Online appendix: A Cardiovascular Disease Policy Model that predicts life expectancy taking into account socio-economic deprivation

This appendix provides an expanded methods section as well as additional model results and is intended to be read in conjunction with the main paper[1].

Model structure

The endpoints for our model are non-fatal CHD hospitalisation, non-fatal cerebrovascular disease (CBVD) hospitalisation and deaths from CVD. However, with the focus on life expectancy we also consider deaths from non-CVD causes and the additional life expectancy experienced after a non-fatal CHD or CBVD event. Figure A1 illustrates the structure of the state transition model. People enter the model in the CVD event free state and then transit into one of four events "competing" to be first. If a hospitalised patient died within 28 days of their admission the first event was re-classified as fatal. If the first event experienced is non-fatal, then there is a final transition to death. Men and women were modelled separately.

Data source

The Scottish Heart Health Extended Cohort (SHHEC) is made up of individuals from the Scottish Heart Health Study[2] which recruited random samples of the Scottish population between 1984 and 1987, and individuals from the Scottish MONICA Project[3] which recruited in Edinburgh in 1986 and north Glasgow in 1986, 1989, 1992 and 1995. The SHHEC participants, aged between 25-74 years, attended a survey clinic where cardiovascular risk factors were measured.

Patients were defined as CVD event free if they did not self-report at recruitment having had angina, myocardial infarction, or a stroke in the past, no ECG appearance of previous myocardial infarction at survey clinic, and also did not have prior hospitalisations with discharge diagnoses of angina, CHD, stroke, acute coronary event, CBVD and transient ischaemic attacks. SHHEC participants gave permission to be followed up through routine records.

The data was linked to hospital admissions using the Scottish Morbidity Record Scheme (SMR) and deaths using the General Register Office (GRO) for Scotland. Follow-up extended from 1981 to the end of 2009. A CHD hospitalisation was identified by ICD9 codes 410-414 and ICD10 codes I20-I25, a CBVD hospitalisation by ICD9 430-438 (ICD10 G45, I60-I69), and a fatal CVD event by ICD9 390-459 (ICD10 I00-I99), with the codes appearing in any diagnostic

position in the SMR/GRO records. Fatal non-CVD events were defined as all deaths not having a CVD cause. Risk factors used for modelling the first event were age at survey (years), systolic blood pressure (SBP) (mm Hg), total cholesterol (TC) (mmol/l), HDL cholesterol (mmol/l), cigarettes per day (CPD), self-reported diabetes, self-reported family history of heart disease, and SIMD score (2004 version). These are the same risk factors that are in the ASSIGN cardiovascular risk score which was also developed using the linked SHHEC data set. Risk factors used for modelling death after a non-fatal first event were age at first event, self-reported family history of heart disease and SIMD. Any missing data in the risk factors was taken into account by using the multiple imputation of chained equations technique[4].

It should be noted that the modifiable risk factors of systolic blood pressure, total cholesterol, HDL cholesterol and cigarettes per day can only directly influence the risk of having a first event as these variables were not measured at time of first event and therefore could not be used in the subsequent modelling of death after a non-fatal first event. Therefore, our policy model is intended to evaluate primary prevention interventions and not secondary prevention interventions.

Modelling stage 1 - estimating risk of having first event (equation 1 in Figure A1)
Survival analysis was used to model the cause specific hazards of the competing first events. By the end of follow-up not all SHHEC participants had experienced a first event so a parametric approach was required to extrapolate the modelling so the total remaining life expectancy could be estimated. Similar to Cox regression, Gompertz regression is a proportional hazards type model but, in addition, an ancillary parameter is estimated from the data which describes how the hazard function is related to time[5]. The model results are shown in Table A1. The associated Choleskey decomposition matrices[6] are shown in Tables A3-A10.

The following was derived from section 3.2 in Putter *et al.* using parametric expressions for the cause specific hazards[7]. The predicted cumulative incidence estimates of first events can be obtained from the Gompertz regression as follows:

$$CI_k\ (t) = \Sigma\ p_k(t_j)$$

i.e., the cumulative incidence at time t, $CI_k\ (t_j)$, is the cumulative sum of the unconditional probabilities of having event type k at time t_j, $\Sigma\ p_k(t_j)$, up to and including time t. The unconditional probabilities are obtained by:

$$p_k(t_j) = h_k(t_j)S(t_{j-1})$$

Where $h_k(t_j)$ is the cause specific hazard for event type k which for the Gompertz regression has the expression:

$$h_k(t_j) = \exp(xb)\exp(\gamma t)$$

Where xb is the linear predictor from the regression and γ is the ancillary shape parameter estimated from the data. S(t) is the probability of surviving from any of the four events at time t and is obtained by:

$$S(t) = \Pi(1 - \Sigma\, h_k(t_j))$$

Where $\Sigma\, h_k(t_j)$ is the sum of the four cause specific hazards at time t_j.

Figure A2a displays CI_k (t) and S(t) for a particular covariate profile. The middle panel of Table 2 in the main paper shows the $p_k(t_j)$ for the same covariate profile.

Modelling stage 2 - estimating life expectancy following non-fatal CHD and CBVD events (equation 2 in Figure A1)

Gompertz regression was also used to model the hazard of death following a first event in hospital. Due to censoring it was necessary to extrapolate the survival analysis to a time point when for a given covariate profile the probability of surviving beyond that time point was zero. The model results are shown in Table A2. The associated Choleskey decomposition matrices are shown in Tables A11-A14. A predicted survival curve extrapolated until the probability of surviving beyond that time point was zero can be obtained for each covariate profile. Figures A2b-A2d show predicted survival curves for a particular covariate profile with different ages at first event. The area under the survival curve was obtained by applying the trapezoidal rule[8] with half cycle correction and this provided an estimate of remaining life expectancy.

Modelling stage 3 - estimating overall life expectancy

The state transition model uses a cycle period of 1 year. At the end of a model cycle an individual can either remain in a CVD free state or move to one of the first four competing events. To calculate remaining life expectancy, the model sums the time before an event and

survival time post non-fatal event (area under the survival curve). The model cycles annually for 100 years and within each cycle the model estimates the consequences if each of the competing first events occurred. For example, if a person has a non-fatal CHD event after 3 years the additional life expectancy is those 3 years added to the life expectancy following the non-fatal event predicted from the survival analysis (modelling stage 2). Whereas, if a person dies of CVD causes after 3 years the additional life expectancy is just those 3 years. All these first event possibilities are weighted by the probability of that event occurring at that particular time which comes from the predicted cumulative incidence estimates (modelling stage 1). Finally, the estimated overall life expectancy is obtained by taking the sum of the expected additional life years and adding this to the age of the person at survey.

For measuring inequalities in life expectancy, it is possible to calculate the Slope Index of Inequality (SII) or Relative Index of Inequality (RII)[9] which takes into account the whole distribution of life expectancy across the range of the SIMD index, not just focusing on the top and bottom of the range.

Discrimination, validation and calibration of the model

The discrimination of the statistical models was assessed using Harrell's concordance statistic (c-statistic)[10]. It is important to note this will only assess discrimination where we have observed events to compare to the model predictions. We will not know how well our model discriminates in the extrapolated period.

As a validation exercise, we used the West of Scotland Coronary Prevention Study (WOSCOPS)[11] to test the extent to which our model can predict events in a Scottish population that did not inform the development of the model. WOSCOPS was a randomised, double-blind, trial investigating the effectiveness of pravastatin in preventing coronary heart disease in asymptomatic males between 45-64 years old. Participants were recruited between 1989 and 1991, which is a slightly more recent cohort of patients than SHHEC (1984-1995). The trial period averaged 4.9 years and there was an additional 10 years of follow-up, where patients had returned to normal care. For the placebo group the validation was over the entire fifteen year period. Baseline risk factors were inputted into the model, and predictive accuracy was assessed by checking whether the predicted cumulative incidence curves fell within the 95% confidence interval limits of the observed cumulative incidence curves. For the intervention group, the validation proceeded indirectly through the effect of treatment on cholesterol in order to mimic the intended use of the model. This was only done for the 5 year trial period, as post-

trial only a proportion of patients continued to take statins (28.6% at 1 year, 33.6% at 3 years, 38.7% at 5 years).

Predicted life expectancies were obtained from a model where the risk factor values are provided by average values from the Scottish Health Survey 2009[12], a sample which is broadly representative of the Scottish population. These predicted life expectancies were compared to life expectancies published in GRO life tables[13]. A calibration factor was used to adjust the linear predictor of the Gompertz regressions for first events to minimise the root mean square error (RMSE) between the predicted and observed life expectancy values for individuals aged 40, 60 and 80 years old. This was undertaken separately for men and women.

The Gompertz regressions were carried out using STATA v12 and the state transition model used to calculate life expectancy was implemented using Microsoft Excel.

Table A1: Gompertz regression modelling of cause specific hazards of first event

a) Men

Covariate	non-fatal CHD		non-fatal CBVD		fatal CVD		fatal non-CVD	
	coeff. (95% CI)	p value	coeff. (95% CI)	p value	coeff. (95% CI)	p value	coeff. (95% CI)	p value
Age	0.045 (0.038, 0.052)	<0.001	0.066 (0.054, 0.078)	<0.001	0.093 (0.082, 0.103)	<0.001	0.094 (0.085, 0.102)	<0.001
SIMD sc.	0.004 (0.001, 0.007)	0.002	0.009 (0.005, 0.014)	<0.001	0.006 (0.003, 0.010)	<0.001	0.009 (0.007, 0.012)	<0.001
Diabetes	0.653 (0.292, 1.014)	<0.001	1.168 (0.664, 1.673)	<0.001	0.863 (0.389, 1.337)	<0.001	0.335 (-0.169, 0.839)	0.192
Fam. his.	0.408 (0.295, 0.522)	<0.001	-0.021 (-0.235, 0.193)	0.847	0.165 (-0.003, 0.332)	0.054	-0.015 (-0.162, 0.133)	0.845
CPD	0.018 (0.013, 0.022)	<0.001	0.024 (0.017, 0.031)	<0.001	0.031 (0.026, 0.037)	<0.001	0.031 (0.026, 0.035)	<0.001
SBP	0.008 (0.005, 0.011)	<0.001	0.012 (0.007, 0.016)	<0.001	0.015 (0.012, 0.019)	<0.001	-0.001 (-0.005, 0.002)	0.391
TC	0.255 (0.208, 0.302)	<0.001	0.083 (-0.002, 0.168)	0.056	0.120 (0.050, 0.189)	0.001	-0.051 (-0.111, 0.008)	0.092
HDL	-0.760 (-0.947, -0.574)	<0.001	-0.125 (-0.394, 0.144)	0.362	-0.143 (-0.370, 0.085)	0.218	0.384 (0.214, 0.554)	<0.001
Constant	-9.54 (-10.12, -8.96)	<0.001	-12.51 (-13.47, -11.54)	<0.001	-14.13 (-14.93, -13.33)	<0.001	-11.22 (-11.91, -10.53)	<0.001
Gamma	0.057 (0.049, 0.065)	<0.001	0.091 (0.076, 0.105)	<0.001	0.079 (0.068, 0.091)	<0.001	0.081 (0.071, 0.091)	<0.001

b) Women

Covariate	non-fatal CHD		non-fatal CBVD		fatal CVD		fatal non-CVD	
	coeff. (95% CI)	p value	coeff. (95% CI)	p value	coeff. (95% CI)	p value	coeff. (95% CI)	p value
Age	0.058 (0.049, 0.067)	<0.001	0.080 (0.065, 0.095)	<0.001	0.102 (0.087, 0.116)	<0.001	0.091 (0.081, 0.101)	<0.001
SIMD sc.	0.009 (0.006, 0.012)	<0.001	0.013 (0.009, 0.018)	<0.001	0.004 (0.000, 0.009)	0.054	0.007 (0.004, 0.010)	<0.001
Diabetes	0.725 (0.343, 1.108)	<0.001	1.101 (0.595, 1.607)	<0.001	1.144 (0.680, 1.609)	<0.001	-0.037 (-0.668, 0.594)	0.908
Fam. his.	0.516 (0.389, 0.643)	<0.001	0.356 (0.150, 0.562)	0.001	0.239 (0.050, 0.428)	0.013	-0.018 (-0.165, 0.129)	0.814
CPD	0.021 (0.014, 0.027)	<0.001	0.027 (0.017, 0.037)	<0.001	0.048 (0.040, 0.056)	<0.001	0.038 (0.032, 0.044)	<0.001
SBP	0.006 (0.003, 0.009)	<0.001	0.014 (0.009, 0.018)	<0.001	0.018 (0.013, 0.022)	<0.001	0.003 (-0.001, 0.006)	0.112
TC	0.188 (0.136, 0.240)	<0.001	-0.051 (-0.150, 0.048)	0.308	0.057 (-0.022, 0.136)	0.159	-0.076 (-0.140, -0.013)	0.018
HDL	-0.746 (-0.937, -0.555)	<0.001	-0.346 (-0.636, -0.056)	0.020	-0.174 (-0.420, 0.073)	0.166	-0.045 (-0.229, 0.138)	0.626
Constant	-10.52 (-11.14, -9.89)	<0.001	-13.01 (-14.02, -12.00)	<0.001	-15.42 (-16.39, -14.46)	<0.001	-11.26 (-11.93, -10.58)	<0.001
Gamma	0.083 (0.073, 0.093)	<0.001	0.096 (0.080, 0.112)	<0.001	0.099 (0.084, 0.114)	<0.001	0.089 (0.078, 0.099)	<0.001

Note: ‘Age’ is age at survey

Table A2: Gompertz regression modelling of survival after non-fatal event

a) Men, after CHD event

Covariate	coeff. (95% CI)	p value
Age at event	0.077 (0.065, 0.090)	<0.001
SIMD score	0.013 (0.009, 0.017)	<0.001
Family history	-0.035 (-0.233, 0.162)	0.725
Constant	-8.597 (-9.479, -7.715)	<0.001
Gamma	0.038 (0.017, 0.059)	<0.001

b) Men, after CBVD event

Covariate	coeff. (95% CI)	p value
Age at event	0.067 (0.048, 0.087)	<0.001
SIMD score	0.009 (0.003, 0.015)	0.004
Family history	0.061 (-0.263, 0.385)	0.711
Constant	-7.447 (-8.852, -6.043)	<0.001
Gamma	0.024 (-0.015, 0.062)	0.226

c) Women, after CHD event

Covariate	coeff. (95% CI)	p value
Age at event	0.074 (0.059, 0.089)	<0.001
SIMD score	0.007 (0.003, 0.012)	0.003
Family history	-0.285 (-0.519, -0.051)	0.017
Constant	-8.360 (-9.488, -7.232)	<0.001
Gamma	0.041 (0.013, 0.068)	0.004

d) Women, after CBVD event

Covariate	coeff. (95% CI)	p value
Age at event	0.070 (0.050, 0.089)	<0.001
SIMD score	0.0002 (-0.007, 0.008)	0.961
Family history	0.181 (-0.152, 0.513)	0.287
Constant	-7.668 (-9.192, -6.144)	<0.001
Gamma	0.036 (-0.008, 0.080)	0.106

Table A3: Cholesky decomposition matrix for model in Table A1a (non-fatal CHD)

	Age	SIMD sc.	Diabetes	Fam. his.	CPD	SBP	TC	HDL	Constant	Gamma
Age	1.26E-05									
SIMD sc.	-5.63E-08	1.67E-06								
Diabetes	-1.9E-05	-9.68E-06	0.03375							
Fam. his.	1.32E-05	-1.65E-06	0.000132	0.003352						
CPD	8.88E-07	-4.29E-07	2.49E-05	-7.14E-07	4.76E-06					
SBP	-1.36E-06	-8.92E-08	-9.51E-06	-2.38E-06	5.41E-08	1.97E-06				
TC	-1.82E-06	2.97E-06	-0.00025	-6.5E-05	-1.65E-06	-3.02E-06	0.000577			
HDL	-1.9E-05	4.02E-06	0.000214	8.21E-06	1.71E-05	-2.24E-06	-0.00022	0.008855		
Constant	-0.00045	-5.9E-05	0.002371	-0.00105	-0.0001	-0.00018	-0.00306	-0.0087	0.086123	
Gamma	1.54E-06	6.02E-07	4.04E-05	4.01E-06	5.24E-07	2.54E-07	2.35E-06	-2.1E-05	-0.00034	1.76E-05

Table A4: Cholesky decomposition matrix for model in Table A1a (non-fatal CBVD)

	Age	SIMD sc.	Diabetes	Fam. his.	CPD	SBP	TC	HDL	Constant	Gamma
Age	3.79E-05									
SIMD sc.	-1.01E-06	4.46E-06								
Diabetes	-5.6E-05	-3.3E-05	0.065828							
Fam. his.	3.75E-05	-4.72E-06	0.000427	0.011873						
CPD	3.28E-06	-1.23E-06	7.57E-05	-7.44E-06	1.32E-05					
SBP	-3.95E-06	-3.16E-07	-1E-05	-1.2E-05	5.24E-08	4.98E-06				
TC	-7.37E-06	9.44E-06	-0.00024	-0.00017	-1.20E-07	-7.77E-06	0.001865			
HDL	-3E-05	3.05E-06	0.002974	-0.00029	2.43E-05	-1.8E-05	-0.00071	0.018683		
Constant	-0.00143	-0.00011	-0.002	-0.00161	-0.00033	-0.00041	-0.00964	-0.01667	0.241253	
Gamma	5.86E-06	1.87E-06	0.000121	6.77E-06	1.76E-06	7.97E-07	3.09E-06	-3.7E-05	-0.00118	5.37E-05

Table A5: Cholesky decomposition matrix for model in Table A1a (fatal CVD)

	Age	SIMD sc.	Diabetes	Fam. his.	CPD	SBP	TC	HDL	Constant	Gamma
Age	2.84E-05									
SIMD sc.	-1.41E-06	3.04E-06								
Diabetes	-2.9E-05	-2.2E-05	0.057734							
Fam. his.	2.89E-05	-4.29E-06	0.000287	0.007269						
CPD	2.89E-06	-8.25E-07	3.37E-05	-7.79E-06	8.31E-06					
SBP	-2.68E-06	-2.19E-07	-3.69E-06	-1E-05	-1.17E-07	2.82E-06				
TC	3.20E-06	6.64E-06	-0.00037	-7.8E-05	4.02E-06	-3.16E-06	0.001252			
HDL	-3E-05	-1.52E-07	-0.00018	-0.00031	7.41E-06	-2.5E-05	-0.0006	0.013304		
Constant	-0.00119	-3.2E-05	0.001989	-0.00097	-0.00026	-0.0002	-0.00717	-0.00859	0.165284	
Gamma	4.71E-06	1.12E-06	0.0001	1.81E-06	1.27E-06	4.50E-07	4.01E-06	-4E-05	-0.00078	3.56E-05

Table A6: Cholesky decomposition matrix for model in Table A1a (fatal non-CVD)

	Age	SIMD sc.	Diabetes	Fam. his.	CPD	SBP	TC	HDL	Constant	Gamma
Age	1.83E-05									
SIMD sc.	-7.87E-07	2.10E-06								
Diabetes	-1.7E-05	-1.3E-05	0.06594							
Fam. his.	1.73E-05	-2.54E-06	0.000451	0.005661						
CPD	1.72E-06	-5.79E-07	3.27E-05	-3.54E-06	5.78E-06					
SBP	-1.63E-06	-1.57E-07	-4.59E-06	-5.03E-06	7.55E-08	2.71E-06				
TC	-2.47E-06	4.63E-06	-0.00014	-8E-05	1.39E-06	-4.19E-06	0.000922			
HDL	-1.6E-05	1.42E-06	0.001089	-1.2E-05	8.01E-06	-9.23E-06	-0.00024	0.007462		
Constant	-0.00076	-3.8E-05	-0.00081	-0.00098	-0.00018	-0.00024	-0.00479	-0.00697	0.123588	
Gamma	3.27E-06	8.97E-07	3.96E-05	1.28E-06	8.05E-07	3.28E-07	2.69E-07	-1.2E-05	-0.00056	2.51E-05

Table A7: Cholesky decomposition matrix for model in Table A1b (non-fatal CHD)

	Age	SIMD sc.	Diabetes	Fam. his.	CPD	SBP	TC	HDL	Constant	Gamma
Age	2.18E-05									
SIMD sc.	-7.96E-07	2.26E-06								
Diabetes	-2.9E-05	-9.53E-06	0.037997							
Fam. his.	0.000018	-2.08E-06	8.26E-05	0.004177						
CPD	2.66E-06	-8.93E-07	2.72E-05	-1.58E-06	9.93E-06					
SBP	-2.46E-06	-1.20E-07	-2.51E-06	-4.40E-06	2.39E-07	2.50E-06				
TC	-3.7E-05	5.10E-06	-0.00027	-0.00013	-1.2E-05	-3.42E-06	0.000695			
HDL	-3.7E-05	3E-05	0.00214	-4E-05	3.5E-05	3.95E-06	-0.00022	0.009329		
Constant	-0.00054	-9.9E-05	-0.00115	-0.00131	-0.00021	-0.00019	-0.00201	-0.01228	0.100345	
Gamma	2.87E-06	8.61E-07	3.61E-05	8.54E-06	7.60E-07	1.70E-07	-2.70E-06	-3.3E-05	-0.00048	2.55E-05

Table A8: Cholesky decomposition matrix for model in Table A1b (non-fatal CBVD)

	Age	SIMD sc.	Diabetes	Fam. his.	CPD	SBP	TC	HDL	Constant	Gamma
Age	5.7E-05									
SIMD sc.	-3.01E-06	5.43E-06								
Diabetes	-8.7E-05	-3E-05	0.066499							
Fam. his.	5.36E-05	-3.65E-06	0.000852	0.011053						
CPD	7.60E-06	-2.08E-06	5.76E-05	2.80E-06	2.46E-05					
SBP	-5.89E-06	-3.39E-07	-1.1E-05	-4.99E-06	4.55E-07	5.78E-06				
TC	-0.00012	1.56E-05	-0.00029	-0.00044	-2.7E-05	-1.4E-05	0.002499			
HDL	-9.3E-05	6.54E-05	0.003344	0.00022	8.84E-05	3.79E-06	-0.00045	0.021592		
Constant	-0.00143	-0.0002	-0.00087	-0.00427	-0.00059	-0.00041	-0.00758	-0.02873	0.264345	
Gamma	9.61E-06	2.25E-06	8.87E-05	2.39E-05	2.09E-06	4.86E-07	-1.4E-05	-7.9E-05	-0.0014	6.83E-05

Table A9: Cholesky decomposition matrix for model in Table A1b (fatal CVD)

	Age	SIMD sc.	Diabetes	Fam. his.	CPD	SBP	TC	HDL	Constant	Gamma
Age	5.22E-05									
SIMD sc.	-3.12E-06	4.91E-06								
Diabetes	-6.5E-05	-3E-05	0.056007							
Fam. his.	4.58E-05	-1.64E-06	0.000961	0.009241						
CPD	6.60E-06	-1.85E-06	3.83E-05	9.60E-06	1.48E-05					
SBP	-4.81E-06	-1.95E-07	-2.57E-06	-4.48E-06	4.62E-07	4.30E-06				
TC	-7.1E-05	1.13E-05	-0.00014	-0.00025	-2E-05	-5.45E-06	0.001614			
HDL	-4.1E-05	4.73E-05	0.002741	0.000329	5.4E-05	3.09E-06	-0.00069	0.015663		
Constant	-0.00173	-0.00012	-0.00286	-0.0045	-0.00049	-0.00032	-0.00528	-0.0204	0.241351	
Gamma	8.99E-06	1.83E-06	8.77E-05	2.29E-05	1.31E-06	4.95E-07	-5.91E-06	-5.4E-05	-0.00128	5.58E-05

Table A10: Cholesky decomposition matrix for model in Table A1b (fatal non-CVD)

	Age	SIMD sc.	Diabetes	Fam. his.	CPD	SBP	TC	HDL	Constant	Gamma
Age	2.61E-05									
SIMD sc.	-1.22E-06	2.61E-06								
Diabetes	-5.4E-05	-1.3E-05	0.103373							
Fam. his.	1.88E-05	-1.43E-06	0.000119	0.005609						
CPD	3.22E-06	-1.10E-06	1.32E-05	2.35E-06	8.98E-06					
SBP	-2.87E-06	-1.45E-07	-8.82E-06	-3.44E-06	2.02E-07	3.01E-06				
TC	-4.9E-05	5.38E-06	0.000137	-0.00016	-1.3E-05	-4.92E-06	0.00103			
HDL	-2.1E-05	2.4E-05	0.000733	0.000174	3.07E-05	7.74E-07	-0.00041	0.008691		
Constant	-0.0007	-7.7E-05	0.000422	-0.00161	-0.00022	-0.00022	-0.00277	-0.01125	0.118397	
Gamma	3.99E-06	1.10E-06	4.08E-05	8.37E-06	5.54E-07	1.90E-07	-4.73E-06	-2.5E-05	-0.00062	3.03E-05

Table A11: Cholesky decomposition matrix for model in Table A2a

	Age at event	SIMD score	Family history	Constant	Gamma
Age at event	3.95E-05				
SIMD score	1.29E-06	4.53E-06			
Family history	5.81E-05	-1.1E-05	0.01014		
Constant	-0.00275	-0.00023	-0.00676	0.202488	
Gamma	2.62E-05	2.19E-06	1.38E-05	-0.00246	0.000116

Table A12: Cholesky decomposition matrix for model in Table A2b

	Age at event	SIMD score	Family history	Constant	Gamma
Age at event	9.59E-05				
SIMD score	2.70E-06	9.60E-06			
Family history	0.000123	6.25E-07	0.027277		
Constant	-0.00685	-0.00052	-0.01452	0.513441	
Gamma	7.25E-05	4.20E-06	-7.7E-05	-0.00675	0.000379

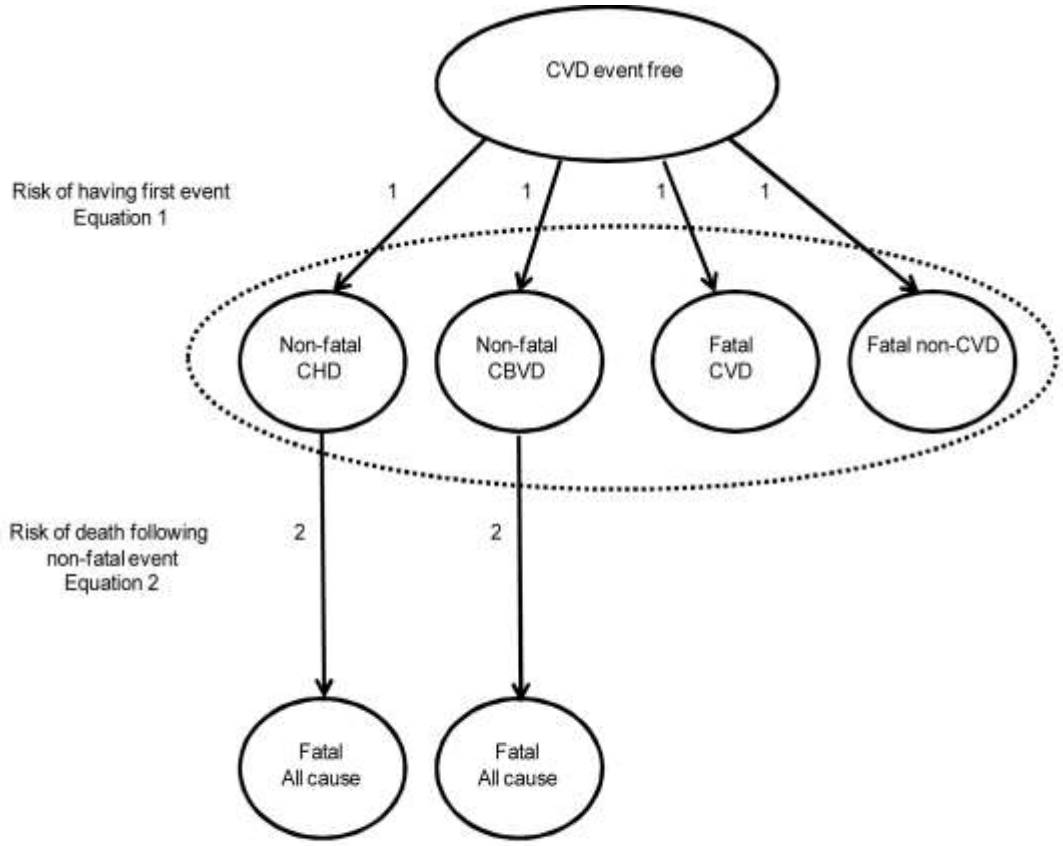
Table A13: Cholesky decomposition matrix for model in Table A2c

	Age at event	SIMD score	Family history	Constant	Gamma
Age at event	6.08E-05				
SIMD score	8.05E-07	6.06E-06			
Family history	5.03E-05	-4.91E-06	0.014259		
Constant	-0.00437	-0.00026	-0.00863	0.3313	
Gamma	4.5E-05	4.42E-07	-6.3E-05	-0.00411	0.000197

Table A14: Cholesky decomposition matrix for model in Table A2d

	Age at event	SIMD score	Family history	Constant	Gamma
Age at event	0.000106				
SIMD score	-2.60E-06	1.41E-05			
Family history	0.000242	-2.6E-05	0.028796		
Constant	-0.00775	-0.00031	-0.02781	0.604536	
Gamma	9.8E-05	7.31E-07	6.96E-05	-0.00917	0.000503

Figure A1: Structure of the state transition model



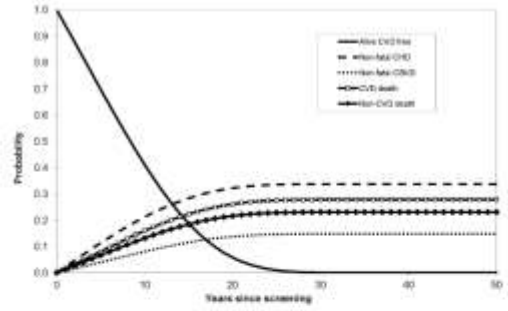
Equation 1: Function (age at survey, SBP, TC, HDL, CPD, family history, SIMD)

Equation 2: Function (age at first event, family history, SIMD)

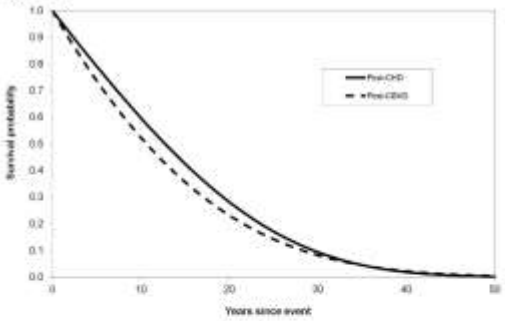
Notes: SBP = systolic blood pressure (mm Hg), TC = total cholesterol (mmol/l), HDL = HDL cholesterol (mmol/l), CPD = cigarettes per day, SIMD = Scottish Index of Multiple Deprivation

Figure A2: Cumulative incidence of first four events and survival probabilities after first non-fatal events

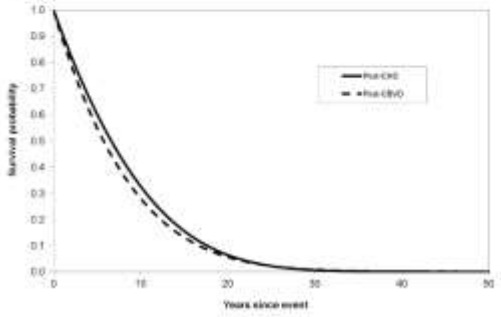
a) Cumulative incidence of first events



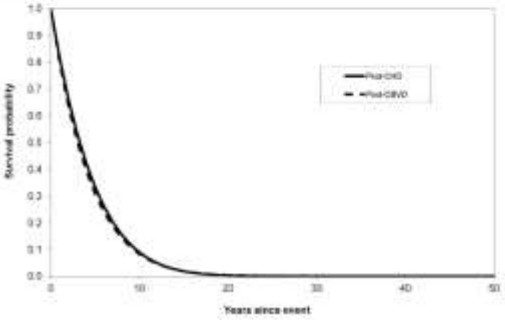
b) Survival probabilities after first non-fatal event (event occurs at age 60)



c) Survival probabilities after first non-fatal event (event occurs at age 70)



d) Survival probabilities after first non-fatal event (event occurs at age 80)



REFERENCES

1. **Lewsey JD**, Lawson KD, Ford I, *et al.* A Cardiovascular Disease Policy Model that predicts life expectancy taking into account socio-economic deprivation.
2. **Tunstall-Pedoe H**, Woodward M, Tavendale R, *et al.* Comparison of the prediction by 27 different factors of coronary heart disease and death in men and women of the Scottish Heart Health Study: cohort study. *BMJ* 1997;**315**:722-9.
3. **Tunstall-Pedoe H**, ed, for the WHO MONICA Project. *MONICA monograph and multimedia sourcebook.* Geneva: World Health Organization, 2003:124.
4. **van Buuren S**, Boshuizen HC and Knook DL. Multiple imputation of missing blood pressure covariates in survival analysis. *Statistics in Medicine* 1999;**18**:681-694.
5. **Kleinbaum DG**, Klein M. *Survival Analysis – A Self-Learning Text, 2nd edition.* New York: Springer, 2005, p285.
6. **Briggs A**, Claxton K, Sculpher M. *Decision Modeling for Health Economic Evaluation*. Oxford: Oxford University Press, 2006, p95.
7. **Putter H**, Fiocco M and Geskus RB. Tutorial in biostatistics: Competing risks and multi-state models. *Statistics in Medicine* 2007;**26**:2389-2430.
8. **Gray AM**, Clarke PM, Wolstenholme JL, Wordsworth S. *Applied Methods of Cost-effectiveness Analysis in Health Care*. Oxford: Oxford University Press, 2012, p72.
9. **ScotPHO** Public Health Information for Scotland. Measuring Socio-Economic Inequalities in Health: A Practical Guide, 2007. http://www.scotpho.org.uk/downloads/scotphoreports/scotpho071009_measuringinequalities_rep.pdf (accessed 13th May 2014).
10. **Harrell FE**, Lee KL and Mark DB . Multivariable prognostic models: issues in developing models, evaluating assumptions and adequacy, and measuring and reducing errors. *Statistics in Medicine* 1996;**15**:361–387.
11. **Shepherd J**, Cobbe S, Ford I, *et al.* Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia. *New England Journal of Medicine* 1995;**333**:1301-1308.
12. **The Scottish Government**. Scottish Health Survey. http://www.scotland.gov.uk/Topics/Statistics/Browse/Health/scottish-health-survey (accessed 30th October 2012).
13. **General Register Office for Scotland**. Life Expectancy at Scotland Level – Scottish Interim Life Tables. http://www.gro-scotland.gov.uk/files2/stats/life-expectancy-at-scotland-level/table2-le-2009-2011.pdf (accessed 30th October 2012).