psychosocial characteristics				
Depression at diagnosis	0.81 (0.73-0.89)	0.80 (0.75-0.84)	0.82 (0.78-0.86)	0.80 (0.76-0.85)
Anxiety at diagnosis	0.83 (0.55-1.25)	0.78 (0.72-0.84)	0.83 (0.78-0.89)	0.82 (0.76-0.88)
Biomarkers				
Heart rate, per 10 b.p.m. increase	0.90 (0.86-0.95)	0.89 (0.87-0.92)	0.91 (0.89-0.93)	0.90 (0.88-0.93)
Creatinine, per 30 micromol/L increase	0.98 (0.93-1.04)	1.00 (0.98-1.02)	0.99 (0.97-1.01)	0.99 (0.97-1.01)
White cell count, per 1.5 10^9/L increase	0.87 (0.82-0.92)	0.85 (0.84-0.87)	0.89 (0.87-0.90)	0.87 (0.86-0.89)
Haemoglobin, per 1.5 g/dL increase	1.38 (1.33-1.42)	1.41 (1.37-1.44)	1.33 (1.30-1.36)	1.38 (1.35-1.41)
Generalised gamma model parameters				
mu	10.1 (10.01-10.19)	10.25 (10.15-10.34)	9.95 (9.87-10.03)	10.32 (10.24-10.40)
sigma	1.37 (1.11-1.70)	1.73 (1.7-1.76)	0.86 (0.85-0.88)	1
Q	0.46 (0.19-0.73)	0	1	1
Model Fit				
Log-likelihood	-87260.46	-87397.88	-87058.62	-87182.58
AIC	174590.93	174863.76	174185.23	174431.16


First Event Fatal Non−CVD: Overall Average (N=8663)
Peicewise Exponential
gengamma (AIC=174591, log−likelihood=−87260)
lognormal (AIC=174864, log−likelihood=−87398)
weibull (AIC=174185, log−likelihood=−87059)
exponential (AIC=174431, log−likelihood=−87183)
hazard
0.00002
0.00004
0.00006
0.00008
0.00010
0.00012
0.00014
0
10
20
30
40
50
60
70
years from SCAD index date

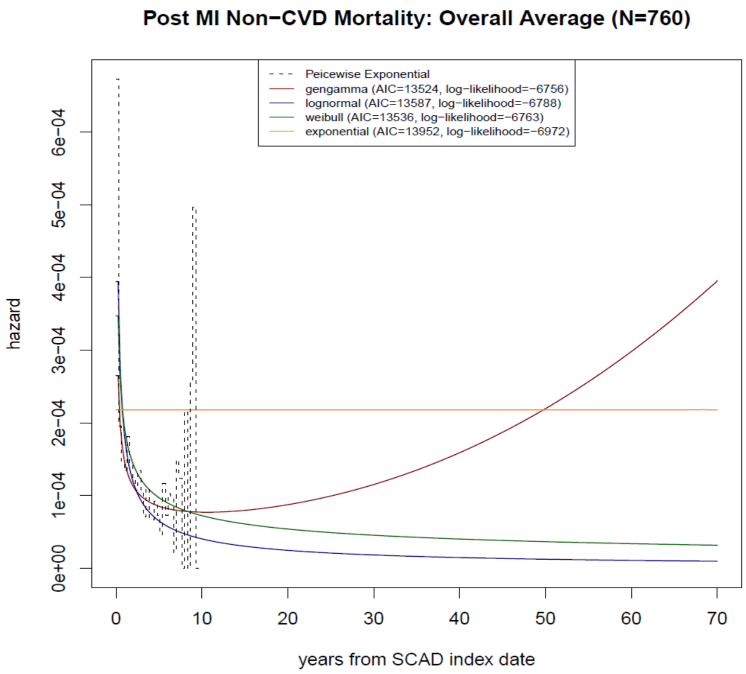

First Event Fatal Non−CVD: Overall Average (N=8663)
Kaplan−Meier
gengamma (AIC=174591, log−likelihood=−87260)
lognormal (AIC=174864, log−likelihood=−87398)
weibull (AIC=174185, log−likelihood=−87059)
exponential (AIC=174431, log−likelihood=−87183)
survival probability
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
0
10
20
30
40
50
60
70
years from SCAD index date

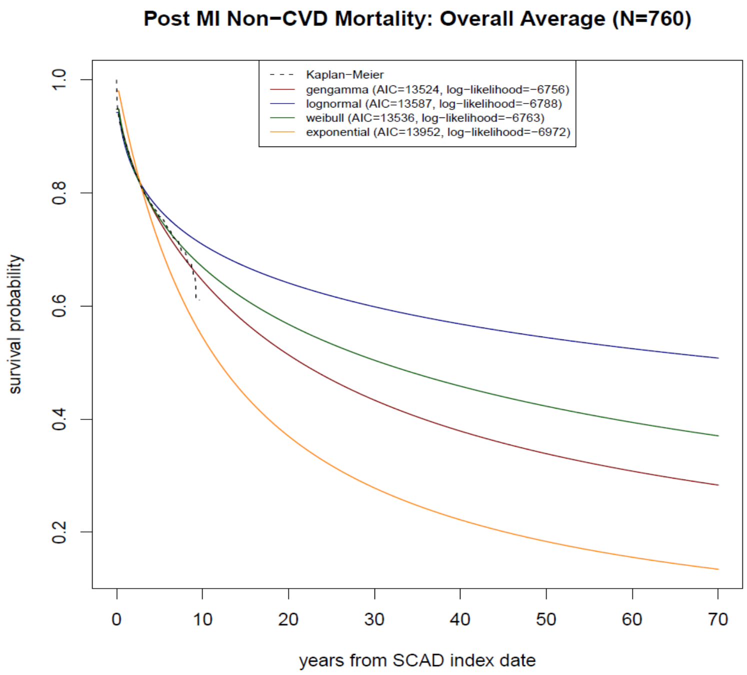
Equation 6: Post MI Fatal CVD	GenGamma	LogNormal	Weibull	Exponential
Sociodemographic characteristics				
Age in men	0.85 (0.83-0.87)	0.85 (0.83-0.87)	0.85 (0.83-0.87)	0.92 (0.91-0.93)
Age in women	0.98 (0.95-1.02)	0.98 (0.95-1.02)	0.98 (0.95-1.02)	0.99 (0.97-1.00)
Women vs men	1.87 (1.12-3.11)	1.87 (1.12-3.11)	1.90 (1.12-3.22)	1.39 (1.11-1.74)
Generalised gamma model parameters				
mu	11.14 (10.71-11.56)	11.13 (10.74-11.51)	11.27 (10.89-11.65)	8.85 (8.74-8.96)
sigma	4.21 (3.60-4.93)	4.24 (4.02-4.48)	2.39 (2.25-2.54)	1
Q	0.02 (-0.32-0.36)	0	1	1
Model Fit				
Log-likelihood	-6781.95	-6781.95	-6798.12	-7388.97
AIC	13575.89	13573.90	13606.23	14785.94



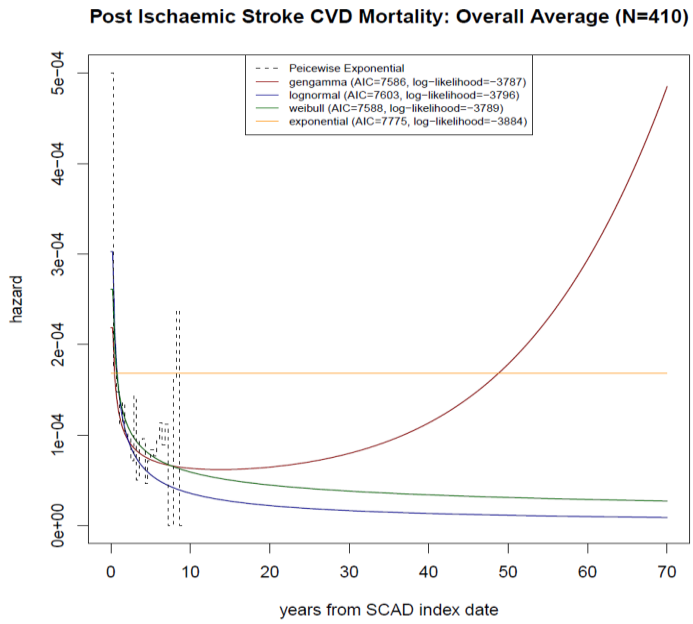


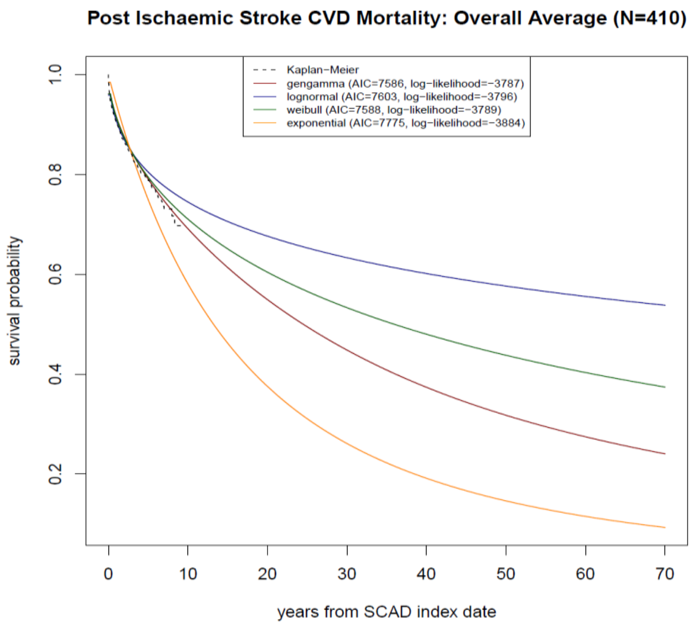
Equation 7: Post MI Fatal Non-CVD	GenGamma	LogNormal	Weibull	Exponential
Sociodemographic characteristics				
Age in men	0.88 (0.86-0.89)	0.87 (0.85-0.88)	0.87 (0.86-0.89)	0.91 (0.90-0.92)
Age in women	1.03 (1.00-1.05)	1.02 (0.99-1.05)	1.03 (1.00-1.05)	1.01 (1.00-1.03)
Women vs men	0.91 (0.64-1.30)	1.04 (0.71-1.52)	0.95 (0.66-1.37)	1.00 (0.81-1.24)
Generalised gamma model parameters				
mu	10.38 (10.02-10.75)	10.38 (10.07-10.69)	10.32 (10.03-10.6)	8.99 (8.87-9.11)
sigma	0.77 (0.37-1.61)	3.27 (3.09-3.45)	1.73 (1.63-1.84)	1
Q	2.47 (0.63-4.3)	0	1	1
Model Fit				
Log-likelihood	-6755.79	-6788.29	-6762.82	-6972.03
AIC	13523.58	13586.59	13535.64	13952.06



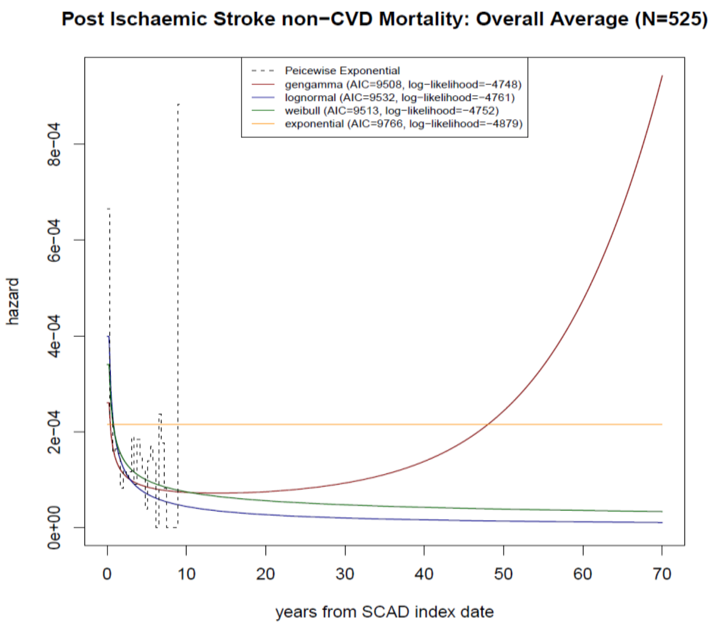


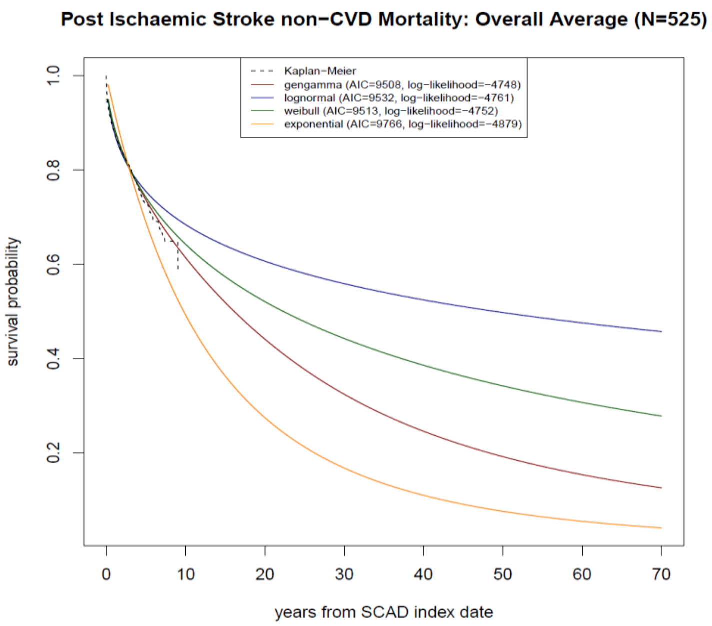
Equation 8: Post Ischaemic Stroke Fatal CVD	GenGamma	LogNormal	Weibull	Exponential
Sociodemographic characteristics				
Age in men	0.91 (0.89-0.93)	0.91 (0.89-0.94)	0.91 (0.89-0.93)	0.94 (0.92-0.95)
Age in women	0.99 (0.96-1.03)	0.99 (0.95-1.03)	0.99 (0.96-1.03)	0.99 (0.97-1.01)
Women vs men	1.52 (0.90-2.54)	1.54 (0.90-2.62)	1.54 (0.91-2.59)	1.35 (0.98-1.86)
Generalised gamma model parameters				
mu	10.42 (9.45-11.39)	10.68 (10.22-11.14)	10.4 (9.98-10.81)	9.08 (8.89-9.27)
sigma	0.59 (0.04-9.78)	3.30 (3.07-3.56)	1.67 (1.54-1.81)	1
Q	3.00 (-5.42-11.42)	0	1	1
Model Fit				
Log-likelihood	-3786.80	-3796.47	-3789.03	-3883.70
AIC	7585.61	7602.95	7588.07	7775.40



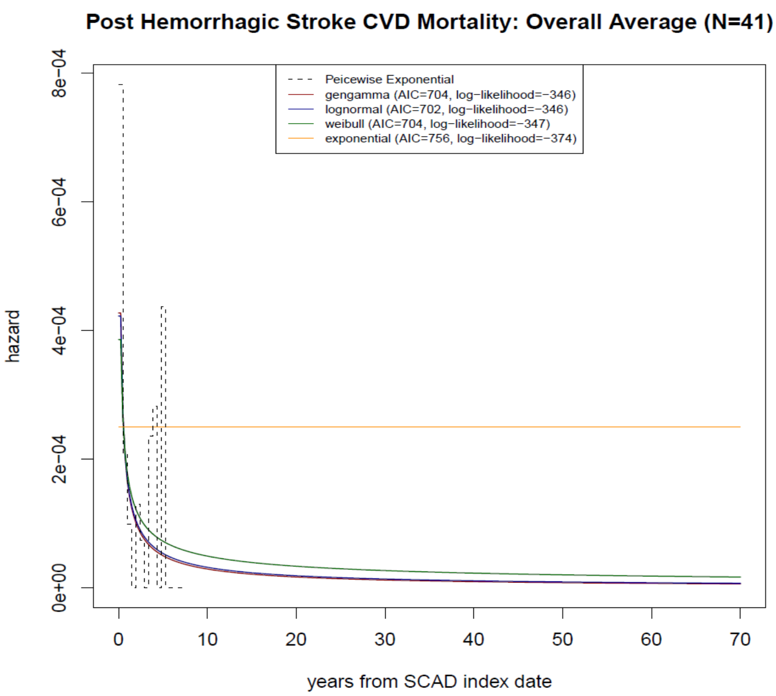


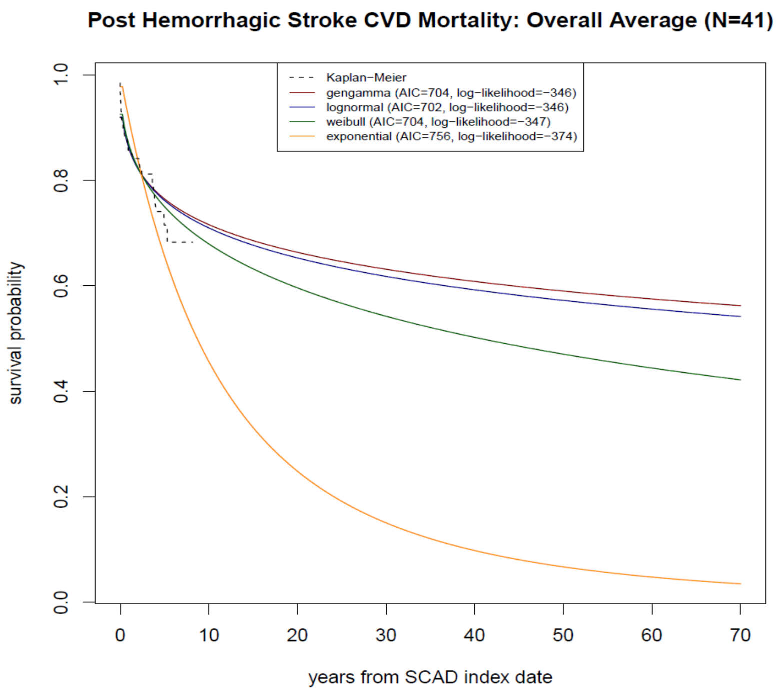
Equation 9: Post Ischaemic Stroke Fatal Non-CVD	GenGamma	LogNormal	Weibull	Exponential
Sociodemographic characteristics				
Age in men	0.93 (0.91-0.95)	0.93 (0.91-0.95)	0.93 (0.91-0.95)	0.95 (0.94-0.96)
Age in women	0.99 (0.97-1.03)	1.01 (0.97-1.04)	1.00 (0.97-1.03)	1.00 (0.98-1.02)
Women vs men	1.48 (0.97-2.26)	1.59 (1.02-2.49)	1.50 (0.97-2.31)	1.32 (1.02-1.71)
Generalised gamma model parameters				
mu	9.92 (8.53-11.3)	9.86 (9.49-10.23)	9.80 (9.47-10.13)	8.70 (8.54-8.85)
sigma	0.53 (0.01-38.25)	3.23 (3.02-3.45)	1.69 (1.57-1.82)	1
Q	3.40 (-11.15-17.96)	0	1	1
Model Fit				
Log-likelihood	-4747.78	-4760.80	-4751.72	-4879.00
AIC	9507.57	9531.60	9513.44	9765.99



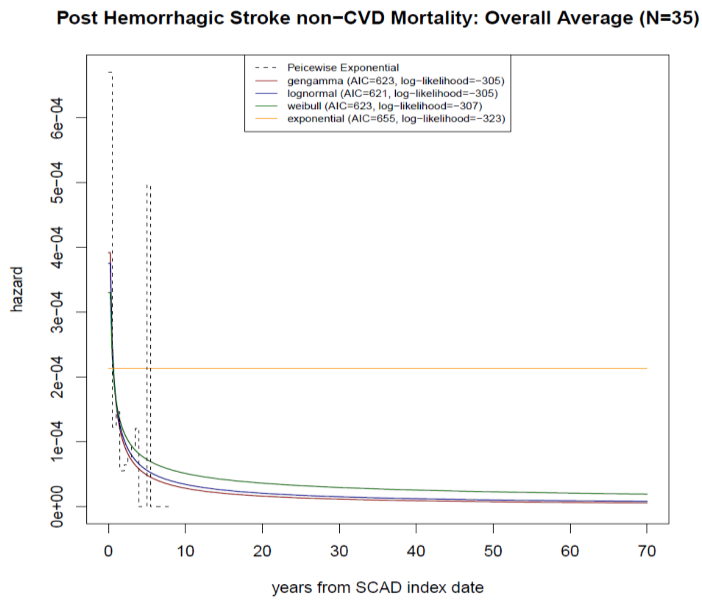


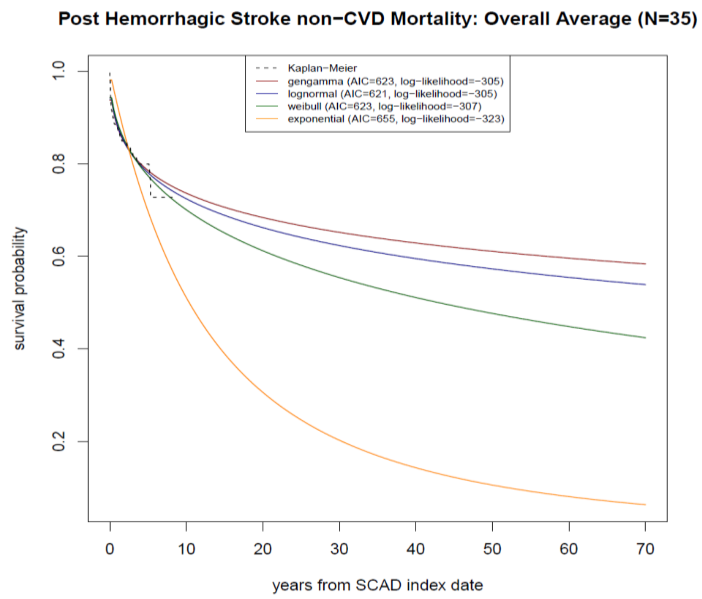
Equation 10: Post Hemorrhagic Stroke Fatal CVD	GenGamma	LogNormal	Weibull	Exponential
Sociodemographic characteristics				
Age in men	0.88 (0.80-0.96)	0.88 (0.80-0.96)	0.89 (0.81-0.97)	0.94 (0.90-0.97)
Age in women	1.02 (0.87-1.20)	1.02 (0.87-1.19)	1.04 (0.90-1.19)	1.02 (0.96-1.08)
Women vs men	0.79 (0.09-6.85)	0.85 (0.11-6.58)	1.06 (0.15-7.27)	1.19 (0.52-2.76)
Generalised gamma model parameters				
mu	10.95 (8.99-12.9)	11.02 (9.31-12.74)	10.79 (9.18-12.41)	8.58 (8.06-9.09)
sigma	4.60 (2.04-10.36)	4.14 (3.27-5.25)	2.25 (1.73-2.92)	1
Q	-0.26 (-2.4-1.89)	0	1	1
Model Fit				
Log-likelihood	-346.21	-346.24	-346.99	-373.82
AIC	704.42	702.48	703.98	755.64





Equation 11: Post Hemorrhagic Stroke Fatal Non-CVD	GenGamma	LogNormal	Weibull	Exponential
Sociodemographic characteristics				
Age in men	0.91 (0.84-0.99)	0.91 (0.84-0.99)	0.92 (0.85-0.99)	0.95 (0.91-0.99)
Age in women	0.95 (0.81-1.12)	0.95 (0.81-1.11)	0.94 (0.8-1.09)	0.97 (0.91-1.04)
Women vs men	5.81 (0.68-49.96)	5.64 (0.62-51.43)	5.70 (0.57-57.48)	2.59 (0.88-7.65)
Generalised gamma model parameters				
mu	9.86 (7.32-12.39)	10.24 (8.70-11.79)	10.22 (8.81-11.63)	8.51 (8.03-9.00)
sigma	4.55 (2.38-8.72)	3.68 (2.85-4.75)	2.01 (1.53-2.66)	1
Q	-0.61 (-2.86-1.64)	0	1	1
Model Fit				
Log-likelihood	-305.31	-305.49	-306.60	-323.30
AIC	622.63	620.97	623.20	654.61





Modelling lifetime costs and health outcomes for patients with stable coronary artery disease

Appendix E: Patient Profiles

Section 1: Patient Risk Deciles

Patient average covariate profiles based on deciles of 5yr risk of composite CVD primary endpoint											
Risk Decile	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**Overall**
5 year risk (average across patients)	3.69%	5.70%	7.37%	9.15%	11.20%	13.71%	17.14%	22.14%	30.42%	52.37%	16.68%
5 year risk (at average covariate values)	3.46%	5.43%	6.95%	8.53%	10.36%	12.57%	15.64%	20.07%	27.23%	44.18%	11.64%
Socio-demographic characteristics											
Sex (% female)	64%	48%	42%	39%	37%	37%	38%	42%	44%	46%	44%
Age (if male)	49	55	59	62	65	67	71	74	77	81	67
Age (if female)	53	62	67	70	73	75	78	80	83	87	72
Age (weighted average)	52	59	62	65	68	70	73	76	80	84	69
Most deprived quintile (%)	15%	17%	18%	19%	20%	21%	21%	22%	22%	24%	20%
SCAD diagnosis											
Other CHD	11%	17%	20%	22%	24%	24%	25%	26%	25%	20%	23%
NSTEMI	0%	1%	3%	5%	8%	10%	12%	17%	23%	43%	10%
STEMI	1%	4%	8%	12%	13%	14%	13%	9%	6%	4%	7%
Unstable angina	10%	13%	12%	12%	12%	12%	13%	15%	17%	15%	14%
Stable angina	78%	65%	56%	49%	43%	39%	37%	34%	29%	18%	47%
SCAD severity											
PCI in last 6 months	9%	12%	13%	14%	13%	13%	11%	9%	6%	4%	9%
CABG in last 6 months	9%	7%	6%	5%	5%	4%	4%	3%	2%	1%	4%
Previous/recurrent MI	2%	6%	10%	14%	18%	23%	26%	29%	32%	43%	18%
Use of nitrates	10%	16%	19%	21%	24%	28%	33%	37%	43%	56%	28%
Smoking status											
Current smoker	31%	35%	36%	37%	38%	38%	37%	35%	32%	30%	35%
Ex-smoker	27%	30%	31%	32%	32%	33%	34%	34%	34%	34%	32%
Never smoked	41%	35%	33%	31%	30%	29%	29%	31%	33%	36%	33%
Other CVD risk factors											
Hypertension	69%	70%	71%	71%	72%	74%	76%	79%	83%	87%	76%
Diabetes	4%	8%	10%	12%	14%	16%	18%	21%	24%	32%	16%
Total cholesterol (mmol/L)	4.95	4.91	4.84	4.79	4.74	4.74	4.70	4.68	4.64	4.54	4.79
HDL (mmol/L)	1.41	1.37	1.35	1.35	1.35	1.35	1.36	1.37	1.37	1.35	1.37
CVD co-morbidities											
Heart failure	5%	7%	9%	12%	15%	19%	27%	37%	52%	73%	26%
Peripheral arterial disease	1%	2%	3%	4%	6%	8%	10%	13%	16%	25%	8%
Atrial fibrillation	3%	5%	7%	9%	10%	13%	16%	21%	29%	43%	15%
Stroke	0%	1%	1%	2%	3%	5%	8%	14%	22%	39%	9%
Non-CVD co-morbidities											
Chronic kidney disease	2%	2%	3%	4%	4%	5%	7%	9%	12%	20%	7%
Chronic obstructive pulmonary disease	20%	20%	20%	21%	22%	23%	25%	27%	28%	30%	23%
Cancer	4%	5%	6%	7%	8%	9%	11%	13%	14%	12%	9%
Chronic liver disease	0%	1%	1%	1%	1%	1%	1%	1%	1%	1%	1%
Psychosocial characteristics											
Depression at diagnosis	20%	17%	15%	15%	14%	14%	15%	17%	18%	21%	17%
Anxiety at diagnosis	7%	6%	6%	7%	7%	7%	8%	8%	10%	12%	8%
Biomarkers											
Heart rate (b.p.m.)	72	71	71	71	71	71	72	73	74	76	72
Creatinine (mmol/L)	88	92	95	96	98	100	101	104	109	125	100
White cell count (10^9/L)	6.81	7.05	7.19	7.31	7.44	7.54	7.62	7.76	7.88	8.22	7.46
Haemoglobin (g/100ml)	14.26	14.26	14.16	14.05	13.88	13.70	13.48	13.16	12.81	12.20	13.61

Section 2: Clinically selected patients

Sample patient covariate profiles for 10 clinically selected patients										
Patient Profile	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
5 year risk	3.68%	5.72%	7.59%	9.26%	11.48%	13.83%	17.41%	22.29%	30.44%	50.11%
Socio-demographic characteristics										
Sex	Female	Female	Male	Male	Male	Male	Male	Male	Male	Male
Age	53	62	59	62	65	67	71	74	76	81
Most deprived quintile	-	-	TRUE	-	-	TRUE			TRUE	-
SCAD diagnosis										
Other CHD	-	-	-	-	TRUE	TRUE	TRUE	TRUE	-	-
NSTEMI	-	-	-	-	-	-	-	-	TRUE	TRUE
STEMI	-	-	-	-	-	-	-	-	-	-
Unstable angina	-	-	-	-	-	-	-	-	-	-
Stable angina	TRUE	TRUE	TRUE	TRUE	-	-	-	-	-	-
SCAD severity										
PCI in last 6 months	-	-	-	-	-	-	-	-	-	-
CABG in last 6 months	-	-	-	-	-	-	-	-	-	-
Previous/recurrent MI	-	-	-	-	TRUE	-	TRUE	-	-	-
Use of nitrates	-	-	-	TRUE	-	TRUE	TRUE	TRUE	-	-
Smoking Status										
Current smoker	-	TRUE	TRUE	-	-	-	TRUE	TRUE	TRUE	-
Ex-smoker	-	-	-	TRUE	-	-	-	-	-	-
Never smoked	TRUE	-	-	-	-	TRUE	-	-	-	TRUE
Other CVD risk factors										
Hypertension	TRUE	TRUE	TRUE	TRUE	TRUE	TRUE	TRUE	TRUE	TRUE	TRUE
Diabetes	-	-	-	-	-	-	-	-	-	TRUE
Total cholesterol (mmol/L)	5.57	4.78	4.30	6.63	4.39	4.80	4.68	4.00	3.23	3.70
HDL (mmol/L)	1.83	1.27	1.39	1.30	1.20	0.71	2.10	0.99	1.61	0.93
CVD co-morbidities										
Heart failure	-	-	-	-	-	-	-	TRUE	TRUE	TRUE
Peripheral arterial disease	-	-	-	-	-	-	-	-	-	-
Atrial fibrillation	-	-	-	-	-	-	TRUE	-	TRUE	-
Stroke	-	-	-	-	-	-	-	-	-	-
Non-CVD co-morbidities										
Chronic kidney disease	-	-	-	-	-	-	-	-	-	-
Chronic obstructive pulmonary disease	-	TRUE	TRUE	-	-	-	TRUE	-	TRUE	-
Cancer	-	-	-	-	-	-	-	-	-	-
Chronic liver disease	-	-	-	-	-	-	-	-	-	-
Psychosocial characteristics										
Depression at diagnosis	-	TRUE	-	TRUE	-	-	-	-	-	TRUE
Anxiety at diagnosis	-	-	-	-	-	-	-	-	-	-
Biomarkers										
Heart rate (b.p.m.)	66	69	77	79	70	65	67	78	79	79
Creatinine (mmol/L)	94.35	116.34	94.00	103.00	99.83	85.00	94.00	113.00	92.54	114.00
White cell count (10^9/L)	10.20	7.75	10.35	8.18	8.37	5.24	7.16	9.30	6.13	9.50
Haemoglobin (g/100ml)	11.05	13.01	15.77	14.39	12.60	10.90	16.00	14.90	15.67	11.70

Section 3: Trial comparable patient populations

Patient average covariate profiles CALIBER patients matching trial criteria		
Trial	**pegasus**	**odyssey**
Socio-demographic characteristics		
Sex (% female)	40%	44%
Age (if male)	75	69
Age (if female)	78	70
Age (weighted average)	76	70
Most deprived quintile (%)	19%	20%
SCAD diagnosis		
Other CHD	0%	22%
NSTEMI	64%	12%
STEMI	36%	8%
Unstable angina	0%	13%
Stable angina	0%	45%
SCAD severity		
PCI in last 6 months	23%	10%
CABG in last 6 months	6%	5%
Previous/recurrent MI	27%	20%
Use of nitrates	27%	29%
Smoking status		
Current smoker	28%	34%
Ex-smoker	35%	32%
Never smoked	37%	33%
Other CVD risk factors		
Hypertension	68%	75%
Diabetes	22%	16%
Total cholesterol (mmol/L)	4.22	4.75
HDL (mmol/L)	1.32	1.36
CVD co-morbidities		
Heart failure	28%	26%
Peripheral arterial disease	11%	9%
Atrial fibrillation	20%	16%
Stroke	0%	10%
Non-CVD co-morbidities		
Chronic kidney disease	11%	7%
Chronic obstructive pulmonary disease	24%	24%
Cancer	11%	9%
Chronic liver disease	1%	1%
Psychosocial characteristics		
Depression at diagnosis	14%	17%
Anxiety at diagnosis	7%	8%
Biomarkers		
Heart rate (b.p.m.)	70	72
Creatinine (mmol/L)	106	101
White cell count (10^9/L)	7.64	7.48
Haemoglobin (g/100ml)	13.27	13.58

Modelling lifetime costs and health outcomes for patients with stable coronary artery disease

Appendix F: Full Results by Risk Decile and Clinical Profiles

Section 1: Results by Risk Deciles

	Risk Decile									
Basecase	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Life years	26.81 (26.63 to 26.98)	19.62 (19.48 to 19.8)	17.34 (17.18 to 17.53)	15.63 (15.47 to 15.84)	14.26 (14.08 to 14.49)	13.03 (12.83 to 13.28)	11.92 (11.69 to 12.21)	10.48 (10.21 to 10.84)	8.52 (8.19 to 8.94)	5.51 (5.09 to 6.02)
QALYs*	19.23 (18.06 to 20.09)	14.08 (13.28 to 14.69)	12.4 (11.7 to 12.95)	11.13 (10.5 to 11.62)	10.09 (9.52 to 10.55)	9.16 (8.64 to 9.58)	8.26 (7.76 to 8.67)	7.13 (6.66 to 7.54)	5.65 (5.2 to 6.06)	3.51 (3.14 to 3.92)
QALYs**	19.11 (18.06 to 19.93)	13.97 (13.26 to 14.54)	12.29 (11.66 to 12.8)	11.01 (10.45 to 11.48)	9.97 (9.44 to 10.41)	9.03 (8.53 to 9.45)	8.13 (7.65 to 8.53)	6.99 (6.54 to 7.4)	5.5 (5.09 to 5.89)	3.34 (3.01 to 3.72)
Total Cost (£)	116,888 (64,743 to 168,032)	81,490 (54,858 to 108,206)	73,057 (53,809 to 92,411)	68,102 (53,588 to 83,062)	64,521 (53,054 to 76,141)	62,034 (53,567 to 71,316)	61,435 (54,672 to 68,506)	59,446 (53,872 to 65,167)	54,345 (49,316 to 59,720)	43,020 (37,731 to 48,842)
CVD Specific Cost (£)	71,943 (28,717 to 113,960)	52,034 (29,821 to 73,886)	47,681 (31,396 to 63,800)	45,251 (32,763 to 57,894)	43,438 (33,616 to 53,321)	42,266 (34,888 to 50,204)	42,301 (36,394 to 48,452)	41,366 (36,735 to 46,148)	38,410 (34,488 to 42,629)	31,199 (27,373 to 35,474)
CHD Specific Cost (£)	46,921 (12,629 to 79,870)	36,069 (18,387 to 53,211)	33,892 (20,897 to 46,637)	32,693 (22,676 to 42,679)	31,741 (23,884 to 39,629)	30,944 (24,902 to 37,252)	30,793 (26,031 to 35,683)	29,885 (26,263 to 33,699)	27,533 (24,555 to 30,719)	22,324 (19,620 to 25,304)
Discounted Life Years	16.77 (16.69 to 16.85)	13.66 (13.58 to 13.75)	12.5 (12.41 to 12.61)	11.56 (11.46 to 11.68)	10.76 (10.65 to 10.89)	9.99 (9.87 to 10.15)	9.26 (9.11 to 9.44)	8.27 (8.1 to 8.5)	6.9 (6.67 to 7.17)	4.67 (4.38 to 5.01)
Discounted QALYs*	12.09 (11.46 to 12.6)	9.84 (9.33 to 10.24)	8.97 (8.51 to 9.34)	8.25 (7.82 to 8.6)	7.63 (7.23 to 7.96)	7.04 (6.66 to 7.34)	6.42 (6.06 to 6.73)	5.64 (5.3 to 5.94)	4.58 (4.25 to 4.88)	2.98 (2.7 to 3.28)
Discounted QALYs**	12.04 (11.45 to 12.53)	9.77 (9.31 to 10.17)	8.9 (8.47 to 9.25)	8.18 (7.78 to 8.51)	7.55 (7.17 to 7.87)	6.95 (6.58 to 7.25)	6.34 (5.98 to 6.63)	5.55 (5.21 to 5.84)	4.47 (4.16 to 4.76)	2.85 (2.6 to 3.13)
Discounted Total Cost (£)	62,210 (33,724 to 90,043)	50,864 (34,490 to 67,270)	48,046 (35,660 to 60,475)	46,535 (37,121 to 56,164)	45,429 (37,877 to 53,081)	44,785 (39,150 to 50,876)	45,283 (40,798 to 49,797)	44,903 (41,160 to 48,628)	42,436 (38,855 to 46,110)	35,549 (31,679 to 39,615)
Discounted CVD Cost (£)	37,857 (14,738 to 60,313)	32,331 (18,671 to 45,751)	31,288 (21,030 to 41,484)	30,896 (22,893 to 38,965)	30,584 (24,097 to 37,099)	30,531 (25,641 to 35,726)	31,211 (27,360 to 35,214)	31,281 (28,197 to 34,361)	30,024 (27,337 to 32,944)	25,801 (22,935 to 28,739)
Discounted CHD Cost (£)	25,316 (7,118 to 42,948)	22,868 (12,077 to 33,360)	22,639 (14,464 to 30,648)	22,672 (16,260 to 29,078)	22,657 (17,508 to 27,823)	22,619 (18,653 to 26,761)	22,946 (19,867 to 26,107)	22,778 (20,345 to 25,211)	21,646 (19,569 to 23,841)	18,522 (16,462 to 20,605)
Time to first event (years)	24.55 (24.31 to 24.76)	17.8 (17.64 to 17.95)	15.62 (15.47 to 15.75)	13.98 (13.85 to 14.11)	12.67 (12.54 to 12.8)	11.49 (11.36 to 11.62)	10.43 (10.29 to 10.57)	9 (8.85 to 9.15)	7.06 (6.91 to 7.22)	4.07 (3.9 to 4.23)
MI as primary endpoint (%)	6 (5.55 to 6.49)	7.11 (6.73 to 7.49)	8.06 (7.72 to 8.43)	8.94 (8.61 to 9.29)	9.84 (9.5 to 10.15)	10.7 (10.39 to 11.01)	11.59 (11.28 to 11.9)	12.33 (12.01 to 12.64)	12.89 (12.57 to 13.22)	14.3 (13.87 to 14.73)
Ischaemic stroke as primary endpoint (%)	5.51 (5.01 to 6.06)	5.7 (5.34 to 6.11)	6.06 (5.73 to 6.43)	6.39 (6.07 to 6.74)	6.8 (6.48 to 7.11)	7.37 (7.05 to 7.68)	8.29 (7.95 to 8.63)	9.31 (8.96 to 9.68)	10.07 (9.72 to 10.43)	9.97 (9.58 to 10.38)
Haemorragic stroke as primary endpoint (%)	0.67 (0.48 to 0.89)	0.67 (0.54 to 0.81)	0.71 (0.59 to 0.82)	0.72 (0.62 to 0.84)	0.74 (0.65 to 0.84)	0.76 (0.67 to 0.86)	0.79 (0.7 to 0.89)	0.78 (0.69 to 0.88)	0.7 (0.61 to 0.81)	0.48 (0.4 to 0.57)
CVD Mortality (%)	4.48 (3.45 to 5.55)	6.6 (5.45 to 7.51)	8.52 (7.22 to 9.47)	10.39 (8.97 to 11.44)	12.63 (11.07 to 13.85)	15.48 (13.78 to 17.07)	20.17 (18.17 to 22.63)	26.29 (23.61 to 30.18)	34.46 (30.65 to 39.32)	45.95 (41.34 to 50.07)
Non-CVD Mortality (%)	95.46 (94.4 to 96.49)	93.4 (92.49 to 94.55)	91.48 (90.53 to 92.78)	89.6 (88.56 to 91.03)	87.37 (86.15 to 88.93)	84.52 (82.93 to 86.22)	79.83 (77.37 to 81.83)	73.71 (69.82 to 76.39)	65.54 (60.68 to 69.35)	54.05 (49.93 to 58.66)

* 1 year decrement post event

** constant decrement post event

					Risk Decile					
Scenario HR=0.9	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Life years	26.82 (26.65 to 26.98)	19.65 (19.52 to 19.81)	17.38 (17.24 to 17.56)	15.69 (15.54 to 15.88)	14.33 (14.17 to 14.55)	13.12 (12.94 to 13.36)	12.05 (11.84 to 12.33)	10.64 (10.39 to 10.98)	8.7 (8.38 to 9.1)	5.65 (5.26 to 6.14)
QALYs*	19.23 (18.06 to 20.1)	14.1 (13.31 to 14.71)	12.44 (11.73 to 12.98)	11.18 (10.55 to 11.67)	10.15 (9.58 to 10.6)	9.22 (8.7 to 9.65)	8.35 (7.85 to 8.76)	7.24 (6.77 to 7.65)	5.77 (5.32 to 6.17)	3.6 (3.23 to 4)
QALYs**	19.13 (18.06 to 19.95)	14 (13.28 to 14.58)	12.33 (11.7 to 12.84)	11.07 (10.5 to 11.53)	10.04 (9.51 to 10.47)	9.11 (8.61 to 9.53)	8.23 (7.75 to 8.63)	7.12 (6.66 to 7.51)	5.63 (5.23 to 6.02)	3.44 (3.12 to 3.81)
Total Cost (£)	116,326 (64,272 to 167,320)	81,135 (54,510 to 107,802)	72,807 (53,450 to 92,149)	67,944 (53,306 to 82,935)	64,464 (52,855 to 76,119)	62,119 (53,512 to 71,443)	61,757 (54,884 to 68,906)	60,001 (54,431 to 65,716)	55,094 (50,093 to 60,425)	43,676 (38,531 to 49,287)
CVD Specific Cost (£)	71,461 (28,231 to 113,373)	51,699 (29,429 to 73,512)	47,415 (31,048 to 63,543)	45,047 (32,473 to 57,691)	43,302 (33,392 to 53,276)	42,226 (34,724 to 50,204)	42,422 (36,418 to 48,621)	41,648 (36,976 to 46,488)	38,835 (34,907 to 43,039)	31,585 (27,807 to 35,723)
CHD Specific Cost (£)	46,551 (12,262 to 79,418)	35,800 (18,125 to 52,914)	33,670 (20,647 to 46,416)	32,513 (22,469 to 42,510)	31,610 (23,696 to 39,506)	30,882 (24,783 to 37,211)	30,844 (26,004 to 35,739)	30,050 (26,380 to 33,921)	27,801 (24,778 to 30,944)	22,571 (19,899 to 25,446)
Discounted Life Years	16.78 (16.71 to 16.85)	13.68 (13.61 to 13.77)	12.53 (12.45 to 12.63)	11.6 (11.51 to 11.71)	10.81 (10.71 to 10.94)	10.06 (9.94 to 10.2)	9.35 (9.21 to 9.52)	8.39 (8.22 to 8.6)	7.03 (6.81 to 7.28)	4.78 (4.5 to 5.11)
Discounted QALYs*	12.1 (11.47 to 12.61)	9.85 (9.35 to 10.26)	8.99 (8.53 to 9.36)	8.28 (7.85 to 8.63)	7.67 (7.27 to 8)	7.08 (6.7 to 7.39)	6.49 (6.13 to 6.79)	5.72 (5.37 to 6.02)	4.66 (4.33 to 4.96)	3.05 (2.77 to 3.35)
Discounted QALYs**	12.05 (11.46 to 12.54)	9.79 (9.33 to 10.19)	8.93 (8.5 to 9.29)	8.22 (7.81 to 8.55)	7.6 (7.22 to 7.91)	7.01 (6.64 to 7.31)	6.41 (6.05 to 6.7)	5.63 (5.29 to 5.92)	4.56 (4.25 to 4.85)	2.93 (2.68 to 3.21)
Discounted Total Cost (£)	61,970 (33,482 to 89,767)	50,675 (34,265 to 67,062)	47,897 (35,481 to 60,325)	46,427 (36,937 to 56,057)	45,373 (37,768 to 53,058)	44,806 (39,089 to 50,926)	45,446 (40,888 to 50,039)	45,219 (41,455 to 48,916)	42,906 (39,371 to 46,580)	36,032 (32,152 to 40,063)
Discounted CVD Cost (£)	37,639 (14,517 to 60,073)	32,144 (18,461 to 45,550)	31,123 (20,815 to 41,320)	30,757 (22,693 to 38,849)	30,477 (23,969 to 37,015)	30,476 (25,520 to 35,707)	31,250 (27,342 to 35,246)	31,423 (28,289 to 34,525)	30,276 (27,547 to 33,156)	26,077 (23,251 to 28,952)
Discounted CHD Cost (£)	25,144 (6,949 to 42,762)	22,715 (11,922 to 33,208)	22,501 (14,300 to 30,506)	22,552 (16,095 to 28,937)	22,559 (17,391 to 27,734)	22,558 (18,566 to 26,735)	22,951 (19,822 to 26,116)	22,856 (20,366 to 25,330)	21,803 (19,688 to 24,006)	18,697 (16,654 to 20,772)
Time to first event (years)	24.76 (24.53 to 24.96)	17.99 (17.84 to 18.13)	15.81 (15.67 to 15.93)	14.18 (14.06 to 14.31)	12.88 (12.76 to 13)	11.72 (11.59 to 11.84)	10.68 (10.55 to 10.81)	9.28 (9.13 to 9.42)	7.35 (7.19 to 7.5)	4.3 (4.13 to 4.47)
MI as primary endpoint (%)	5.44 (5.03 to 5.89)	6.46 (6.11 to 6.81)	7.33 (7.02 to 7.67)	8.15 (7.84 to 8.47)	8.98 (8.67 to 9.27)	9.8 (9.5 to 10.08)	10.65 (10.36 to 10.94)	11.38 (11.09 to 11.68)	11.99 (11.68 to 12.31)	13.47 (13.05 to 13.87)
Ischaemic stroke as primary endpoint (%)	5 (4.54 to 5.51)	5.18 (4.86 to 5.56)	5.52 (5.21 to 5.87)	5.84 (5.54 to 6.16)	6.22 (5.92 to 6.51)	6.76 (6.46 to 7.05)	7.64 (7.32 to 7.97)	8.64 (8.3 to 8.99)	9.43 (9.08 to 9.78)	9.48 (9.1 to 9.89)
Haemorragic stroke as primary endpoint (%)	0.67 (0.49 to 0.9)	0.68 (0.55 to 0.82)	0.71 (0.6 to 0.84)	0.73 (0.63 to 0.85)	0.75 (0.66 to 0.86)	0.77 (0.68 to 0.87)	0.81 (0.72 to 0.91)	0.8 (0.71 to 0.9)	0.73 (0.64 to 0.84)	0.51 (0.43 to 0.6)
CVD Mortality (%)	4.09 (3.14 to 5.07)	6.02 (4.97 to 6.86)	7.79 (6.59 to 8.66)	9.52 (8.21 to 10.49)	11.59 (10.15 to 12.72)	14.24 (12.67 to 15.73)	18.65 (16.77 to 20.96)	24.46 (21.94 to 28.11)	32.35 (28.74 to 36.88)	43.8 (39.38 to 47.72)
Non-CVD Mortality (%)	95.85 (94.88 to 96.79)	93.98 (93.14 to 95.03)	92.21 (91.34 to 93.41)	90.48 (89.51 to 91.79)	88.41 (87.28 to 89.85)	85.76 (84.27 to 87.33)	81.35 (79.04 to 83.23)	75.54 (71.89 to 78.06)	67.65 (63.12 to 71.26)	56.2 (52.28 to 60.62)

* 1 year decrement post event

** constant decrement post event

					Risk Decile					
Scenario HR=0.8	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Life years	26.83 (26.67 to 26.97)	19.68 (19.56 to 19.83)	17.43 (17.3 to 17.59)	15.75 (15.61 to 15.93)	14.41 (14.26 to 14.61)	13.22 (13.06 to 13.44)	12.19 (11.99 to 12.44)	10.81 (10.58 to 11.12)	8.89 (8.59 to 9.26)	5.81 (5.43 to 6.27)
QALYs*	19.24 (18.07 to 20.11)	14.12 (13.34 to 14.73)	12.47 (11.77 to 13.01)	11.22 (10.59 to 11.71)	10.2 (9.63 to 10.65)	9.3 (8.77 to 9.72)	8.45 (7.95 to 8.86)	7.36 (6.88 to 7.77)	5.89 (5.45 to 6.29)	3.71 (3.34 to 4.1)
QALYs**	19.14 (18.06 to 19.97)	14.03 (13.31 to 14.62)	12.37 (11.74 to 12.88)	11.12 (10.55 to 11.59)	10.1 (9.57 to 10.53)	9.19 (8.7 to 9.6)	8.34 (7.85 to 8.74)	7.24 (6.79 to 7.63)	5.77 (5.36 to 6.15)	3.56 (3.23 to 3.92)
Total Cost (£)	115,756 (63,795 to 166,598)	80,773 (54,120 to 107,389)	72,551 (53,082 to 91,896)	67,781 (53,014 to 82,803)	64,405 (52,651 to 76,101)	62,207 (53,455 to 71,622)	62,097 (55,108 to 69,331)	60,594 (54,973 to 66,325)	55,914 (50,957 to 61,211)	44,438 (39,264 to 49,876)
CVD Specific Cost (£)	70,971 (27,738 to 112,777)	51,358 (29,040 to 73,130)	47,143 (30,692 to 63,247)	44,839 (32,205 to 57,488)	43,163 (33,161 to 53,177)	42,185 (34,553 to 50,181)	42,551 (36,444 to 48,767)	41,950 (37,232 to 46,828)	39,303 (35,345 to 43,456)	32,038 (28,346 to 36,032)
CHD Specific Cost (£)	46,175 (11,891 to 78,959)	35,525 (17,858 to 52,611)	33,442 (20,394 to 46,174)	32,330 (22,210 to 42,337)	31,475 (23,530 to 39,414)	30,817 (24,670 to 37,225)	30,900 (25,961 to 35,827)	30,228 (26,517 to 34,109)	28,096 (25,049 to 31,237)	22,861 (20,245 to 25,719)
Discounted Life Years	16.79 (16.73 to 16.86)	13.7 (13.64 to 13.78)	12.56 (12.49 to 12.66)	11.64 (11.56 to 11.75)	10.86 (10.77 to 10.98)	10.13 (10.02 to 10.26)	9.44 (9.31 to 9.6)	8.5 (8.35 to 8.7)	7.16 (6.96 to 7.4)	4.91 (4.64 to 5.21)
Discounted QALYs*	12.11 (11.47 to 12.62)	9.87 (9.36 to 10.28)	9.01 (8.55 to 9.39)	8.31 (7.88 to 8.66)	7.71 (7.3 to 8.03)	7.13 (6.75 to 7.44)	6.55 (6.19 to 6.85)	5.8 (5.45 to 6.1)	4.75 (4.42 to 5.05)	3.13 (2.85 to 3.42)
Discounted QALYs**	12.06 (11.47 to 12.56)	9.82 (9.35 to 10.21)	8.96 (8.52 to 9.32)	8.25 (7.85 to 8.59)	7.64 (7.26 to 7.96)	7.06 (6.69 to 7.36)	6.48 (6.13 to 6.78)	5.72 (5.38 to 6.01)	4.66 (4.35 to 4.94)	3.02 (2.77 to 3.3)
Discounted Total Cost (£)	61,727 (33,236 to 89,489)	50,483 (34,036 to 66,850)	47,745 (35,300 to 60,172)	46,317 (36,748 to 55,994)	45,314 (37,691 to 53,033)	44,829 (39,027 to 51,018)	45,617 (41,061 to 50,263)	45,555 (41,805 to 49,261)	43,414 (39,829 to 47,104)	36,583 (32,756 to 40,495)
Discounted CVD Cost (£)	37,418 (14,294 to 59,830)	31,953 (18,248 to 45,346)	30,956 (20,596 to 41,151)	30,615 (22,490 to 38,731)	30,368 (23,839 to 36,906)	30,419 (25,391 to 35,688)	31,291 (27,335 to 35,254)	31,575 (28,357 to 34,715)	30,551 (27,749 to 33,423)	26,395 (23,621 to 29,239)
Discounted CHD Cost (£)	24,970 (6,780 to 42,575)	22,560 (11,764 to 33,053)	22,361 (14,139 to 30,360)	22,428 (15,925 to 28,821)	22,459 (17,272 to 27,665)	22,494 (18,470 to 26,702)	22,957 (19,776 to 26,161)	22,941 (20,424 to 25,455)	21,974 (19,859 to 24,145)	18,899 (16,854 to 20,921)
Time to first event (years)	24.97 (24.76 to 25.15)	18.18 (18.04 to 18.31)	16.01 (15.88 to 16.12)	14.39 (14.27 to 14.51)	13.09 (12.98 to 13.21)	11.95 (11.83 to 12.07)	10.94 (10.81 to 11.07)	9.57 (9.43 to 9.71)	7.65 (7.49 to 7.81)	4.56 (4.38 to 4.73)
MI as primary endpoint (%)	4.87 (4.5 to 5.28)	5.79 (5.48 to 6.11)	6.58 (6.3 to 6.9)	7.33 (7.05 to 7.63)	8.1 (7.81 to 8.36)	8.85 (8.58 to 9.12)	9.66 (9.39 to 9.94)	10.39 (10.11 to 10.67)	11.03 (10.73 to 11.33)	12.56 (12.16 to 12.94)
Ischaemic stroke as primary endpoint (%)	4.48 (4.07 to 4.94)	4.65 (4.36 to 5)	4.97 (4.69 to 5.28)	5.26 (4.99 to 5.56)	5.62 (5.35 to 5.89)	6.13 (5.85 to 6.4)	6.96 (6.66 to 7.26)	7.92 (7.6 to 8.26)	8.72 (8.39 to 9.07)	8.93 (8.56 to 9.33)
Haemorragic stroke as primary endpoint (%)	0.68 (0.49 to 0.9)	0.69 (0.55 to 0.83)	0.72 (0.61 to 0.85)	0.75 (0.64 to 0.86)	0.76 (0.67 to 0.87)	0.79 (0.7 to 0.89)	0.83 (0.74 to 0.93)	0.83 (0.73 to 0.93)	0.76 (0.67 to 0.88)	0.54 (0.45 to 0.64)
CVD Mortality (%)	3.7 (2.84 to 4.57)	5.43 (4.48 to 6.2)	7.04 (5.96 to 7.84)	8.62 (7.43 to 9.5)	10.51 (9.2 to 11.54)	12.95 (11.52 to 14.32)	17.04 (15.31 to 19.19)	22.49 (20.16 to 25.85)	30.02 (26.63 to 34.22)	41.36 (37.16 to 45.06)
Non-CVD Mortality (%)	96.25 (95.37 to 97.1)	94.56 (93.8 to 95.52)	92.96 (92.16 to 94.04)	91.38 (90.5 to 92.57)	89.49 (88.46 to 90.8)	87.05 (85.68 to 88.48)	82.96 (80.81 to 84.69)	77.5 (74.15 to 79.84)	69.98 (65.78 to 73.37)	58.64 (54.94 to 62.84)

* 1 year decrement post event

** constant decrement post event

	Risk Decile									
Scenario HR=0.7	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Life years	26.83 (26.69 to 26.97)	19.71 (19.6 to 19.84)	17.47 (17.35 to 17.62)	15.81 (15.68 to 15.97)	14.49 (14.36 to 14.67)	13.33 (13.18 to 13.53)	12.33 (12.15 to 12.56)	10.99 (10.77 to 11.28)	9.1 (8.82 to 9.44)	5.99 (5.63 to 6.43)
QALYs*	19.25 (18.08 to 20.11)	14.14 (13.36 to 14.75)	12.5 (11.8 to 13.04)	11.26 (10.63 to 11.75)	10.26 (9.68 to 10.71)	9.37 (8.84 to 9.79)	8.55 (8.04 to 8.95)	7.49 (7.01 to 7.88)	6.03 (5.59 to 6.42)	3.82 (3.46 to 4.2)
QALYs**	19.16 (18.08 to 19.99)	14.06 (13.34 to 14.65)	12.42 (11.77 to 12.93)	11.18 (10.6 to 11.65)	10.17 (9.64 to 10.6)	9.28 (8.78 to 9.68)	8.45 (7.97 to 8.85)	7.38 (6.92 to 7.76)	5.92 (5.51 to 6.29)	3.69 (3.36 to 4.04)
Total Cost (£)	115,177 (63,233 to 165,863)	80,405 (53,673 to 106,949)	72,288 (52,706 to 91,587)	67,615 (52,735 to 82,667)	64,345 (52,458 to 76,100)	62,300 (53,397 to 71,782)	62,454 (55,341 to 69,736)	61,227 (55,536 to 66,892)	56,812 (51,829 to 62,081)	45,327 (40,267 to 50,662)
CVD Specific Cost (£)	70,475 (27,238 to 112,172)	51,010 (28,659 to 72,740)	46,865 (30,328 to 63,028)	44,624 (31,910 to 57,279)	43,019 (32,975 to 53,046)	42,144 (34,377 to 50,231)	42,688 (36,474 to 48,945)	42,274 (37,502 to 47,186)	39,817 (35,815 to 43,938)	32,570 (28,996 to 36,421)
CHD Specific Cost (£)	45,795 (11,515 to 78,492)	35,246 (17,587 to 52,302)	33,210 (20,136 to 45,964)	32,141 (21,989 to 42,159)	31,337 (23,351 to 39,320)	30,751 (24,552 to 37,240)	30,959 (25,924 to 35,994)	30,419 (26,620 to 34,296)	28,422 (25,320 to 31,527)	23,203 (20,580 to 25,947)
Discounted Life Years	16.8 (16.74 to 16.86)	13.73 (13.67 to 13.8)	12.59 (12.53 to 12.68)	11.68 (11.61 to 11.78)	10.92 (10.83 to 11.02)	10.19 (10.1 to 10.32)	9.53 (9.42 to 9.68)	8.62 (8.48 to 8.8)	7.31 (7.12 to 7.52)	5.05 (4.8 to 5.34)
Discounted QALYs*	12.12 (11.48 to 12.62)	9.89 (9.38 to 10.29)	9.04 (8.58 to 9.42)	8.34 (7.91 to 8.69)	7.75 (7.34 to 8.07)	7.18 (6.8 to 7.49)	6.62 (6.25 to 6.92)	5.88 (5.53 to 6.18)	4.85 (4.51 to 5.14)	3.22 (2.95 to 3.51)
Discounted QALYs**	12.08 (11.48 to 12.57)	9.84 (9.37 to 10.24)	8.99 (8.55 to 9.36)	8.29 (7.88 to 8.63)	7.69 (7.3 to 8.01)	7.12 (6.75 to 7.42)	6.55 (6.2 to 6.85)	5.81 (5.47 to 6.1)	4.77 (4.45 to 5.05)	3.12 (2.87 to 3.38)
Discounted Total Cost (£)	61,482 (32,989 to 89,207)	50,287 (33,804 to 66,634)	47,589 (35,114 to 60,015)	46,203 (36,555 to 55,929)	45,254 (37,557 to 53,008)	44,852 (38,964 to 51,038)	45,796 (41,154 to 50,445)	45,911 (42,152 to 49,609)	43,966 (40,329 to 47,635)	37,216 (33,401 to 41,056)
Discounted CVD Cost (£)	37,194 (14,078 to 59,582)	31,760 (18,041 to 45,139)	30,785 (20,372 to 40,974)	30,470 (22,281 to 38,569)	30,256 (23,707 to 36,829)	30,360 (25,265 to 35,669)	31,335 (27,307 to 35,354)	31,738 (28,495 to 34,931)	30,850 (28,072 to 33,706)	26,762 (24,002 to 29,540)
Discounted CHD Cost (£)	24,794 (6,608 to 42,411)	22,403 (11,605 to 32,895)	22,218 (13,976 to 30,212)	22,302 (15,752 to 28,716)	22,356 (17,139 to 27,583)	22,429 (18,374 to 26,666)	22,965 (19,726 to 26,217)	23,031 (20,502 to 25,571)	22,161 (19,992 to 24,353)	19,133 (17,135 to 21,134)
Time to first event (years)	25.19 (25 to 25.35)	18.38 (18.25 to 18.49)	16.21 (16.09 to 16.32)	14.6 (14.49 to 14.71)	13.31 (13.21 to 13.42)	12.19 (12.08 to 12.3)	11.22 (11.09 to 11.34)	9.88 (9.73 to 10.01)	7.97 (7.82 to 8.13)	4.84 (4.66 to 5.02)
MI as primary endpoint (%)	4.3 (3.97 to 4.65)	5.11 (4.83 to 5.4)	5.82 (5.57 to 6.11)	6.5 (6.24 to 6.76)	7.19 (6.93 to 7.43)	7.88 (7.63 to 8.12)	8.63 (8.38 to 8.89)	9.33 (9.07 to 9.6)	9.99 (9.72 to 10.27)	11.55 (11.17 to 11.92)
Ischaemic stroke as primary endpoint (%)	3.96 (3.59 to 4.36)	4.11 (3.85 to 4.42)	4.4 (4.15 to 4.69)	4.67 (4.43 to 4.94)	5 (4.76 to 5.24)	5.47 (5.22 to 5.71)	6.24 (5.97 to 6.52)	7.15 (6.85 to 7.46)	7.96 (7.64 to 8.28)	8.31 (7.95 to 8.69)
Haemorragic stroke as primary endpoint (%)	0.69 (0.49 to 0.91)	0.7 (0.56 to 0.84)	0.73 (0.62 to 0.86)	0.76 (0.65 to 0.87)	0.78 (0.68 to 0.89)	0.8 (0.71 to 0.91)	0.85 (0.75 to 0.95)	0.85 (0.75 to 0.96)	0.8 (0.7 to 0.91)	0.57 (0.48 to 0.68)
CVD Mortality (%)	3.29 (2.53 to 4.07)	4.83 (3.98 to 5.52)	6.27 (5.3 to 6.98)	7.68 (6.62 to 8.48)	9.39 (8.21 to 10.33)	11.61 (10.31 to 12.85)	15.34 (13.79 to 17.31)	20.38 (18.25 to 23.45)	27.47 (24.35 to 31.3)	38.57 (34.65 to 42.03)
Non-CVD Mortality (%)	96.65 (95.87 to 97.41)	95.17 (94.48 to 96.02)	93.73 (93.02 to 94.7)	92.32 (91.52 to 93.38)	90.61 (89.67 to 91.79)	88.39 (87.15 to 89.69)	84.66 (82.69 to 86.21)	79.62 (76.55 to 81.75)	72.53 (68.7 to 75.65)	61.43 (57.97 to 65.35)

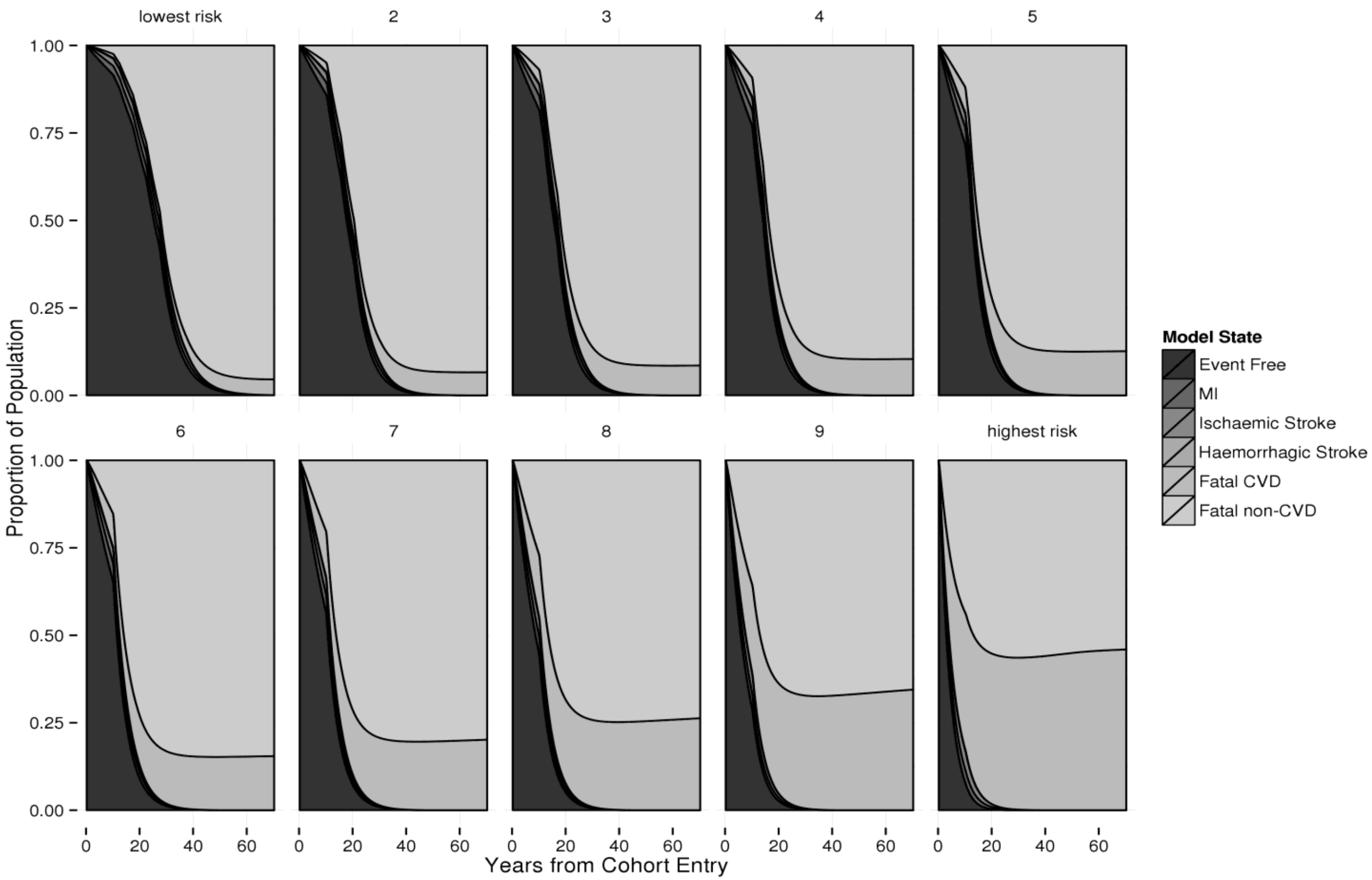
* 1 year decrement post event

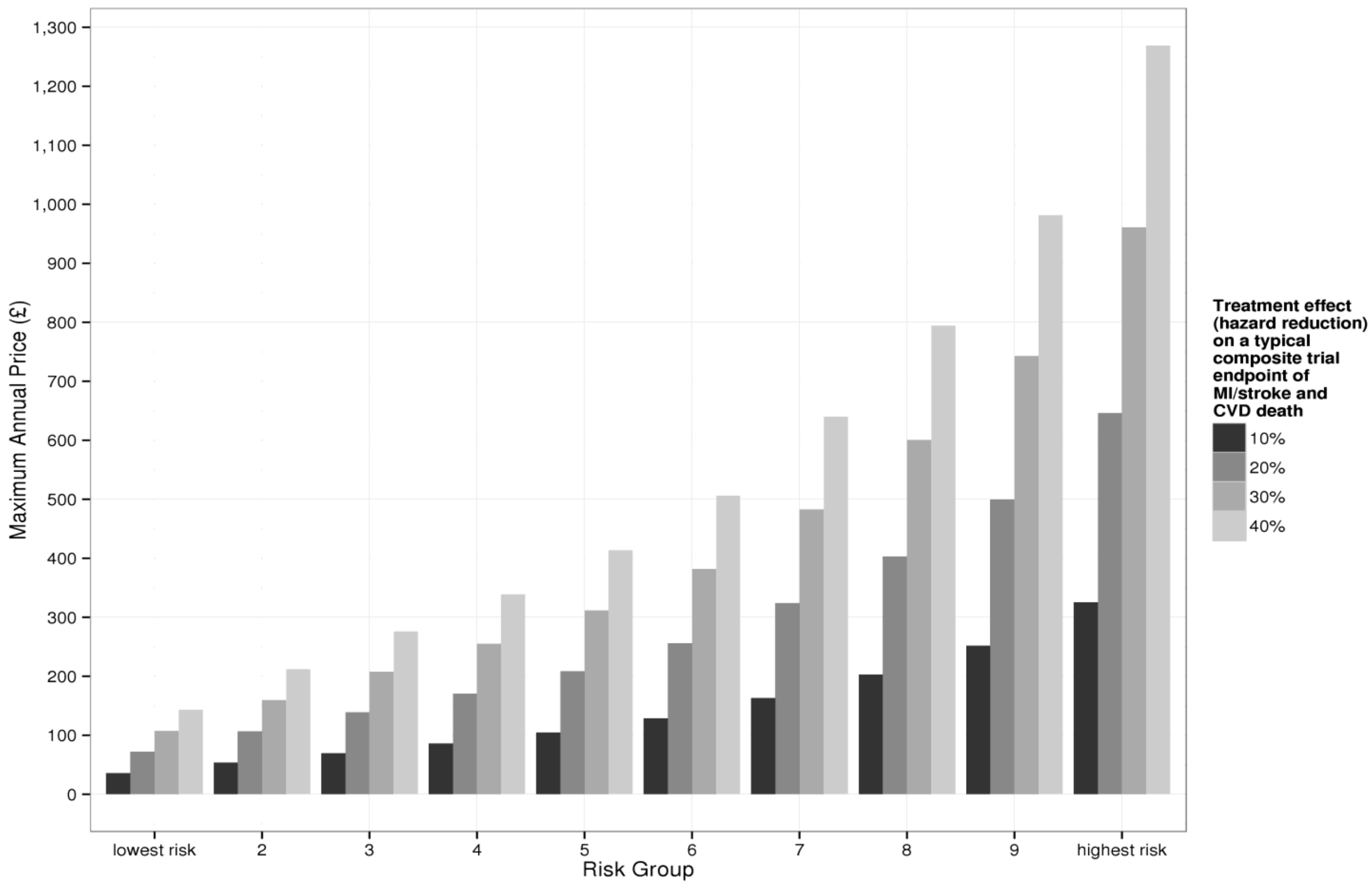
** constant decrement post event

	Risk Decile									
Scenario HR=0.6	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Life years	26.84 (26.71 to 26.96)	19.74 (19.64 to 19.86)	17.52 (17.41 to 17.65)	15.87 (15.76 to 16.02)	14.57 (14.45 to 14.73)	13.43 (13.3 to 13.61)	12.48 (12.32 to 12.69)	11.18 (10.99 to 11.44)	9.32 (9.07 to 9.63)	6.2 (5.85 to 6.59)
QALYs*	19.25 (18.09 to 20.12)	14.17 (13.38 to 14.77)	12.54 (11.84 to 13.07)	11.31 (10.68 to 11.8)	10.32 (9.74 to 10.77)	9.45 (8.91 to 9.87)	8.65 (8.14 to 9.05)	7.62 (7.13 to 8.01)	6.18 (5.73 to 6.57)	3.96 (3.6 to 4.32)
QALYs**	19.18 (18.08 to 20.01)	14.09 (13.36 to 14.69)	12.46 (11.81 to 12.99)	11.23 (10.65 to 11.71)	10.24 (9.7 to 10.67)	9.36 (8.86 to 9.77)	8.56 (8.08 to 8.97)	7.52 (7.06 to 7.91)	6.08 (5.66 to 6.45)	3.83 (3.51 to 4.18)
Total Cost (£)	114,589 (62,629 to 165,153)	80,029 (53,217 to 106,536)	72,020 (52,323 to 91,300)	67,443 (52,434 to 82,527)	64,283 (52,406 to 76,127)	62,397 (53,341 to 71,876)	62,832 (55,638 to 70,110)	61,906 (56,117 to 67,617)	57,799 (52,769 to 63,033)	46,370 (41,440 to 51,583)
CVD Specific Cost (£)	69,971 (26,732 to 111,558)	50,656 (28,272 to 72,342)	46,581 (30,007 to 62,763)	44,404 (31,581 to 57,064)	42,872 (32,790 to 52,950)	42,103 (34,254 to 50,298)	42,833 (36,510 to 49,136)	42,623 (37,821 to 47,567)	40,383 (36,362 to 44,471)	33,199 (29,645 to 36,932)
CHD Specific Cost (£)	45,409 (11,140 to 78,019)	34,962 (17,312 to 51,987)	32,973 (19,872 to 45,761)	31,948 (21,773 to 41,976)	31,194 (23,113 to 39,221)	30,684 (24,409 to 37,185)	31,022 (25,896 to 36,120)	30,625 (26,717 to 34,582)	28,780 (25,670 to 31,945)	23,609 (21,053 to 26,297)
Discounted Life Years	16.81 (16.76 to 16.87)	13.75 (13.69 to 13.81)	12.63 (12.57 to 12.7)	11.73 (11.66 to 11.81)	10.97 (10.89 to 11.07)	10.27 (10.18 to 10.38)	9.63 (9.53 to 9.76)	8.75 (8.63 to 8.91)	7.46 (7.29 to 7.66)	5.21 (4.96 to 5.47)
Discounted QALYs*	12.13 (11.49 to 12.63)	9.9 (9.4 to 10.31)	9.06 (8.6 to 9.44)	8.38 (7.95 to 8.72)	7.79 (7.38 to 8.11)	7.23 (6.85 to 7.54)	6.69 (6.31 to 6.99)	5.97 (5.62 to 6.27)	4.95 (4.61 to 5.24)	3.33 (3.05 to 3.6)
Discounted QALYs**	12.09 (11.48 to 12.59)	9.86 (9.38 to 10.26)	9.02 (8.58 to 9.39)	8.33 (7.92 to 8.67)	7.74 (7.35 to 8.05)	7.18 (6.81 to 7.48)	6.63 (6.27 to 6.93)	5.91 (5.56 to 6.2)	4.88 (4.56 to 5.16)	3.24 (2.98 to 3.49)
Discounted Total Cost (£)	61,233 (32,738 to 88,921)	50,089 (33,569 to 66,414)	47,430 (34,955 to 59,854)	46,087 (36,357 to 55,823)	45,193 (37,422 to 52,982)	44,876 (38,931 to 51,071)	45,984 (41,303 to 50,665)	46,289 (42,418 to 49,997)	44,565 (40,929 to 48,237)	37,944 (34,172 to 41,744)
Discounted CVD Cost (£)	36,968 (13,867 to 59,331)	31,563 (17,844 to 44,928)	30,611 (20,147 to 40,772)	30,322 (22,069 to 38,417)	30,141 (23,569 to 36,749)	30,301 (25,165 to 35,650)	31,382 (27,283 to 35,469)	31,911 (28,661 to 35,135)	31,176 (28,361 to 34,031)	27,188 (24,466 to 29,914)
Discounted CHD Cost (£)	24,616 (6,435 to 42,245)	22,243 (11,423 to 32,734)	22,072 (13,810 to 30,061)	22,173 (15,605 to 28,608)	22,250 (16,989 to 27,496)	22,362 (18,271 to 26,630)	22,973 (19,663 to 26,264)	23,129 (20,522 to 25,716)	22,365 (20,170 to 24,561)	19,407 (17,431 to 21,396)
Time to first event (years)	25.4 (25.24 to 25.55)	18.57 (18.46 to 18.68)	16.42 (16.31 to 16.51)	14.81 (14.71 to 14.91)	13.54 (13.44 to 13.64)	12.43 (12.33 to 12.54)	11.5 (11.38 to 11.62)	10.2 (10.06 to 10.33)	8.32 (8.17 to 8.48)	5.17 (4.97 to 5.35)
MI as primary endpoint (%)	3.71 (3.42 to 4.02)	4.42 (4.18 to 4.67)	5.05 (4.83 to 5.29)	5.64 (5.41 to 5.87)	6.25 (6.02 to 6.47)	6.87 (6.65 to 7.09)	7.56 (7.34 to 7.79)	8.22 (7.98 to 8.46)	8.88 (8.62 to 9.14)	10.44 (10.09 to 10.78)
Ischaemic stroke as primary endpoint (%)	3.42 (3.1 to 3.78)	3.56 (3.34 to 3.84)	3.82 (3.6 to 4.07)	4.06 (3.85 to 4.3)	4.36 (4.14 to 4.57)	4.78 (4.56 to 5)	5.48 (5.24 to 5.73)	6.33 (6.05 to 6.61)	7.12 (6.82 to 7.42)	7.59 (7.26 to 7.96)
Haemorragic stroke as primary endpoint (%)	0.69 (0.5 to 0.92)	0.7 (0.57 to 0.85)	0.74 (0.62 to 0.87)	0.77 (0.66 to 0.89)	0.79 (0.69 to 0.9)	0.82 (0.73 to 0.93)	0.87 (0.77 to 0.98)	0.88 (0.78 to 1)	0.83 (0.73 to 0.96)	0.61 (0.52 to 0.73)
CVD Mortality (%)	2.87 (2.2 to 3.58)	4.22 (3.47 to 4.82)	5.47 (4.62 to 6.1)	6.72 (5.78 to 7.42)	8.23 (7.19 to 9.06)	10.2 (9.05 to 11.3)	13.54 (12.16 to 15.32)	18.12 (16.21 to 20.87)	24.67 (21.84 to 28.1)	35.36 (31.76 to 38.53)
Non-CVD Mortality (%)	97.07 (96.36 to 97.73)	95.78 (95.18 to 96.53)	94.53 (93.9 to 95.38)	93.28 (92.58 to 94.22)	91.77 (90.94 to 92.81)	89.8 (88.7 to 90.95)	86.46 (84.68 to 87.84)	81.88 (79.13 to 83.79)	75.33 (71.9 to 78.16)	64.64 (61.47 to 68.23)

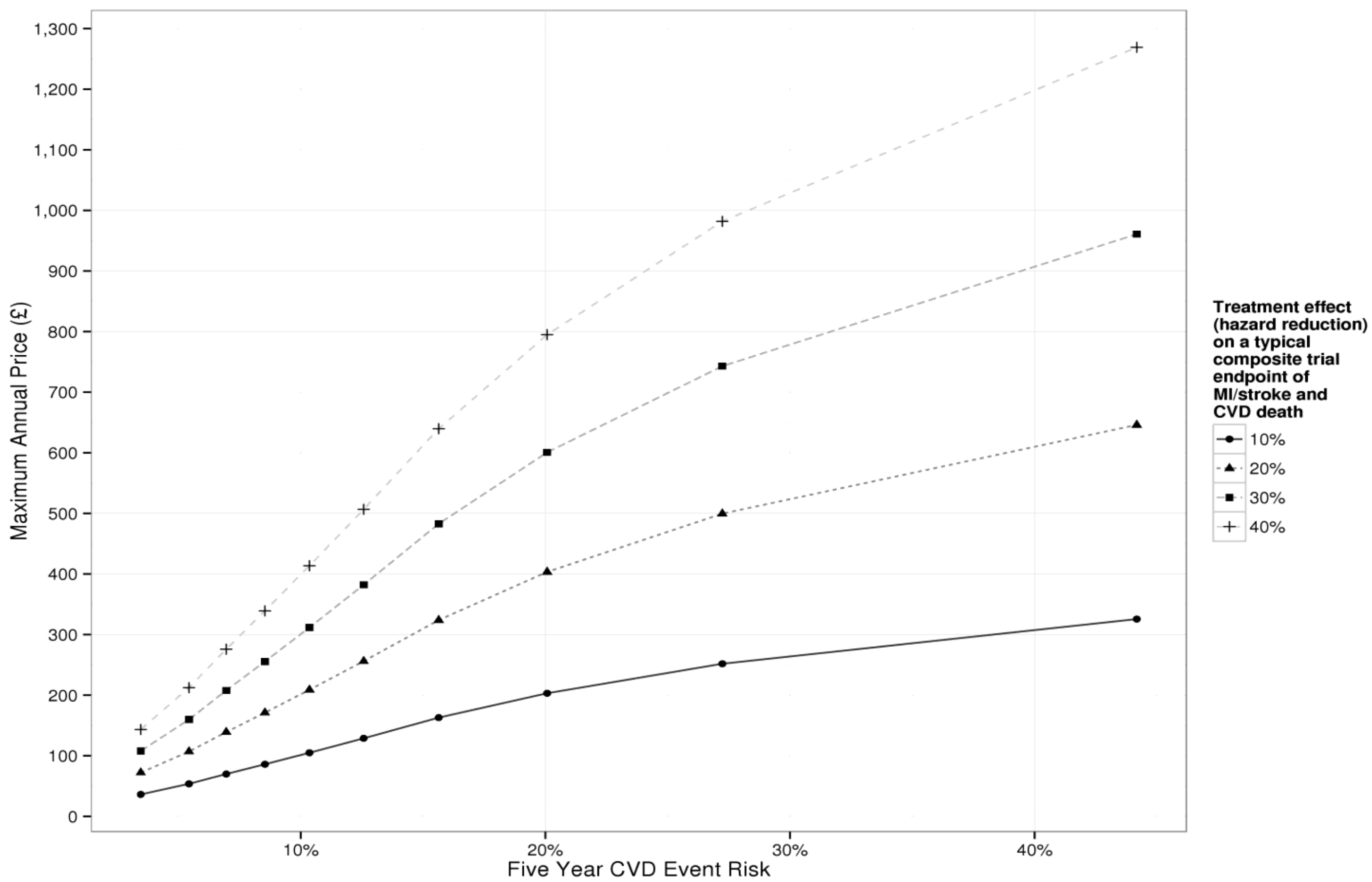
* 1 year decrement post event

** constant decrement post event


lowest risk
2
3
4
5
6
7
8
9
highest risk
1.00
0.75
0.50
0.25
0.00
Proportion of Population
0
20
40
60
Years from Cohort Entry
Model State
Event Free
MI
Ischaemic Stroke
Haemorrhagic Stroke
Fatal CVD
Fatal non-CVD



Maximum Annual Price (£)
1,300
1,200
1,100
1,000
900
800
700
600
500
400
300
200
100
0
lowest risk
2
3
4
5
6
7
8
9
highest risk
Risk Group
Treatment effect (hazard reduction) on a typical composite trial endpoint of MI/stroke and CVD death
10%
20%
30%
40%



1,300
1,200
1,100
1,000
900
800
700
600
500
400
300
200
100
0
Maximum Annual Price (£)
10%
20%
30%
40%
Five Year CVD Event Risk
Treatment effect (hazard reduction) on a typical composite trial endpoint of MI/stroke and CVD death
10%
20%
30%
40%

Section 2: Results Based on Selected Clinical Profiles

	Patient Profile									
Basecase	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Life years	25.61 (25.33 to 25.84)	18.6 (18.29 to 18.87)	18.41 (18.14 to 18.69)	16.55 (16.23 to 16.88)	15.01 (14.77 to 15.35)	13.5 (13.11 to 13.9)	12.41 (11.93 to 12.84)	10.41 (9.98 to 10.82)	9.04 (8.35 to 9.74)	5.48 (4.99 to 6.07)
QALYs*	18.51 (17.4 to 19.34)	13.47 (12.69 to 14.09)	13.36 (12.59 to 13.98)	12.02 (11.33 to 12.57)	10.9 (10.32 to 11.43)	9.81 (9.22 to 10.34)	9.01 (8.4 to 9.51)	6.34 (5.73 to 6.84)	5.5 (4.88 to 6.08)	3.33 (2.95 to 3.75)
QALYs**	18.4 (17.39 to 19.2)	13.37 (12.65 to 13.99)	13.26 (12.56 to 13.85)	11.93 (11.29 to 12.47)	10.76 (10.19 to 11.28)	9.66 (9.1 to 10.18)	8.84 (8.29 to 9.34)	6.22 (5.63 to 6.71)	5.34 (4.73 to 5.93)	3.22 (2.83 to 3.62)
Total Cost (£)	97,039 (49,388 to 143,478)	82,964 (60,489 to 106,300)	81,898 (58,414 to 106,229)	56,502 (38,504 to 74,266)	49,665 (35,461 to 63,564)	44,497 (33,681 to 55,477)	63,359 (55,253 to 72,133)	50,352 (44,884 to 56,263)	68,067 (61,550 to 74,877)	42,529 (37,990 to 47,382)
CVD Specific Cost (£)	58,657 (19,082 to 96,458)	51,727 (32,888 to 71,095)	52,296 (33,045 to 72,395)	36,941 (21,875 to 51,656)	33,987 (22,071 to 45,875)	30,821 (21,659 to 40,068)	48,232 (41,260 to 55,659)	35,462 (31,008 to 40,395)	51,822 (46,701 to 57,265)	30,566 (27,267 to 33,973)
CHD Specific Cost (£)	35,950 (4,550 to 65,628)	34,931 (19,966 to 50,241)	36,125 (20,724 to 52,053)	24,542 (12,542 to 36,201)	27,987 (18,501 to 37,393)	25,520 (18,181 to 32,893)	34,655 (29,155 to 40,573)	26,699 (23,119 to 30,529)	37,519 (33,671 to 41,528)	24,279 (21,793 to 26,868)
Discounted Life Years	16.27 (16.14 to 16.38)	13.06 (12.89 to 13.22)	12.93 (12.77 to 13.1)	11.98 (11.78 to 12.19)	11.16 (11 to 11.36)	10.23 (9.97 to 10.49)	9.59 (9.27 to 9.87)	8.23 (7.93 to 8.51)	7.26 (6.78 to 7.75)	4.64 (4.27 to 5.07)
Discounted QALYs*	11.82 (11.21 to 12.31)	9.49 (8.98 to 9.91)	9.42 (8.94 to 9.83)	8.73 (8.27 to 9.1)	8.12 (7.72 to 8.49)	7.45 (7.04 to 7.82)	6.97 (6.54 to 7.33)	5.02 (4.57 to 5.39)	4.42 (3.96 to 4.86)	2.83 (2.53 to 3.15)
Discounted QALYs**	11.77 (11.19 to 12.25)	9.43 (8.96 to 9.84)	9.36 (8.9 to 9.75)	8.67 (8.24 to 9.05)	8.03 (7.64 to 8.4)	7.36 (6.96 to 7.72)	6.86 (6.45 to 7.21)	4.94 (4.5 to 5.31)	4.31 (3.85 to 4.75)	2.74 (2.43 to 3.06)
Discounted Total Cost (£)	51,587 (25,308 to 76,991)	52,614 (38,840 to 66,986)	51,998 (37,350 to 67,021)	36,514 (25,099 to 47,787)	33,301 (24,026 to 42,212)	30,690 (23,448 to 37,856)	46,305 (40,908 to 52,152)	37,856 (34,171 to 41,732)	52,947 (48,530 to 57,385)	35,084 (31,596 to 38,769)
Discounted CVD Cost (£)	30,666 (9,115 to 51,409)	32,587 (21,083 to 44,440)	33,049 (21,154 to 45,279)	23,805 (14,252 to 33,081)	22,826 (14,984 to 30,469)	21,306 (15,246 to 27,335)	35,458 (30,850 to 40,399)	26,713 (23,719 to 29,981)	40,433 (36,920 to 44,039)	25,227 (22,734 to 27,750)
Discounted CHD Cost (£)	19,118 (2,134 to 35,549)	22,399 (13,269 to 31,756)	23,243 (13,848 to 32,937)	16,060 (8,520 to 23,477)	19,356 (13,131 to 25,442)	18,118 (13,283 to 22,916)	25,707 (22,029 to 29,616)	20,326 (17,873 to 22,917)	29,414 (26,822 to 32,126)	20,117 (18,226 to 22,068)
Time to first event (years)	23.4 (22.98 to 23.79)	16.82 (16.4 to 17.24)	16.31 (15.89 to 16.72)	14.72 (14.25 to 15.21)	13.24 (12.84 to 13.6)	11.81 (11.26 to 12.34)	10.65 (10.07 to 11.19)	9.12 (8.65 to 9.61)	7.31 (6.55 to 8.11)	4.13 (3.62 to 4.65)
MI as primary endpoint (%)	5.82 (4.96 to 6.76)	5.93 (5.19 to 6.7)	8.32 (7.44 to 9.19)	8.86 (7.78 to 9.87)	11.2 (10.3 to 12.21)	11.51 (10.25 to 12.85)	11.57 (10.33 to 12.86)	10.17 (9.29 to 11.08)	15 (13.4 to 16.61)	16.81 (15.81 to 17.77)
Ischaemic stroke as primary endpoint (%)	5.84 (4.9 to 6.72)	6.99 (5.94 to 8.01)	6.94 (6.07 to 7.88)	6.15 (5.26 to 7.02)	5.62 (4.96 to 6.33)	5.94 (4.92 to 7.02)	10.05 (8.5 to 11.65)	7.32 (6.56 to 8.04)	9.95 (8.61 to 11.27)	5.89 (5.33 to 6.51)
Haemorragic stroke as primary endpoint (%)	0.64 (0.42 to 0.99)	0.66 (0.49 to 0.89)	0.71 (0.56 to 0.89)	0.74 (0.61 to 0.9)	0.78 (0.65 to 0.91)	0.76 (0.65 to 0.89)	0.84 (0.7 to 0.99)	0.83 (0.68 to 0.98)	0.73 (0.59 to 0.91)	0.53 (0.41 to 0.67)
CVD Mortality (%)	4.51 (3.21 to 6.05)	6.82 (5.25 to 8.71)	9.64 (8.01 to 11.18)	13.33 (11.34 to 15.28)	15.84 (13.78 to 17.34)	18.52 (16.22 to 20.65)	22.08 (19.08 to 25.21)	32.49 (29.49 to 35.87)	35.15 (30.94 to 40.6)	47.28 (44.52 to 50.44)
Non-CVD Mortality (%)	95.44 (93.91 to 96.74)	93.18 (91.29 to 94.75)	90.36 (88.82 to 91.99)	86.67 (84.72 to 88.66)	84.16 (82.66 to 86.22)	81.48 (79.35 to 83.78)	77.92 (74.79 to 80.92)	67.51 (64.13 to 70.51)	64.85 (59.4 to 69.06)	52.72 (49.56 to 55.48)

* 1 year decrement post event

** constant decrement post event

	Patient Profile									
Scenario HR=0.9	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Life years	25.62 (25.36 to 25.83)	18.63 (18.34 to 18.89)	18.46 (18.2 to 18.72)	16.63 (16.33 to 16.94)	15.12 (14.88 to 15.43)	13.62 (13.24 to 14)	12.55 (12.1 to 12.96)	10.61 (10.2 to 11.01)	9.22 (8.55 to 9.91)	5.64 (5.14 to 6.22)
QALYs*	18.52 (17.41 to 19.34)	13.49 (12.71 to 14.11)	13.4 (12.63 to 14.02)	12.08 (11.39 to 12.63)	10.98 (10.39 to 11.51)	9.89 (9.32 to 10.42)	9.11 (8.5 to 9.61)	6.46 (5.86 to 6.96)	5.61 (5 to 6.2)	3.43 (3.04 to 3.85)
QALYs**	18.42 (17.41 to 19.21)	13.4 (12.66 to 14.02)	13.3 (12.6 to 13.9)	12 (11.36 to 12.54)	10.84 (10.28 to 11.36)	9.76 (9.2 to 10.28)	8.95 (8.4 to 9.44)	6.35 (5.76 to 6.84)	5.46 (4.86 to 6.06)	3.32 (2.93 to 3.73)
Total Cost (£)	96,485 (48,868 to 142,792)	82,651 (60,084 to 105,889)	81,602 (58,059 to 105,970)	56,373 (38,270 to 74,247)	49,603 (35,239 to 63,636)	44,507 (33,514 to 55,525)	63,671 (55,554 to 72,503)	51,081 (45,539 to 56,973)	69,059 (62,597 to 75,932)	43,211 (38,644 to 47,975)
CVD Specific Cost (£)	58,183 (18,584 to 96,005)	51,424 (32,565 to 70,764)	51,983 (32,673 to 72,094)	36,747 (21,576 to 51,557)	33,841 (21,836 to 45,815)	30,728 (21,468 to 40,049)	48,389 (41,342 to 55,926)	35,881 (31,279 to 40,876)	52,485 (47,383 to 57,956)	30,953 (27,600 to 34,392)
CHD Specific Cost (£)	35,591 (4,179 to 65,238)	34,700 (19,717 to 49,980)	35,867 (20,411 to 51,780)	24,355 (12,238 to 36,056)	27,856 (18,299 to 37,339)	25,433 (18,015 to 32,911)	34,736 (29,139 to 40,717)	26,985 (23,325 to 30,912)	37,957 (34,083 to 42,009)	24,549 (21,993 to 27,129)
Discounted Life Years	16.28 (16.16 to 16.38)	13.08 (12.92 to 13.23)	12.97 (12.81 to 13.13)	12.04 (11.85 to 12.23)	11.23 (11.07 to 11.42)	10.31 (10.06 to 10.56)	9.68 (9.38 to 9.94)	8.37 (8.09 to 8.64)	7.39 (6.92 to 7.87)	4.77 (4.39 to 5.2)
Discounted QALYs*	11.83 (11.21 to 12.32)	9.5 (9 to 9.92)	9.45 (8.96 to 9.85)	8.77 (8.31 to 9.15)	8.17 (7.77 to 8.54)	7.51 (7.11 to 7.87)	7.04 (6.62 to 7.4)	5.11 (4.65 to 5.48)	4.51 (4.05 to 4.94)	2.9 (2.6 to 3.23)
Discounted QALYs**	11.78 (11.2 to 12.26)	9.45 (8.98 to 9.86)	9.39 (8.93 to 9.79)	8.72 (8.29 to 9.1)	8.09 (7.7 to 8.45)	7.42 (7.03 to 7.79)	6.94 (6.53 to 7.28)	5.03 (4.59 to 5.4)	4.4 (3.94 to 4.84)	2.82 (2.51 to 3.15)
Discounted Total Cost (£)	51,342 (25,061 to 76,713)	52,441 (38,615 to 66,779)	51,836 (37,149 to 66,887)	36,425 (24,925 to 47,761)	33,239 (23,924 to 42,230)	30,666 (23,325 to 37,832)	46,467 (40,985 to 52,319)	38,295 (34,568 to 42,160)	53,587 (49,192 to 58,106)	35,583 (32,027 to 39,279)
Discounted CVD Cost (£)	30,444 (8,896 to 51,182)	32,412 (20,889 to 44,247)	32,867 (20,914 to 45,124)	23,674 (14,084 to 33,008)	22,713 (14,813 to 30,411)	21,220 (15,099 to 27,307)	35,525 (30,895 to 40,460)	26,953 (23,866 to 30,246)	40,851 (37,331 to 44,467)	25,499 (22,984 to 28,085)
Discounted CHD Cost (£)	18,946 (1,943 to 35,380)	22,264 (13,129 to 31,612)	23,092 (13,665 to 32,810)	15,936 (8,324 to 23,396)	19,258 (12,998 to 25,375)	18,044 (13,162 to 22,903)	25,735 (21,999 to 29,689)	20,492 (17,981 to 23,127)	29,689 (27,075 to 32,416)	20,306 (18,406 to 22,293)
Time to first event (years)	23.6 (23.22 to 23.96)	17.01 (16.61 to 17.4)	16.54 (16.14 to 16.93)	14.96 (14.51 to 15.42)	13.49 (13.11 to 13.84)	12.07 (11.54 to 12.58)	10.93 (10.37 to 11.45)	9.43 (8.96 to 9.9)	7.62 (6.87 to 8.41)	4.37 (3.84 to 4.91)
MI as primary endpoint (%)	5.28 (4.49 to 6.13)	5.39 (4.71 to 6.1)	7.58 (6.77 to 8.39)	8.08 (7.09 to 9.02)	10.25 (9.41 to 11.19)	10.55 (9.38 to 11.81)	10.65 (9.48 to 11.86)	9.41 (8.58 to 10.28)	13.98 (12.43 to 15.54)	15.85 (14.88 to 16.79)
Ischaemic stroke as primary endpoint (%)	5.3 (4.45 to 6.11)	6.36 (5.4 to 7.3)	6.33 (5.53 to 7.2)	5.62 (4.8 to 6.43)	5.15 (4.53 to 5.82)	5.46 (4.51 to 6.48)	9.28 (7.82 to 10.79)	6.8 (6.08 to 7.5)	9.33 (8.04 to 10.61)	5.61 (5.05 to 6.22)
Haemorragic stroke as primary endpoint (%)	0.65 (0.42 to 0.99)	0.67 (0.49 to 0.9)	0.72 (0.57 to 0.9)	0.76 (0.62 to 0.91)	0.79 (0.67 to 0.93)	0.78 (0.66 to 0.91)	0.86 (0.72 to 1.01)	0.86 (0.71 to 1.01)	0.77 (0.61 to 0.94)	0.56 (0.43 to 0.71)
CVD Mortality (%)	4.12 (2.92 to 5.52)	6.23 (4.78 to 7.98)	8.83 (7.32 to 10.25)	12.23 (10.38 to 14.04)	14.56 (12.65 to 15.96)	17.07 (14.92 to 19.08)	20.45 (17.65 to 23.42)	30.29 (27.41 to 33.48)	33.07 (28.99 to 38.32)	45.15 (42.44 to 48.26)
Non-CVD Mortality (%)	95.83 (94.44 to 97.02)	93.77 (92.02 to 95.21)	91.17 (89.75 to 92.67)	87.77 (85.96 to 89.62)	85.44 (84.04 to 87.35)	82.93 (80.92 to 85.08)	79.55 (76.58 to 82.35)	69.71 (66.52 to 72.59)	66.93 (61.68 to 71.01)	54.85 (51.74 to 57.56)

* 1 year decrement post event
** constant decrement post event

	Patient Profile									
Scenario HR=0.8	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Life years	25.63 (25.38 to 25.82)	18.66 (18.39 to 18.91)	18.51 (18.26 to 18.76)	16.72 (16.43 to 17.01)	15.22 (15 to 15.51)	13.74 (13.38 to 14.1)	12.7 (12.27 to 13.08)	10.83 (10.43 to 11.21)	9.43 (8.76 to 10.1)	5.81 (5.3 to 6.4)
QALYs*	18.52 (17.42 to 19.33)	13.51 (12.74 to 14.14)	13.44 (12.67 to 14.05)	12.14 (11.45 to 12.69)	11.06 (10.46 to 11.58)	9.98 (9.41 to 10.5)	9.21 (8.63 to 9.71)	6.6 (5.99 to 7.1)	5.74 (5.12 to 6.33)	3.54 (3.14 to 3.96)
QALYs**	18.44 (17.41 to 19.23)	13.43 (12.69 to 14.05)	13.35 (12.64 to 13.94)	12.07 (11.43 to 12.61)	10.93 (10.38 to 11.45)	9.86 (9.3 to 10.37)	9.07 (8.51 to 9.55)	6.5 (5.9 to 6.99)	5.6 (4.99 to 6.18)	3.44 (3.04 to 3.86)
Total Cost (£)	95,922 (48,341 to 142,167)	82,332 (59,672 to 105,476)	81,298 (57,695 to 105,704)	56,240 (38,071 to 74,228)	49,540 (35,031 to 63,711)	44,520 (33,403 to 55,609)	63,999 (55,728 to 72,915)	51,861 (46,260 to 57,771)	70,142 (63,621 to 77,035)	44,009 (39,340 to 48,836)
CVD Specific Cost (£)	57,701 (18,079 to 95,545)	51,115 (32,236 to 70,426)	51,662 (32,253 to 71,783)	36,547 (21,280 to 51,443)	33,691 (21,594 to 45,727)	30,633 (21,271 to 40,110)	48,555 (41,424 to 56,149)	36,330 (31,632 to 41,362)	53,210 (48,062 to 58,630)	31,410 (28,020 to 34,900)
CHD Specific Cost (£)	35,228 (3,802 to 64,885)	34,465 (19,463 to 49,734)	35,603 (20,091 to 51,513)	24,163 (11,976 to 35,919)	27,720 (18,092 to 37,274)	25,343 (17,843 to 32,903)	34,822 (29,179 to 40,814)	27,292 (23,487 to 31,333)	38,435 (34,513 to 42,530)	24,869 (22,288 to 27,583)
Discounted Life Years	16.29 (16.18 to 16.39)	13.1 (12.95 to 13.25)	13 (12.86 to 13.15)	12.1 (11.92 to 12.28)	11.3 (11.15 to 11.48)	10.4 (10.15 to 10.63)	9.78 (9.5 to 10.03)	8.52 (8.24 to 8.78)	7.53 (7.06 to 8)	4.91 (4.52 to 5.34)
Discounted QALYs*	11.84 (11.22 to 12.33)	9.52 (9.02 to 9.94)	9.47 (8.99 to 9.88)	8.81 (8.36 to 9.19)	8.23 (7.82 to 8.59)	7.57 (7.17 to 7.93)	7.11 (6.7 to 7.47)	5.2 (4.74 to 5.58)	4.59 (4.13 to 5.03)	2.99 (2.68 to 3.32)
Discounted QALYs**	11.79 (11.2 to 12.27)	9.47 (9 to 9.88)	9.42 (8.96 to 9.82)	8.77 (8.34 to 9.14)	8.15 (7.76 to 8.51)	7.49 (7.09 to 7.86)	7.02 (6.61 to 7.36)	5.13 (4.68 to 5.51)	4.5 (4.04 to 4.93)	2.92 (2.6 to 3.24)
Discounted Total Cost (£)	51,093 (24,811 to 76,431)	52,265 (38,386 to 66,568)	51,670 (36,942 to 66,748)	36,333 (24,782 to 47,735)	33,176 (23,824 to 42,248)	30,642 (23,215 to 37,869)	46,635 (41,131 to 52,533)	38,761 (35,000 to 42,676)	54,278 (49,862 to 58,878)	36,156 (32,540 to 39,848)
Discounted CVD Cost (£)	30,219 (8,678 to 50,952)	32,234 (20,692 to 44,050)	32,682 (20,669 to 44,986)	23,540 (13,891 to 32,934)	22,597 (14,643 to 30,311)	21,131 (14,947 to 27,279)	35,595 (30,935 to 40,625)	27,208 (24,014 to 30,581)	41,304 (37,805 to 44,953)	25,815 (23,300 to 28,466)
Discounted CHD Cost (£)	18,771 (1,749 to 35,209)	22,128 (12,987 to 31,465)	22,937 (13,475 to 32,678)	15,810 (8,126 to 23,289)	19,158 (12,862 to 25,292)	17,967 (13,037 to 22,902)	25,765 (21,967 to 29,778)	20,667 (18,126 to 23,356)	29,987 (27,342 to 32,777)	20,528 (18,602 to 22,585)
Time to first event (years)	23.81 (23.46 to 24.15)	17.2 (16.83 to 17.56)	16.77 (16.4 to 17.14)	15.21 (14.79 to 15.64)	13.75 (13.39 to 14.08)	12.33 (11.83 to 12.81)	11.22 (10.68 to 11.71)	9.75 (9.29 to 10.2)	7.95 (7.21 to 8.73)	4.64 (4.09 to 5.19)
MI as primary endpoint (%)	4.73 (4.02 to 5.5)	4.84 (4.22 to 5.48)	6.82 (6.08 to 7.55)	7.29 (6.38 to 8.15)	9.26 (8.49 to 10.14)	9.56 (8.48 to 10.72)	9.68 (8.6 to 10.81)	8.61 (7.83 to 9.42)	12.88 (11.41 to 14.38)	14.8 (13.86 to 15.71)
Ischaemic stroke as primary endpoint (%)	4.75 (3.98 to 5.48)	5.71 (4.84 to 6.58)	5.71 (4.97 to 6.51)	5.08 (4.33 to 5.82)	4.67 (4.1 to 5.28)	4.96 (4.08 to 5.9)	8.47 (7.11 to 9.88)	6.25 (5.57 to 6.91)	8.66 (7.43 to 9.88)	5.3 (4.75 to 5.89)
Haemorragic stroke as primary endpoint (%)	0.66 (0.43 to 1)	0.67 (0.5 to 0.91)	0.73 (0.58 to 0.92)	0.77 (0.63 to 0.93)	0.81 (0.68 to 0.95)	0.8 (0.67 to 0.93)	0.88 (0.74 to 1.04)	0.89 (0.73 to 1.04)	0.8 (0.65 to 0.98)	0.59 (0.46 to 0.76)
CVD Mortality (%)	3.72 (2.64 to 5)	5.63 (4.32 to 7.22)	7.99 (6.62 to 9.28)	11.08 (9.38 to 12.76)	13.22 (11.47 to 14.52)	15.55 (13.56 to 17.42)	18.73 (16.11 to 21.53)	27.91 (25.17 to 30.89)	30.78 (26.85 to 35.85)	42.71 (40.02 to 45.7)
Non-CVD Mortality (%)	96.23 (94.96 to 97.31)	94.37 (92.78 to 95.68)	92.01 (90.72 to 93.38)	88.92 (87.24 to 90.62)	86.78 (85.48 to 88.53)	84.45 (82.58 to 86.44)	81.27 (78.47 to 83.89)	72.09 (69.11 to 74.83)	69.22 (64.15 to 73.15)	57.29 (54.3 to 59.98)

* 1 year decrement post event

** constant decrement post event

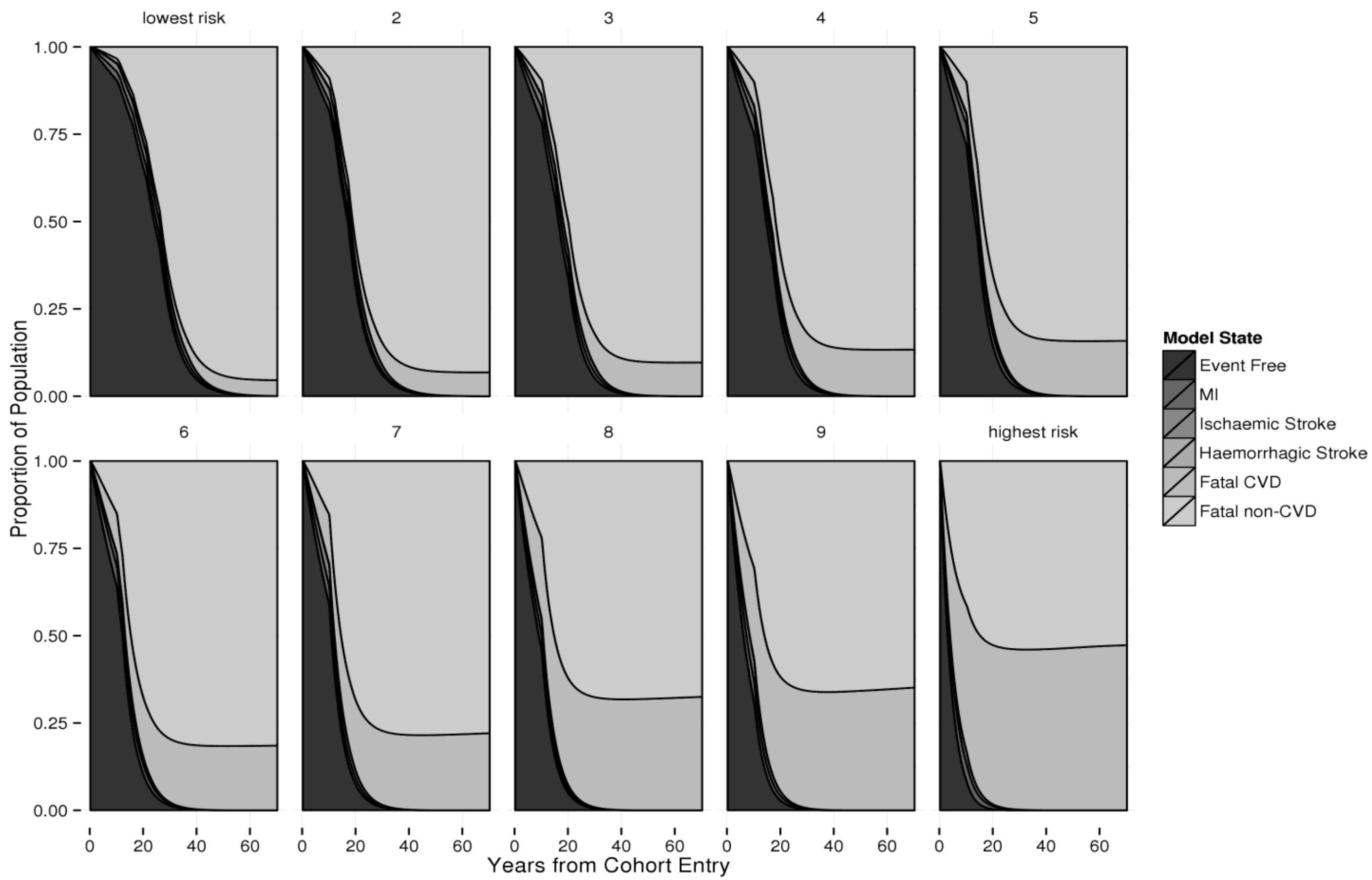
	Patient Profile									
Scenario HR=0.7	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Life years	25.63 (25.41 to 25.81)	18.69 (18.43 to 18.92)	18.56 (18.33 to 18.79)	16.81 (16.54 to 17.08)	15.33 (15.12 to 15.6)	13.87 (13.52 to 14.21)	12.85 (12.45 to 13.2)	11.06 (10.67 to 11.43)	9.64 (8.98 to 10.3)	6.02 (5.5 to 6.6)
QALYs*	18.53 (17.44 to 19.34)	13.53 (12.76 to 14.16)	13.47 (12.72 to 14.08)	12.21 (11.52 to 12.75)	11.14 (10.54 to 11.65)	10.07 (9.51 to 10.59)	9.33 (8.75 to 9.82)	6.74 (6.13 to 7.25)	5.87 (5.24 to 6.46)	3.66 (3.25 to 4.1)
QALYs**	18.45 (17.43 to 19.25)	13.46 (12.73 to 14.08)	13.4 (12.67 to 13.98)	12.14 (11.51 to 12.68)	11.03 (10.46 to 11.53)	9.97 (9.41 to 10.48)	9.2 (8.65 to 9.67)	6.65 (6.04 to 7.15)	5.75 (5.13 to 6.34)	3.57 (3.16 to 4)
Total Cost (£)	95,350 (47,753 to 141,540)	82,007 (59,251 to 105,219)	80,986 (57,322 to 105,431)	56,104 (37,866 to 74,146)	49,475 (34,845 to 63,790)	44,535 (33,299 to 55,682)	64,344 (55,974 to 73,352)	52,696 (47,028 to 58,676)	71,327 (64,740 to 78,249)	44,946 (40,207 to 49,952)
CVD Specific Cost (£)	57,213 (17,566 to 95,080)	50,800 (31,902 to 70,084)	51,332 (31,868 to 71,465)	36,342 (20,964 to 51,283)	33,537 (21,345 to 45,638)	30,536 (21,068 to 40,167)	48,729 (41,505 to 56,357)	36,811 (32,008 to 41,968)	54,003 (48,813 to 59,461)	31,952 (28,526 to 35,655)
CHD Specific Cost (£)	34,859 (3,421 to 64,528)	34,225 (19,204 to 49,464)	35,332 (19,764 to 51,271)	23,966 (11,740 to 35,774)	27,581 (17,879 to 37,170)	25,251 (17,666 to 32,894)	34,912 (29,141 to 41,051)	27,620 (23,666 to 31,793)	38,960 (34,957 to 43,106)	25,250 (22,617 to 28,090)
Discounted Life Years	16.3 (16.2 to 16.39)	13.12 (12.98 to 13.26)	13.04 (12.9 to 13.18)	12.16 (11.99 to 12.33)	11.37 (11.24 to 11.54)	10.48 (10.24 to 10.7)	9.88 (9.62 to 10.12)	8.68 (8.42 to 8.93)	7.69 (7.23 to 8.15)	5.07 (4.67 to 5.49)
Discounted QALYs*	11.85 (11.23 to 12.33)	9.54 (9.04 to 9.96)	9.5 (9.01 to 9.9)	8.86 (8.4 to 9.24)	8.28 (7.87 to 8.64)	7.63 (7.23 to 7.99)	7.19 (6.78 to 7.54)	5.3 (4.84 to 5.68)	4.69 (4.22 to 5.12)	3.09 (2.77 to 3.42)
Discounted QALYs**	11.81 (11.22 to 12.28)	9.49 (9.01 to 9.9)	9.45 (8.99 to 9.85)	8.82 (8.38 to 9.19)	8.21 (7.82 to 8.56)	7.56 (7.16 to 7.93)	7.1 (6.71 to 7.45)	5.23 (4.78 to 5.61)	4.6 (4.15 to 5.03)	3.02 (2.7 to 3.35)
Discounted Total Cost (£)	50,840 (24,558 to 76,145)	52,086 (38,153 to 66,352)	51,500 (36,731 to 66,607)	36,238 (24,636 to 47,649)	33,111 (23,721 to 42,241)	30,618 (23,119 to 37,930)	46,812 (41,313 to 52,758)	39,257 (35,408 to 43,235)	55,027 (50,596 to 59,614)	36,818 (33,232 to 40,644)
Discounted CVD Cost (£)	29,992 (8,449 to 50,718)	32,052 (20,491 to 43,850)	32,492 (20,439 to 44,823)	23,402 (13,723 to 32,860)	22,477 (14,472 to 30,209)	21,039 (14,790 to 27,285)	35,668 (30,916 to 40,786)	27,479 (24,203 to 30,925)	41,796 (38,337 to 45,452)	26,185 (23,622 to 28,883)
Discounted CHD Cost (£)	18,595 (1,554 to 35,036)	21,989 (12,843 to 31,315)	22,780 (13,281 to 32,542)	15,680 (7,972 to 23,191)	19,056 (12,721 to 25,204)	17,888 (12,907 to 22,891)	25,797 (21,936 to 29,888)	20,854 (18,233 to 23,604)	30,311 (27,637 to 33,127)	20,787 (18,831 to 22,867)
Time to first event (years)	24.02 (23.7 to 24.33)	17.39 (17.04 to 17.73)	17.01 (16.66 to 17.36)	15.46 (15.07 to 15.86)	14.01 (13.68 to 14.32)	12.61 (12.12 to 13.06)	11.52 (11.02 to 11.98)	10.08 (9.64 to 10.52)	8.31 (7.57 to 9.07)	4.94 (4.37 to 5.5)
MI as primary endpoint (%)	4.17 (3.54 to 4.85)	4.27 (3.72 to 4.85)	6.04 (5.38 to 6.7)	6.47 (5.65 to 7.25)	8.24 (7.54 to 9.03)	8.52 (7.54 to 9.58)	8.67 (7.68 to 9.7)	7.75 (7.03 to 8.51)	11.7 (10.29 to 13.11)	13.64 (12.74 to 14.52)
Ischaemic stroke as primary endpoint (%)	4.2 (3.51 to 4.85)	5.05 (4.28 to 5.83)	5.07 (4.41 to 5.78)	4.52 (3.84 to 5.19)	4.16 (3.65 to 4.72)	4.44 (3.64 to 5.29)	7.61 (6.37 to 8.91)	5.66 (5.03 to 6.28)	7.92 (6.76 to 9.06)	4.94 (4.42 to 5.51)
Haemorragic stroke as primary endpoint (%)	0.66 (0.43 to 1.01)	0.68 (0.5 to 0.92)	0.74 (0.59 to 0.93)	0.78 (0.64 to 0.94)	0.82 (0.69 to 0.97)	0.81 (0.69 to 0.95)	0.91 (0.76 to 1.07)	0.92 (0.76 to 1.08)	0.84 (0.68 to 1.02)	0.63 (0.5 to 0.81)
CVD Mortality (%)	3.32 (2.34 to 4.48)	5.02 (3.84 to 6.44)	7.12 (5.89 to 8.29)	9.89 (8.36 to 11.42)	11.83 (10.24 to 13.01)	13.95 (12.14 to 15.67)	16.9 (14.47 to 19.44)	25.35 (22.76 to 28.09)	28.25 (24.52 to 33.12)	39.91 (37.3 to 42.76)
Non-CVD Mortality (%)	96.64 (95.47 to 97.61)	94.98 (93.56 to 96.16)	92.88 (91.71 to 94.11)	90.11 (88.58 to 91.64)	88.17 (86.99 to 89.76)	86.05 (84.33 to 87.86)	83.1 (80.56 to 85.53)	74.65 (71.91 to 77.24)	71.75 (66.88 to 75.48)	60.09 (57.24 to 62.7)

* 1 year decrement post event

** constant decrement post event

	Patient Profile									
Scenario HR=0.6	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Life years	25.64 (25.43 to 25.81)	18.72 (18.48 to 18.93)	18.61 (18.39 to 18.83)	16.9 (16.65 to 17.16)	15.44 (15.25 to 15.69)	14 (13.66 to 14.32)	13.01 (12.64 to 13.34)	11.3 (10.94 to 11.65)	9.88 (9.24 to 10.54)	6.25 (5.72 to 6.83)
QALYs*	18.53 (17.46 to 19.35)	13.56 (12.78 to 14.18)	13.51 (12.76 to 14.12)	12.28 (11.59 to 12.83)	11.22 (10.63 to 11.73)	10.17 (9.6 to 10.68)	9.44 (8.87 to 9.93)	6.89 (6.27 to 7.39)	6.01 (5.39 to 6.6)	3.8 (3.39 to 4.24)
QALYs**	18.47 (17.44 to 19.27)	13.49 (12.76 to 14.11)	13.44 (12.72 to 14.03)	12.22 (11.58 to 12.76)	11.12 (10.55 to 11.62)	10.07 (9.52 to 10.58)	9.33 (8.79 to 9.8)	6.8 (6.19 to 7.31)	5.9 (5.28 to 6.49)	3.72 (3.31 to 4.16)
Total Cost (£)	94,770 (47,219 to 140,903)	81,676 (58,823 to 104,885)	80,665 (56,938 to 105,151)	55,964 (37,658 to 73,948)	49,409 (34,656 to 63,823)	44,552 (33,195 to 55,889)	64,708 (56,217 to 73,723)	53,591 (47,784 to 59,809)	72,628 (65,926 to 79,557)	46,051 (41,137 to 51,152)
CVD Specific Cost (£)	56,717 (17,046 to 94,607)	50,479 (31,563 to 69,733)	50,994 (31,442 to 71,139)	36,131 (20,675 to 51,117)	33,378 (21,088 to 45,544)	30,436 (20,859 to 40,115)	48,913 (41,574 to 56,703)	37,327 (32,307 to 42,633)	54,873 (49,624 to 60,397)	32,597 (29,054 to 36,334)
CHD Specific Cost (£)	34,485 (3,034 to 64,166)	33,981 (18,939 to 49,234)	35,054 (19,429 to 50,946)	23,763 (11,499 to 35,597)	27,437 (17,659 to 37,111)	25,156 (17,483 to 32,847)	35,007 (29,125 to 41,280)	27,972 (23,854 to 32,253)	39,535 (35,430 to 43,770)	25,705 (23,009 to 28,568)
Discounted Life Years	16.31 (16.22 to 16.4)	13.15 (13.01 to 13.28)	13.07 (12.94 to 13.21)	12.22 (12.06 to 12.38)	11.45 (11.32 to 11.6)	10.57 (10.34 to 10.78)	9.99 (9.74 to 10.21)	8.84 (8.6 to 9.08)	7.85 (7.4 to 8.3)	5.24 (4.84 to 5.66)
Discounted QALYs*	11.85 (11.24 to 12.34)	9.55 (9.06 to 9.97)	9.53 (9.03 to 9.93)	8.9 (8.45 to 9.28)	8.34 (7.92 to 8.69)	7.69 (7.3 to 8.05)	7.26 (6.86 to 7.61)	5.4 (4.94 to 5.78)	4.79 (4.32 to 5.22)	3.19 (2.87 to 3.53)
Discounted QALYs**	11.82 (11.23 to 12.3)	9.52 (9.04 to 9.93)	9.49 (9.01 to 9.89)	8.87 (8.43 to 9.25)	8.28 (7.88 to 8.63)	7.63 (7.24 to 7.99)	7.19 (6.81 to 7.53)	5.34 (4.89 to 5.72)	4.71 (4.25 to 5.15)	3.13 (2.81 to 3.47)
Discounted Total Cost (£)	50,584 (24,303 to 75,854)	51,903 (37,916 to 66,162)	51,327 (36,516 to 66,462)	36,142 (24,488 to 47,536)	33,044 (23,585 to 42,216)	30,594 (23,020 to 37,973)	46,996 (41,366 to 53,069)	39,783 (35,838 to 43,908)	55,840 (51,382 to 60,404)	37,585 (33,889 to 41,411)
Discounted CVD Cost (£)	29,761 (8,221 to 50,480)	31,868 (20,286 to 43,646)	32,299 (20,207 to 44,658)	23,261 (13,539 to 32,797)	22,355 (14,311 to 30,135)	20,945 (14,628 to 27,275)	35,745 (30,895 to 40,959)	27,768 (24,445 to 31,302)	42,329 (38,845 to 46,060)	26,617 (23,951 to 29,343)
Discounted CHD Cost (£)	18,416 (1,374 to 34,848)	21,848 (12,697 to 31,162)	22,619 (13,083 to 32,403)	15,548 (7,815 to 23,110)	18,950 (12,577 to 25,131)	17,807 (12,773 to 22,833)	25,830 (21,899 to 30,004)	21,053 (18,329 to 23,888)	30,662 (27,953 to 33,524)	21,092 (19,070 to 23,216)
Time to first event (years)	24.23 (23.95 to 24.51)	17.59 (17.26 to 17.9)	17.26 (16.93 to 17.58)	15.72 (15.36 to 16.09)	14.29 (13.98 to 14.57)	12.89 (12.43 to 13.31)	11.84 (11.37 to 12.27)	10.44 (10.02 to 10.85)	8.69 (7.97 to 9.44)	5.27 (4.7 to 5.85)
MI as primary endpoint (%)	3.6 (3.05 to 4.2)	3.7 (3.22 to 4.2)	5.24 (4.66 to 5.82)	5.62 (4.9 to 6.32)	7.18 (6.56 to 7.89)	7.44 (6.57 to 8.39)	7.6 (6.72 to 8.54)	6.84 (6.19 to 7.53)	10.42 (9.12 to 11.73)	12.35 (11.5 to 13.19)
Ischaemic stroke as primary endpoint (%)	3.63 (3.03 to 4.2)	4.38 (3.7 to 5.06)	4.4 (3.82 to 5.04)	3.94 (3.34 to 4.53)	3.64 (3.18 to 4.13)	3.89 (3.18 to 4.65)	6.7 (5.59 to 7.88)	5.02 (4.44 to 5.59)	7.1 (6.02 to 8.17)	4.52 (4.03 to 5.07)
Haemorragic stroke as primary endpoint (%)	0.67 (0.44 to 1.02)	0.69 (0.51 to 0.93)	0.75 (0.59 to 0.95)	0.8 (0.65 to 0.96)	0.84 (0.7 to 0.98)	0.83 (0.7 to 0.98)	0.93 (0.79 to 1.1)	0.95 (0.79 to 1.11)	0.88 (0.71 to 1.07)	0.68 (0.53 to 0.86)
CVD Mortality (%)	2.9 (2.04 to 3.97)	4.38 (3.35 to 5.65)	6.23 (5.13 to 7.26)	8.66 (7.3 to 10.02)	10.38 (8.97 to 11.43)	12.28 (10.65 to 13.82)	14.95 (12.77 to 17.27)	22.57 (20.19 to 25.09)	25.44 (21.99 to 29.88)	36.67 (34.08 to 39.35)
Non-CVD Mortality (%)	97.05 (95.99 to 97.91)	95.61 (94.35 to 96.65)	93.77 (92.74 to 94.87)	91.34 (89.98 to 92.7)	89.62 (88.57 to 91.03)	87.72 (86.18 to 89.35)	85.05 (82.73 to 87.23)	77.43 (74.91 to 79.81)	74.56 (70.12 to 78.01)	63.33 (60.65 to 65.92)

* 1 year decrement post event
** constant decrement post event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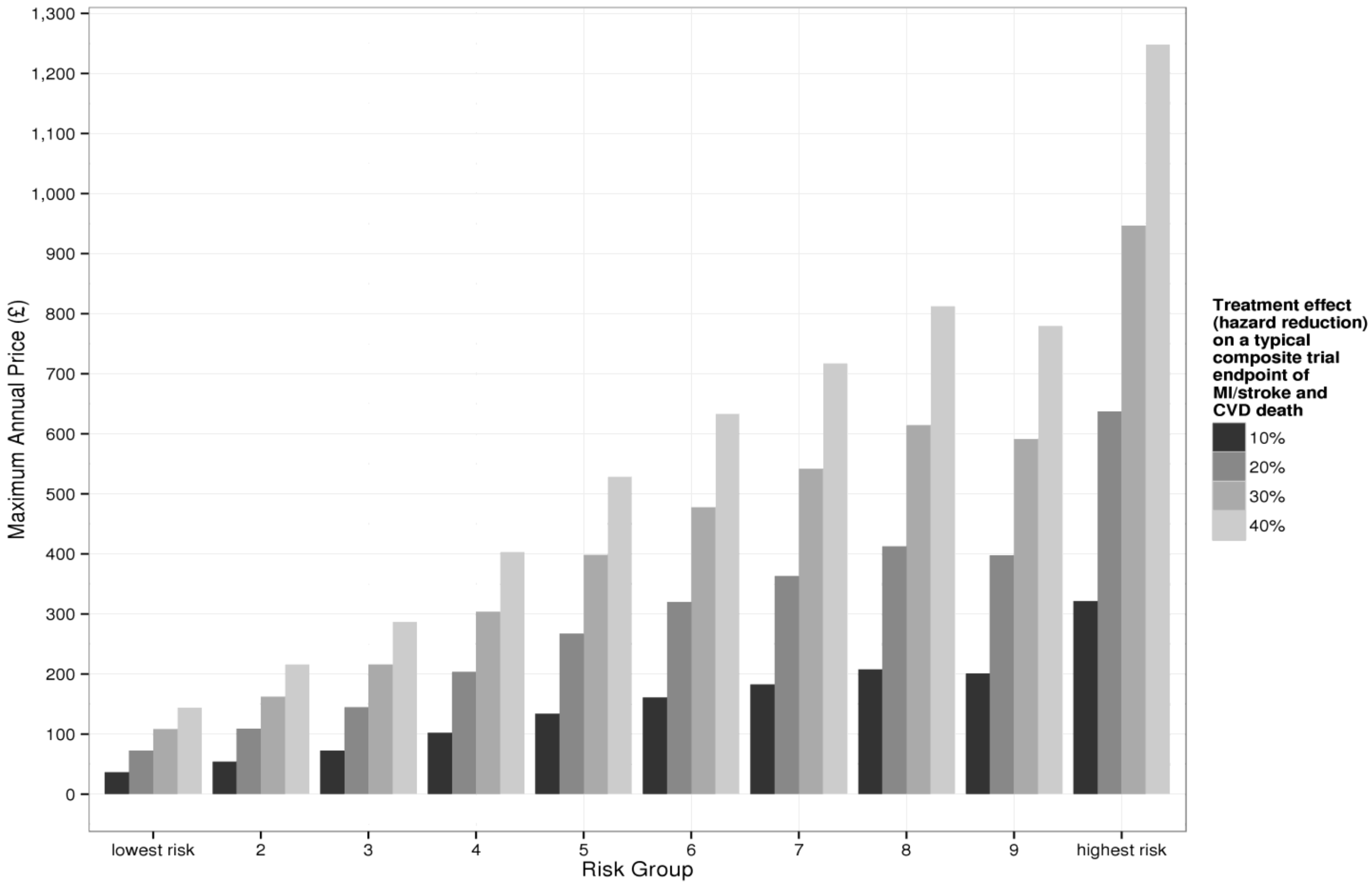
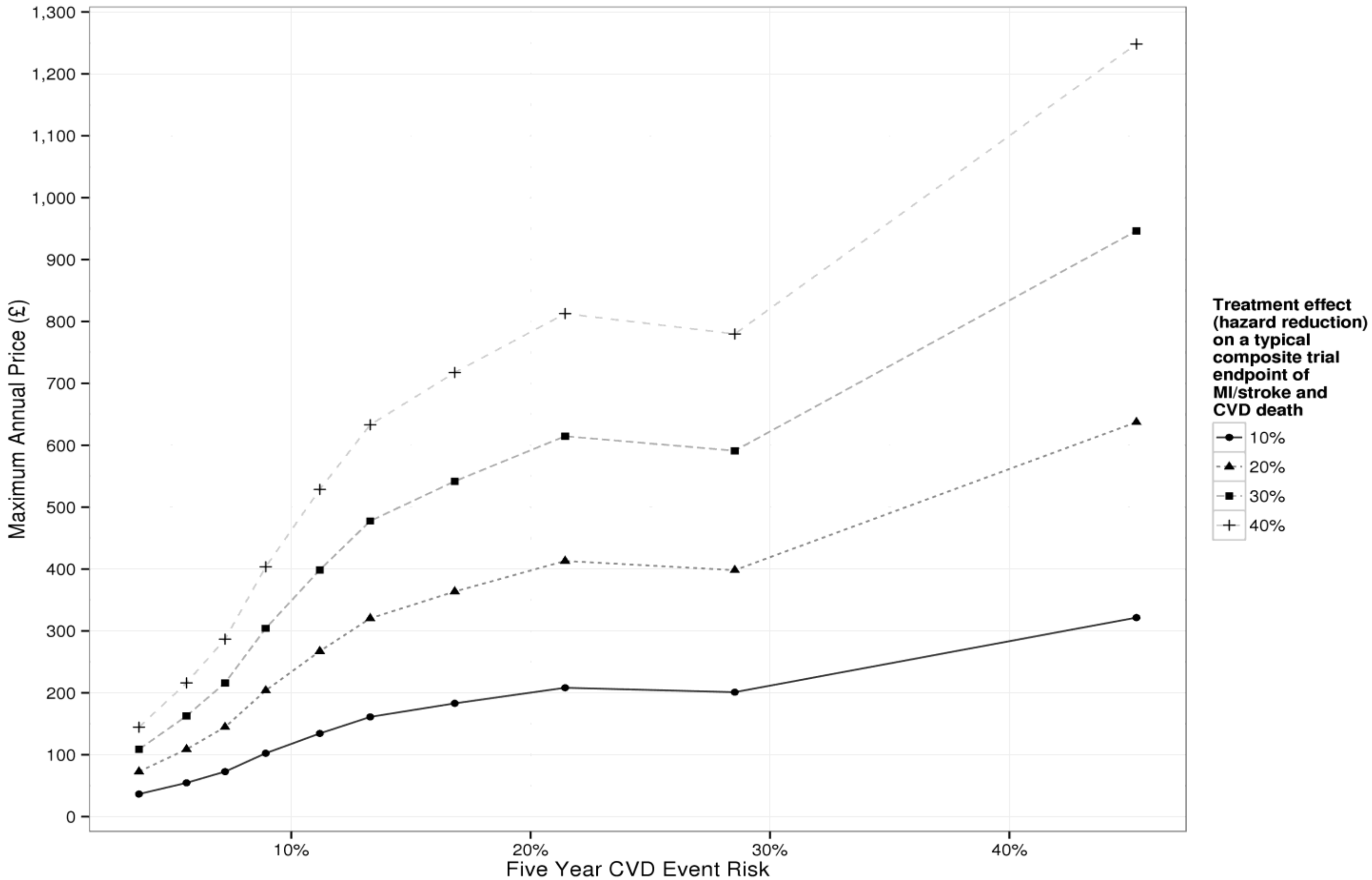
2
3
4
5
6
7
8
9
highest risk
1.00
0.75
0.50
0.25
0.00
0
20
40
60
Proportion of Population
Years from Cohort Entry
Model State
Event Free
MI
Ischaemic Stroke
Haemorrhagic Stroke
Fatal CVD
Fatal non-CVD



1,300
1,200
1,100
1,000
900
800
700
600
500
400
300
200
100
0
Maximum Annual Price (£)
lowest risk
2
3
4
5
6
7
8
9
highest risk
Risk Group
Treatment effect (hazard reduction) on a typical composite trial endpoint of MI/stroke and CVD death
10%
20%
30%
40%

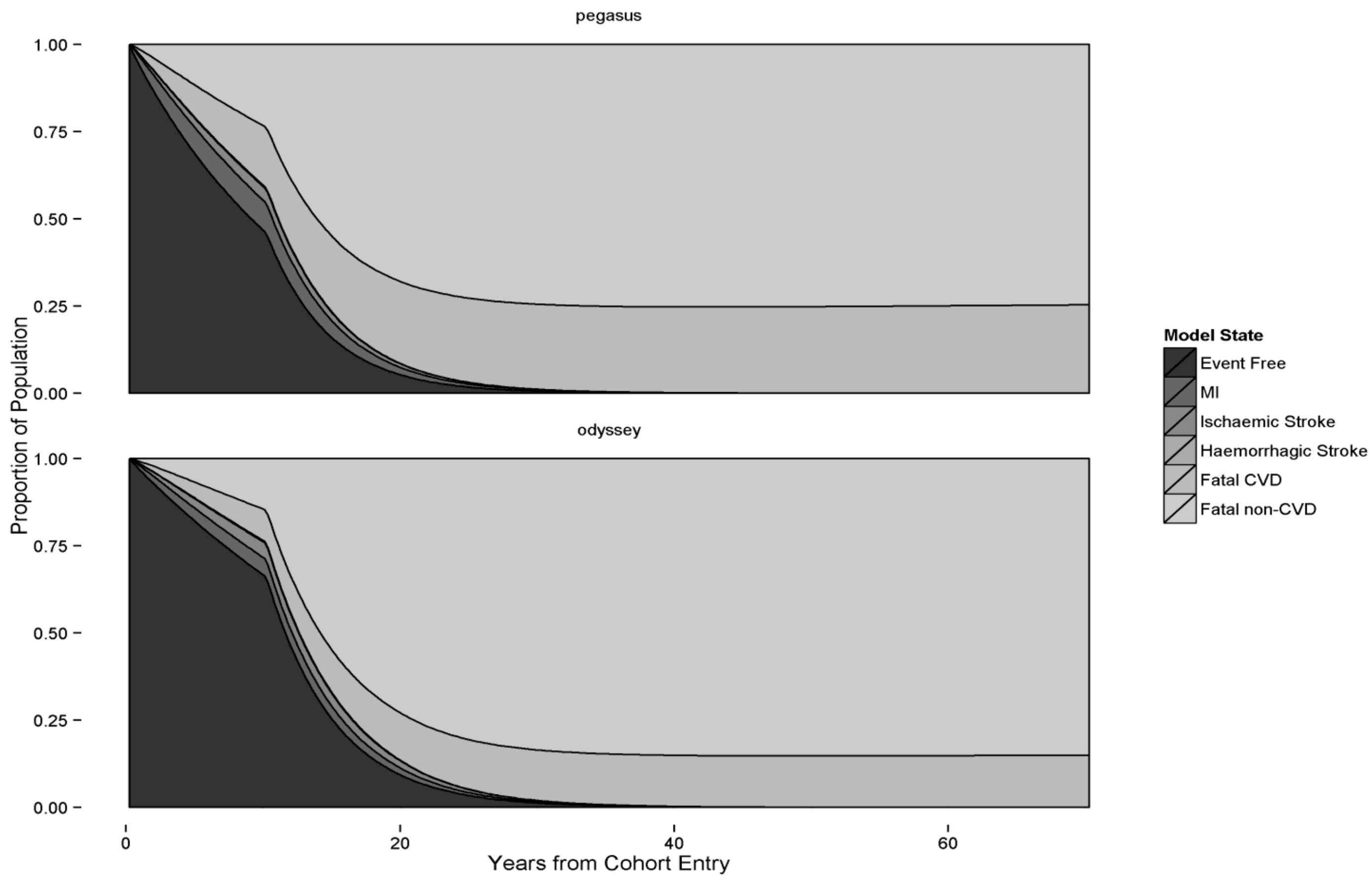


1,300
1,200
1,100
1,000
900
800
700
600
500
400
300
200
100
0
Maximum Annual Price (£)
10%
20%
30%
40%
Five Year CVD Event Risk
Treatment effect (hazard reduction) on a typical composite trial endpoint of MI/stroke and CVD death
10%
20%
30%
40%

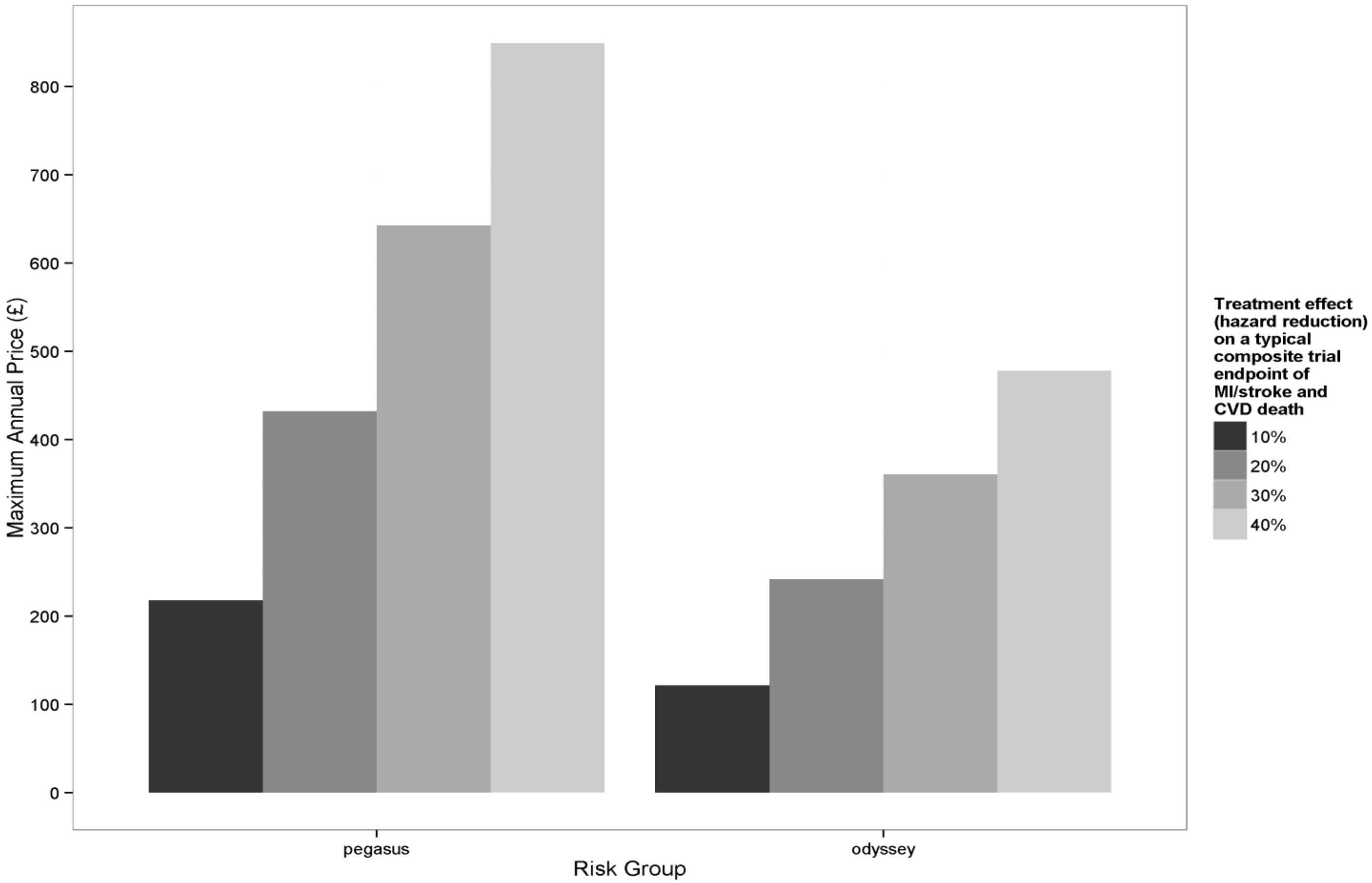
Section 3: Results for trial comparable patients

	pegasus					odyssey				
Scenario HR	**1**	**0.9**	**0.8**	**0.7**	**0.6**	**1**	**0.9**	**0.8**	**0.7**	**0.6**
Life years	10.97 (10.65 to 11.32)	11.14 (10.83 to 11.47)	11.31 (11.02 to 11.62)	11.5 (11.22 to 11.79)	11.7 (11.43 to 11.96)	13.18 (12.99 to 13.43)	13.27 (13.09 to 13.5)	13.36 (13.19 to 13.57)	13.46 (13.3 to 13.65)	13.56 (13.42 to 13.73)
QALYs*	7.59 (7.09 to 8.01)	7.7 (7.21 to 8.12)	7.83 (7.32 to 8.24)	7.96 (7.44 to 8.37)	8.09 (7.57 to 8.51)	9.16 (8.63 to 9.6)	9.22 (8.69 to 9.65)	9.29 (8.75 to 9.72)	9.36 (8.82 to 9.78)	9.43 (8.88 to 9.85)
QALYs**	7.44 (6.95 to 7.86)	7.57 (7.07 to 7.99)	7.7 (7.19 to 8.12)	7.84 (7.34 to 8.27)	7.99 (7.48 to 8.42)	9.03 (8.52 to 9.45)	9.1 (8.59 to 9.52)	9.18 (8.67 to 9.6)	9.26 (8.74 to 9.67)	9.34 (8.82 to 9.75)
Total Cost (£)	63,576 (57,426 to 69,784)	64,058 (57,853 to 70,298)	64,575 (58,308 to 70,873)	65,131 (58,761 to 71,536)	65,729 (59,306 to 72,117)	65,510 (56,422 to 75,258)	65,563 (56,366 to 75,362)	65,619 (56,275 to 75,470)	65,678 (56,223 to 75,587)	65,740 (56,239 to 75,728)
CVD Specific Cost (£)	45,358 (40,271 to 50,611)	45,578 (40,412 to 50,892)	45,815 (40,616 to 51,180)	46,073 (40,711 to 51,439)	46,352 (40,815 to 51,844)	44,459 (36,587 to 52,829)	44,397 (36,440 to 52,818)	44,334 (36,257 to 52,805)	44,269 (36,088 to 52,731)	44,203 (35,976 to 52,656)
CHD Specific Cost (£)	35,489 (31,406 to 39,666)	35,604 (31,416 to 39,804)	35,730 (31,448 to 39,965)	35,866 (31,524 to 40,185)	36,016 (31,606 to 40,388)	31,905 (25,558 to 38,565)	31,826 (25,394 to 38,523)	31,745 (25,262 to 38,442)	31,662 (25,098 to 38,363)	31,576 (24,929 to 38,327)
Discounted Life Years	8.61 (8.4 to 8.84)	8.73 (8.52 to 8.94)	8.85 (8.65 to 9.05)	8.97 (8.78 to 9.16)	9.1 (8.93 to 9.28)	10.09 (9.97 to 10.24)	10.15 (10.04 to 10.29)	10.21 (10.11 to 10.34)	10.28 (10.18 to 10.4)	10.34 (10.26 to 10.45)
Discounted QALYs*	5.97 (5.6 to 6.28)	6.05 (5.68 to 6.36)	6.13 (5.76 to 6.44)	6.22 (5.84 to 6.53)	6.31 (5.93 to 6.62)	7.03 (6.65 to 7.35)	7.07 (6.69 to 7.39)	7.11 (6.73 to 7.43)	7.16 (6.77 to 7.48)	7.21 (6.81 to 7.52)
Discounted QALYs**	5.86 (5.5 to 6.18)	5.95 (5.59 to 6.27)	6.04 (5.67 to 6.36)	6.14 (5.77 to 6.46)	6.24 (5.87 to 6.56)	6.94 (6.57 to 7.25)	6.99 (6.61 to 7.3)	7.04 (6.67 to 7.35)	7.1 (6.72 to 7.4)	7.15 (6.78 to 7.46)
Discounted Total Cost (£)	47,695 (43,550 to 51,732)	47,954 (43,716 to 51,981)	48,231 (43,972 to 52,314)	48,527 (44,213 to 52,644)	48,843 (44,533 to 53,049)	47,262 (41,188 to 53,678)	47,269 (41,144 to 53,706)	47,276 (41,102 to 53,730)	47,284 (41,028 to 53,768)	47,291 (40,999 to 53,808)
Discounted CVD Cost (£)	34,093 (30,689 to 37,556)	34,187 (30,744 to 37,685)	34,288 (30,801 to 37,840)	34,398 (30,862 to 37,999)	34,517 (30,927 to 38,155)	32,084 (26,847 to 37,563)	32,019 (26,724 to 37,525)	31,951 (26,622 to 37,486)	31,882 (26,488 to 37,426)	31,811 (26,351 to 37,364)
Discounted CHD Cost (£)	26,929 (24,194 to 29,707)	26,966 (24,182 to 29,763)	27,007 (24,171 to 29,834)	27,052 (24,176 to 29,928)	27,102 (24,170 to 30,025)	23,272 (19,049 to 27,623)	23,203 (18,933 to 27,575)	23,131 (18,815 to 27,526)	23,058 (18,694 to 27,462)	22,983 (18,569 to 27,388)
Time to first event (years)	9.11 (8.79 to 9.4)	9.42 (9.11 to 9.7)	9.74 (9.44 to 10.02)	10.09 (9.79 to 10.35)	10.45 (10.16 to 10.7)	11.6 (11.47 to 11.72)	11.82 (11.7 to 11.94)	12.05 (11.93 to 12.16)	12.28 (12.17 to 12.39)	12.53 (12.42 to 12.63)
MI as primary endpoint (%)	20.59 (19.89 to 21.36)	19.06 (18.39 to 19.8)	17.44 (16.79 to 18.15)	15.71 (15.11 to 16.39)	13.88 (13.32 to 14.5)	10.15 (9.85 to 10.48)	9.29 (9 to 9.59)	8.39 (8.13 to 8.67)	7.47 (7.23 to 7.72)	6.51 (6.29 to 6.73)
Ischaemic stroke as primary endpoint (%)	6.88 (6.4 to 7.46)	6.4 (5.94 to 6.95)	5.89 (5.45 to 6.41)	5.33 (4.93 to 5.82)	4.73 (4.36 to 5.18)	7.7 (7.37 to 8.03)	7.06 (6.76 to 7.37)	6.4 (6.12 to 6.68)	5.7 (5.45 to 5.96)	4.99 (4.76 to 5.22)
Haemorragic stroke as primary endpoint (%)	0.75 (0.66 to 0.84)	0.77 (0.69 to 0.87)	0.8 (0.71 to 0.9)	0.83 (0.74 to 0.93)	0.86 (0.76 to 0.97)	0.73 (0.64 to 0.82)	0.74 (0.65 to 0.84)	0.75 (0.67 to 0.86)	0.77 (0.68 to 0.87)	0.78 (0.69 to 0.89)
CVD Mortality (%)	25.3 (23.14 to 28.22)	23.59 (21.53 to 26.39)	21.75 (19.8 to 24.38)	19.76 (17.98 to 22.21)	17.61 (16 to 19.84)	14.92 (13.15 to 16.44)	13.72 (12.09 to 15.14)	12.48 (10.98 to 13.78)	11.17 (9.83 to 12.36)	9.81 (8.63 to 10.87)
Non-CVD Mortality (%)	74.7 (71.78 to 76.86)	76.41 (73.61 to 78.47)	78.25 (75.62 to 80.2)	80.24 (77.79 to 82.02)	82.39 (80.16 to 84)	85.08 (83.56 to 86.84)	86.28 (84.86 to 87.91)	87.52 (86.22 to 89.02)	88.83 (87.64 to 90.17)	90.19 (89.13 to 91.37)

* 1 year decrement post event
** constant decrement post event



pegasus
odyssey
1.00
0.75
0.50
0.25
0.00
Proportion of Population
0
20
40
60
Years from Cohort Entry
Model State
Event Free
MI
Ischaemic Stroke
Haemorrhagic Stroke
Fatal CVD
Fatal non-CVD



800
700
600
500
400
300
200
100
0
Maximum Annual Price (£)
pegasus
odyssey
Risk Group
Treatment effect (hazard reduction) on a typical composite trial endpoint of MI/stroke and CVD death
10%
20%
30%
40%