TECHNICAL APPENDIX FOR THE IMPACT$_{SEC}$ MODEL

Contents

1 Overview of the IMPACT$_{SEC}$ model

The IMPACT model accommodates sub-national variation in CHD mortality trends by socioeconomic circumstances (IMPACT$_{SEC}$ model). We used the Index of Multiple Deprivation 2007 (IMD) quintiles as a proxy indicator of socioeconomic circumstances. This model examines the effects of changes in treatment uptake and risk factor trends on changes in mortality from coronary heart disease (CHD) among adults in England aged 25 years and over, stratified into equal quintiles by population size. The tables included in this Technical Appendix provide details about the sources and methods that were used.

2 METHOD AND EXAMPLES OF DEATHS PREVENTED OR POSTPONED (DPP) CALCULATIONS

2.1. Changes in mortality rates from CHD, England 2000 to 2007

Data sources used in examining the changes in CHD mortality rates over 2000 to 2007 are shown in Table A. Mortality rates from CHD were calculated using the underlying cause of death (*2000*: ICD9 410-414; *2007*: ICD10 I20-I25). Both unadjusted and age-adjusted mortality rates were calculated. The direct method of age-standardisation was used with the European Union reference population as standard.

2.2. Expected and observed number of deaths from CHD

Data sources used to estimate the observed and expected number of deaths from CHD for 2000 and 2007 are shown in Table A. The expected number of CHD deaths in 2007 was calculated by multiplying the age-sex-IMD quintile specific mortality rates from CHD in 2000 by the population counts for 2007 in that age-sex-IMD quintile stratum. Summing over all strata then yielded the expected number of deaths in 2007 had mortality rates remained unchanged. The difference between the number of expected and observed deaths from CHD represented the mortality fall, or the total DPPs in 2007 relative to 2000. Population counts, CHD mortality rates, observed and expected numbers of deaths are shown in sections 3.1and 3.2

2.3. Treatment component of IMPACT$_{SEC}$ model

The treatment component of the IMPACT$_{SEC}$ model included nine mutually exclusive CHD patient groups (see below). However, **<u>for the purposes of our model, we just take into account groups 8 and 9</u>**

1. Patients treated in hospital for acute myocardial infarction (ST-elevation myocardial infarction and non-ST elevation acute coronary syndrome)
2. Patients admitted to hospital with unstable angina
3. Community-dwelling patients who have survived a myocardial infarction for over a year
4. Patients who have undergone a revascularisation procedure up to and including the years 2000 and 2007: Coronary Artery Bypass Grafting (CABG), or a Percutaneous Coronary Intervention (PCI)
5. Community-dwelling patients with stable coronary artery disease
6. Patients admitted to hospital with heart failure (due to CHD)
7. Community-dwelling patients with heart failure (due to CHD)
8. **<u>Hypercholesterolaemic subjects without CHD eligible for cholesterol lowering therapy such as statins</u>**
9. **<u>Hypertensive individuals without CHD eligible for anti-hypertensive therapy</u>**

The general approach to calculating the number of DPPs from an intervention among a particular patient group was first to stratify by age, sex and IMD quintile; then to multiply the estimated number of patients in 2007 in turn by: the proportion of these patients receiving a particular treatment; the one-year case fatality rate; and the relative reduction in the case fatality rate due to the administered treatment. Sources for treatment uptake are shown in sections 3.3 and 3.4. Sources for estimates of treatment efficacy (relative risk reductions) are shown in section 3.5 . We obtained the relative risks based on the most recent published systematic reviews and meta-analyses of epidemiological studies. Each treatment relative risk value in the model was based on a meta-analysis comparison with an older therapy, or in some cases with a placebo if relevant. Age-sex specific case fatality rates for each patient group are presented in section 3.6

It was assumed that compliance (adherence), i.e. the proportion of treated patients actually taking therapeutically effective levels of medication, was 100% among hospital patients, 70% among symptomatic community patients, and 50% among asymptomatic community patients taking lipid-lowering drugs or anti-hypertensive medication for primary prevention. An adjustment was also made in certain cases for sub-optimal dose.

Example 1: Estimation of DPPs from a specific treatment

Mortality fall as a result of taking statins in men aged 55-64 in the most affluent quintile

For example, in 2007, about 685,000 men aged 55-64 were classified as the most affluent quintile. Uptake of statins in primary prevention was estimated to be approximately 15% with 100% assumed to comply. Statins in primary prevention reduces case fatality in patients by approximately 35%. The underlying one-year case fatality rate in these men was approximately 0.6%. The DPPs for at least a year were therefore calculated as:

Patient numbers × treatment uptake × compliance × relative mortality reduction × one year case fatality

$= 685{,}000 \times 15\% \times 50\% \times 35\% \times 0.6\% \approx 108$ DPPs

This calculation was then repeated for each age-sex-IMD quintile group.

2.4. Risk factor component of $\text{IMPACT}_{\text{SEC}}$ model

The second part of the $\text{IMPACT}_{\text{SEC}}$ model estimated the number of DPPs related to changes in cardiovascular risk factor levels in the population. The risk factors considered were total cholesterol and systolic blood pressure. The Health Survey for England was used to calculate trends in the prevalence (or mean values) of each risk factor (section 3.7). For the purposes of this paper, we used the regression approach to calculate DPPs from changes in risk factors.

In this approach regression approach the number of CHD deaths in 2000 (the start year) after adjusting for population change between 2000 and 2007 were multiplied by the absolute change in risk factor level, and by a regression coefficient ('beta') quantifying the estimated relative change in CHD mortality that would result from a one-unit change in risk factor level (see section 3.9). Natural logarithms were used, as is conventional, in order to best describe the log-linear relationship between absolute changes in risk factor levels and relative change in mortality. Levels of risk factors in 2000 and 2007 by sex and IMD quintile are shown in section 3.8.

Example 2: Estimation of DPPs from risk factor changes using regression method

Mortality fall due to reduction in SBP in women aged 55-64 in the most affluent quintile

For example, in 2000, there were 227 CHD deaths among 573,291 women aged 55-64 years in the most affluent quintile. The population total had increased to 714,111 in 2007. Applying the CHD death rate from 2000 (39.6 per 100,000) to the 2007 population gives an (adjusted) total of 283 expected deaths in 2007.

Mean SBP in this group fell by an estimated 4.28 millimetres of mercury (mmHg) (from 133.8 in 2000 to 129.5 in 2007). The largest meta-analysis reports an estimated age-sex specific reduction in mortality of 50% for every 20 mmHg reduction in SBP, generating a logarithmic coefficient of -0.035 (i.e. natural logarithm of 0.5 divided by 20). The subsequent reduction in CHD deaths between 2000 and 2007 was then estimated as the product of three variables:

DPPs = expected CHD deaths in 2007 (had mortality rates in 2000 remained constant) × absolute risk factor reduction between 2000 and 2007 × regression coefficient exponentiated

DPPs = (1-(exponential (regression coefficient × absolute change))) × expected deaths in 2007

DPPs = (1-(exponential (-0.035 × 4.28))) × 283 ≈ 39

This calculation was then repeated for each age-sex-quintile group.

The regression coefficients were assumed equal across deprivation quintiles. A 'fixed gradient' approach was used to stabilise estimates of risk factor change across the quintiles; this method is discussed in 2.5.5

2.5. Cumulative risk-reduction

2.5.1. Background

CHD deaths are usually caused by multiple risk factors acting simultaneously. Hence, part of the effect of one risk factor may be mediated through another. For example, physical inactivity may have a direct effect on CHD but may also partly be mediated through its effects on BMI and blood pressure. It is recommended therefore that mortality benefits attributable to risk factors which may be causally related, or which overlap in population groups, should not be combined by simple addition. Ideally, their effects should instead be jointly estimated [12-16].

We do not currently have sources that allow joint estimation of relative risks for combinations of risk factors in this English population. However, several large cohort studies and meta-analyses have published independent risk reduction coefficients for each risk factor included in this study. One approach commonly used is to calculate the **cumulative risk-**reduction [17]. This approach accounts for risk factor prevalence overlap but assumes independence of effects [14-15]. The general equation for cumulative risk-reduction is stated as:

Combined (or cumulative) effect (CR) =

$$1 - ((1\text{-}a) \times (1\text{-}b) \times (1\text{-}c) \times \ldots \times (1\text{-}n)) \qquad \textbf{[1]}$$

Thus for CHD risk factors, the specific equation is stated as:

$$\mathbf{CR} = 1 - ((1\text{-}R_{SBP}) \times (1\text{-}R_{smoke}) \times (1\text{-}R_{diabetes}) \times \ldots \times (1\text{-}R_n))$$

where R denotes the mortality change attributable to a specific risk factor.

This is in contrast to additive risk-reduction (AR):

$$\mathbf{AR} = (R_{SBP}) + (R_{smoke}) + (R_{diabetes}) + \ldots + (R_n) \qquad \textbf{[2]}$$

2.5.2. 1.3.2 Implementation

For the purposes of this modelling study we first calculated the (additive) DPPs attributed to risk factor change. These were then adjusted down by using the ratio:

Adjustment factor = CR/AR

The adjustment factor would always be expected to be less than 1. In other words, cumulative risk factor reduction would be smaller than the mortality benefits arrived at by a simple summation of the benefits of each risk factor in turn.

The proportional change in the CHD mortality rate between two time points (denoted by R) was calculated using the following formulas [14-15]:

Continuous risk factors:

$R_{continuous}$ = 1 – exp(beta × absolute mean risk factor change) **[3]**

and P denotes prevalence at the start-year; RR the relative risk in CHD mortality associated with risk factor presence; and ΔP the change in prevalence between the start and final years.

Formulas [3] and [4] were used to calculate the proportional change in the CHD mortality rate (R) for each risk factor and the steps involved in their estimation are detailed below. However, we made two modifications to the methodology used in previous work [14-15]. First, we estimated aggregate change over a seven year period (2000-2007) rather than average annual change. Second, additive and cumulative risk-reduction was calculated by using the **absolute** values of R (i.e. disregarding the direction of risk factor change). These are discussed in turn below.

2.5.3. Calculating aggregate change in risk factors over 2000 and 2007

Previous studies [14-15] estimating cumulative risk factor reduction calculated the average annual percentage change in CHD mortality attributable to annual falls in levels of smoking, blood pressure and cholesterol (where annual falls in CHD mortality and risk factor levels were estimated over a specified number of years). Rather than estimate the average annual change over a specific range of years, we were interested in calculating the R values between two fixed points in time (start and end years of the model), seven years apart, 2000 and 2007. We therefore adapted formulas [3] and [4], substituting change over the seven year study period for the estimation of annual average change. We checked our resulting estimates of cumulative risk reduction calculated over seven years against uprating the annual average by a factor of seven. The two sets of estimates were found to be virtually identical.

2.5.4. Regression models to estimate risk factor change, 2000-2007

Formula [3] requires estimates of absolute and relative change in risk factors, respectively. Regression modelling was used to estimate the magnitude of absolute and relative change. In order to smooth fluctuations in Health Survey for England data, we obtained estimates of risk factor change for each risk factor over 2000-2007 by using the predicted values from regression models. Separate models were fitted by sex and seven ten-year age-bands.

The dependent variable was the risk-factor level for each survey respondent; calendar year (i.e. year of interview) was the explanatory variable entered in the model as a continuous term.

Absolute change was measured as the difference between the predicted values for 2000 and 2007, by age and sex.

Estimates of risk factor change were not calculated separately by deprivation quintile owing to small sample sizes, especially in those risk factors covered by the survey in intermittent years. Data since 2003 were weighted for non-response at each stage of data collection. Although it was just beyond the time period covered by the $IMPACT_{SEC}$ model, the most recent survey data available (2008) was included in fitting the regressions to improve estimation of the underlying change. Analyses were conducted using Stata Version 11.1.

2.5.5. Adjustment factors by age-sex-IMD

The adjustment factors (section 3.10) fell within the range of 0.83 to 0.96. The largest adjustment (0.83) was applied to the DPPs for women aged 65-74 resident in the most deprived areas (IMDQ5). The adjustment factors for the deprivation quintiles were, on average, ± 0.01 of the overall adjustment ratio for England across the 14 age and sex groups. The adjustments were on average, slightly higher for women (0.89) than men (0.92); and were higher in IMDQ5 than in IMDQ1 (mean values 0.8924 and 0.9089, respectively). Hence the adjustment values indicated a larger downward adjustment to the additive DPPs in the most deprived areas relative to the most affluent.

2.6. Overlap between pharmacological and non-pharmacological contributions to risk factor DPPs

Risk factor improvements, such as lower blood pressure or lower total cholesterol, may be achieved through medications, lifestyle changes, or a combination. In order to separate the DPPs from pharmacological versus non-pharmacological contributions to CHD mortality, we subtracted the DPPs calculated in the treatment (primary prevention) component of the model from the DPPs calculated in the risk factor component. That is, to estimate the impact of population-wide reduction in total cholesterol due to non-pharmacological change, we subtracted the estimated effect of statins for the primary prevention of CHD from the overall number of DPPs due to change in mean total cholesterol. Similarly, to estimate the impact of the population-wide reduction in SBP we subtracted the estimated effect of anti-hypertensive medication for primary prevention from the overall number of DPPs due to change in mean SBP levels.

2.7. Net effects

As all treatments were in use in 2000, the net benefit of an intervention in 2007 was calculated by subtracting the expected number of deaths prevented if the uptake rates in 2000 remained constant from the estimated number of deaths prevented calculated using the 2007 uptake rates. This is illustrated in the example below.

Example 5: Net effects for treatments

For example, in 2007, about 685,000 men aged 55-64 were classified as the most affluent quintile. Uptake of statins in primary prevention was estimated to be approximately 15% with 50% assumed to comply. Statins in primary prevention reduces case fatality in patients by approximately 35%. The underlying one-year case fatality rate in these men was approximately 0.6%. The DPPs for at least a year were therefore calculated as:

Patient numbers × treatment uptake × compliance × relative mortality reduction × one year case fatality

$= 685{,}000 \times 15\% \times 50\% \times 35\% \times 0.6\% \approx 108$ *DPPs*

Applying the uptake rate in 2000 (2.7%) gave a total of 19 DPPs:

The net DPPs were therefore:

Net DPPs = DPPs using uptake$_{2007}$ – DPPs using uptake$_{2000}$

= 108 –19 = 89

The estimated changes in treatment uptake between 2000 and 2007 by deprivation quintile are shown in Table H.

2.8. Uncertainty analyses

We implemented uncertainty analysis in Excel using Ersatz (version 1.0 available at http://www.epigear.com). This is an add-on which allows probabilistic bootstrapping in Excel. Ersatz allows repeated random draws from specified distributions for input variables and then calculates the 95% uncertainty intervals from the realised values of the output variable (deaths prevented or postponed). For the $\text{IMPACT}_{\text{SEC}}$ model, we calculated the uncertainty intervals based on 1000 draws – taking the 95% uncertainty intervals from the 2.5^{th} and 97.5^{th} percentiles. The parameter distributions used for the input variables to the DPP calculations are shown in Table M. Worked examples using Ersatz are shown below Table M.

2.8.1. Allocating areas to socioeconomic quintiles using the Index of Multiple Deprivation, 2007

The Index of Multiple Deprivation (IMD) is a composite index of relative deprivation at small area level based on seven domains: income; employment; health deprivation and disability; education, skills and training; barriers to housing and services; crime and disorder; and living environment [19]. The IMD 2007 score of all small areas in England (average population 1,500) were ranked in ascending order and grouped into equal quintiles (about 6,500 areas in each), with quintile one (IMDQ1) including the most affluent and quintile five (IMDQ5) the most deprived areas. Based on their postcode of residence, patients treated in hospital (e.g. recorded in Hospital Episode Statistics) or in the community (e.g. in the General Practice Research Database) were matched via their area of residence to the corresponding deprivation quintile by the data providers to protect patient anonymity. Mortality counts were similarly aggregated into deprivation quintiles by the Office for National Statistics before being released to us for research purposes.

As the IMD 2007 includes rates of premature total mortality in the health deprivation and disability domain, its use to quantify health inequalities risks a tautology. However UK studies have shown that removing the health domain had little effect on either the assignment of areas into their deprivation quintile or the relationship between area-based deprivation and health [20].

Conceptually, the IMD 2007 is a measure of deprivation, not a measure of affluence. Hence, areas with the lowest scores are not necessarily the most affluent; rather they have the lowest concentration of deprived people. In this paper for clarity and to easily distinguish between the extreme ends of the deprivation spectrum, we have used the term ‘most affluent’ and ‘most deprived’ rather than ‘least deprived’ and ‘most deprived’.

3 Data sources

3.1. Population and patient data sources used in the IMPACTSEC model

Information	Source
Population data	
Population counts and CHD deaths stratified by age, sex, and Index of Multiple Deprivation quintiles	Office for National Statistics (ONS): (*2000*: ICD9 410-414) (*2007*: ICD10 I20-I25)
Patients eligible for primary prevention therapies:	
Lipid-lowering drugs	Prevalence of never having had angina or heart attack and currently taking lipid lowering drugs prescribed by a doctor from the Health Survey for England (HSfE 1998, 2003, and 2006) (http://www.ic.nhs.uk/statistics-and-data-collections/health-and-lifestyles-related-surveys/health-survey-for-england)
Hypertension treatment	Prevalence of never having had angina or heart attack and currently taking medication specifically prescribed to treat high blood pressure from the Health Survey for England (HSfE 1998, 2003, and 2006)

Table A: Population and patient data sources used in the IMPACTSEC model

3.2. Demographic data 2000 and 2007 by sex and deprivation quintiles

	Year	England	IMDQ1	IMDQ2	IMDQ3	IMDQ4	IMDQ5
Male							
Population (000s)	**2000**	16242	3353	3372	3321	3186	3011
	2007	17002	3525	3542	3486	3335	3114
Observed CHD deaths	**2000**	56713	9146	10868	11671	12094	12934
	2007	41713	6962	8129	8535	8723	9364
Age-standardised rate (00,000)	**2000**	310	238	270	301	349	415
	2007	200	147	170	191	231	294
Annual % fall†		6.0	6.6	6.4	6.3	5.7	4.8
Expected deaths††	**2007**	63685	11207	12856	13348	13098	13176
Target DPPs‡	**2007**	21972	4245	4727	4813	4375	3812
% of expected deaths prevented	**2007**	34.5	37.9	36.8	36.1	33.4	28.9
Female							
Population (000s)	**2000**	17710	3618	3663	3618	3493	3318
	2007	18279	3803	3820	3747	3571	3337
Observed CHD deaths	**2000**	46530	7383	8959	9789	10093	10306
	2007	32461	5350	6315	6812	6953	7031
Age-standardised rate (00,000)	**2000**	148	115	128	143	164	198
	2007	94	70	79	90	107	136
Annual % fall†		6.3	6.7	6.7	6.4	5.9	5.2
Expected deaths††	**2007**	48559	8458	9812	10348	10162	9778
Target DPPs‡	**2007**	16098	3108	3497	3536	3209	2747
% of expected deaths prevented	**2007**	33.2	36.7	35.6	34.2	31.6	28.1
Total							
Population (000s)	**2000**	33952	6972	7035	6939	6678	6329
	2007	35281	7328	7363	7233	6906	6451
Observed CHD deaths	**2000**	103243	16529	19827	21460	22187	23240
	2007	74174	12312	14444	15347	15676	16395
Age-standardised rate (00,000)	**2000**	229	177	199	222	257	306
	2007	147	109	124	141	169	215
Annual % fall†		6.1	6.7	6.5	6.3	5.8	4.9
Expected deaths††	**2007**	112244	19665	22669	23696	23260	22953
Total DPPs‡	**2007**	38070	7353	8225	8349	7584	6558
% of expected deaths prevented	**2007**	33.9	37.4	36.3	35.2	32.6	28.6

Table B: Demographic data 2000 and 2007 by sex and deprivation quintiles

† Annual % fall = (1-(2007 rate/2000 rate)^(1/7))

†† Expected deaths = CHD deaths expected in 2007 had 2000 CHD rates remained.

‡ DPPs, deaths prevented or postponed. DPPs = expected – observed deaths in 2007

3.3. Data sources for treatment uptake levels

Primary prevention therapies:	
Lipid-lowering drugs	Prevalence of never having had angina or heart attack and currently taking lipid lowering drugs prescribed by a doctor from the Health Survey for England (HSfE 1998, 2003, and 2006).
Anti-hypertensive medication	Prevalence of never having had angina or heart attack and currently taking medication specifically prescribed to treat high blood pressure from the Health Survey for England (HSfE 1998, 2003, and 2006).

Table C: Data sources for treatment uptake levels

3.4. Treatment uptake in 2000 and 2007

	England			IMDQ1			IMDQ2			IMDQ3			IMDQ4			IMDQ5		
	N	**Uptake (%)**		**N**	**Uptake (%)**		**N**	**Uptake (%)**		**N**	**Uptake (%)**		**N**	**Uptake (%)**		**N**	**Uptake (%)**	
		2000	**2007**		**2000**	**2007**		**2000**	**2007**		**2000**	**2007**		**2000**	**2007**		**2000**	**2007**
Anti-hypertension	35,280,843	8.3	13.5	7,328,217	8.3	14.0	7,362,561	8.2	13.8	7,232,779	8.6	13.9	6,905,987	8.2	13.0	6,451,299	8.3	12.7
Statins	35,280,843	1.1	9.0	7,328,217	1.0	7.9	7,362,561	1.1	8.5	7,232,779	1.1	9.1	6,905,987	1.4	10.3	6,451,299	1.3	9.1

Table D: Treatment uptake in 2000 and 2007

†† We assumed no change in community-based CPR between 2000 and 2007

3.5. Clinical efficacy of interventions: relative risk reductions obtained from meta-analyses, and randomised clinical trials

Treatments	Relative risk reduction†	Comments	Source paper: First author (year), notes
Primary prevention therapies:			
Treatments for high blood pressure	13% (95% CI: 6,19)	OR=0.87 (95% CI: 0.81,0.94); RRR=13% (95% CI: 6,19) in those with high blood pressure without disease at entry. [RRR=29% (95% CI: 17,37) those with average blood pressure and CHD, treated with ACE inhibitors]	Law (2003) [51]
Statins	35% (95% CI: 11,52)	OR=0.65 (95% CI: 0.48,0.89); RRR=35% (95% CI: 11,52) for CHD mortality (only trials using statins), Figure 3 on page 4	Pignone (2000) [52]

Table E; Relatives risk reductions used in the model

†Relative risk reduction (RRR) calculated as 1 – odds ratio

3.6. Case fatality rates for each patient group

Patient group	Hypertension		Statins	
	Men	**Women**	**Men**	**Women**
25-34	0.000	0.000	0.000	0.000
35-44	0.001	0.001	0.001	0.001
45-54	0.002	0.002	0.002	0.002
55-64	0.006	0.004	0.006	0.004
65-74	0.014	0.014	0.014	0.014
75-84	0.035	0.035	0.035	0.035
85+	0.094	0.094	0.094	0.094

Table F: Case-fatality rates. Source Wijeysundera et.al (2010) [5]

3.7. Risk factors: variable definitions and source

The Health Survey for England (HSfE), an annual nationwide household survey of the English population, has been described in detail elsewhere [24]. Briefly, members of a stratified random sample (drawn from the Postcode Address File) that is socio-demographically representative of the English population were invited to participate. The annual household response rate was 75% in 2000, falling steadily to 66% in 2007. Data were collected at two visits: an interviewer's visit, during which a questionnaire was administered, followed by a visit from a trained nurse for all those interviewed who agreed. The nurse visit, which did not take place in 2004 among the general population sample, includes measurements and collection of blood, as well as additional questioning including use of prescribed medication (1998, 2003, and 2006).

Risk factor	**HSfE survey years**	**Description**
SBP (mmHg)	All years between 2000-7 except 2004	Calculated as the mean of the 2nd and 3rd readings for those who had not eaten, consumed alcohol or smoked in the 30 minutes prior to measurement. Those reporting taking blood pressure lowering drugs were included
Total cholesterol (mmol/l)	1998,2003,2006	Those reporting taking lipid lowering drugs were included

Table G: Definition of risk fators

3.8. Risk factor levels in 2000 and 2007 by sex and deprivation quintiles

The annual sample size of the Health Survey for England (HSE), roughly 14,000 adults aged 16 years and over, was not large enough to provide accurate and precise estimates of risk factor levels, and hence rates of change over time by age, sex, and deprivation quintiles. We considered a 'fixed gradient approach' for estimating risk factors changes.

The fixed gradient approach is based on the assumption that changes in pace and direction for each deprivation quintile were similar and therefore, most accurately measured by the overall national rates of change (across all age-sex groups). If this assumption holds, then relatively stable and plausible estimates for each quintile could be derived by scaling the national age-sex risk factor levels up or down using a fixed ratio/gradient.

The fixed gradient was derived by pooling together survey data for all available years from 2000 to 2007 to calculate risk factor estimates by age, sex, and deprivation quintiles. Then the pooled national estimate for 14 age-by-sex groups was set notionally to one, and the corresponding estimates for each deprivation quintile re-indexed to be below or above one (i.e. expressing the ratio of the deprivation quintile to national estimate). These index rates were then applied to the single year national estimates to derive the corresponding risk factor levels for that year. The fixed gradient was applied to both the start and end years of the model. The next table shows the risk factor levels in 2000 and 2007 by gender and deprivation quintiles using this approach.

	England		**IMDQ1**		**IMDQ2**		**IMDQ3**		**IMDQ4**		**IMDQ5**	
	2000	**2007**	**2000**	**2007**	**2000**	**2007**	**2000**	**2007**	**2000**	**2007**	**2000**	**2007**
Systolic blood pressure, mmHg												
Male	133.1	130.6	133.1	130.5	133.4	130.8	133.3	130.7	133.0	130.6	133.0	130.6
Female	131.0	125.6	130.7	125.3	131.6	126.6	131.2	125.7	131.1	125.6	130.6	125.1
Cholesterol, mmol/L												
Male	5.6	5.4	5.6	5.4	5.6	5.5	5.6	5.4	5.5	5.4	5.5	5.4
Female	5.7	5.5	5.7	5.6	5.8	5.6	5.7	5.5	5.6	5.4	5.6	5.5

Table H: Risk factor levels in 2000 and 2007

3.9. Beta coefficients for risk factors

Estimated β coefficients from multiple regression analyses for the relationship between absolute changes in population mean risk factors and percentage changes in coronary heart disease mortality for men and women, stratified by age. Data sources, values and comments.

Systolic blood pressure	**Age group (years)**				
	25-44	**45-54**	**55-64**	**65-74**	**75+**
Men (hazard ratio per 20 mmHg)	0.49	0.49	0.52	0.58	0.65
Men (log hazard ratio per 1 mmHg)	**-0.036**	**-0.035**	**-0.032**	**-0.027**	**-0.021**
Minimum	*-0.029*	*-0.028*	*-0.026*	*-0.022*	*-0.017*
Maximum	*-0.043*	*-0.042*	*-0.039*	*-0.032*	*-0.025*
Women (hazard ratio per 20 mmHg)	0.40	0.40	0.49	0.52	0.59
Women (log hazard ratio per 1 mmHg)	**-0.046**	**-0.046**	**-0.035**	**-0.032**	**-0.026**
Minimum	*-0.037*	*-0.037*	*-0.028*	*-0.026*	*-0.021*
Maximum	*-0.055*	*-0.055*	*-0.042*	*-0.039*	*-0.031*

Source: Prospective studies collaborative meta-analysis, Lancet 2002 [53]

Units: Percentage change in CHD mortality per 20 mmHg change in systolic blood pressure

Strengths: Large dataset, includes US data, adjusted for regression dilution bias, consistent with randomised controlled trials, results stratified by age and sex, with 95% confidence intervals

Limitations: Some publication bias still possible

Table I: Beta coefficients for SBP.

† **Risk reduction = 1 – hazard ratio**

Cholesterol	Age groups (years)					
	25-44	**45-54**	**55-64**	**65-74**	**75-84**	**85+**
Mortality reduction per 1 mmol/l						
Men	0.55	0.53	0.36	0.21	0.21	0.21
Women	0.57	0.52	0.35	0.23	0.23	0.23
Log coefficient						
Men	**-0.799**	**-0.755**	**-0.446**	**-0.236**	**-0.117**	**-0.083**
Minimum	*-0.639*	*-0.604*	*-0.357*	*-0.189*	*-0.093*	*-0.067*
Maximum	*-0.958*	*-0.906*	*-0.536*	*-0.283*	*-0.140*	*-0.100*
Women	**-0.844**	**-0.734**	**-0.431**	**-0.261**	**-0.174**	**-0.051**
Minimum	*-0.675*	*-0.587*	*-0.345*	*-0.209*	*-0.139*	*-0.041*
Maximum	*-1.013*	*-0.881*	*-0.517*	*-0.314*	*-0.209*	*-0.062*

Source: Prospective studies collaborative meta-analysis, Lancet 2007 [54]

Units:	Percentage change in CHD mortality per 1 mmol/l change in total cholesterol
Strengths:	Includes US data, adjusted for regression dilution bias, includes randomised controlled trials, RCT values consistent with observational data, results stratified by age and sex, with 95% confidence intervals
Limitations:	Some publication bias still possible

Table J: Beta coefficients for cholesterol

[†] Risk reduction = 1 – hazard ratio

3.10. Cumulative benefit: Adjustment factors by age, sex and IMD quintile

In Section 1.2 we described how we adjusted down the DPPs calculated in an additive fashion over the risk factors by using the ratio of cumulative to additive risk-reduction. The 70 age-sex-IMD specific adjustment factors are shown below.

	Deprivation quintile					
	IMDQ1	IMDQ2	IMDQ3	IMDQ4	IMDQ5	England
			Men			
25-34	0.9464	0.9449	0.9463	0.9462	0.9434	0.9453
35-44	0.9196	0.9169	0.9179	0.9126	0.9110	0.9153
45-54	0.9335	0.9278	0.9205	0.9193	0.9083	0.9219
55-64	0.8957	0.8957	0.8883	0.8851	0.8762	0.8886
65-74	0.8885	0.8843	0.8846	0.8817	0.8720	0.8827
75-84	0.9182	0.9146	0.9134	0.9214	0.9149	0.9162
85+	0.9561	0.9569	0.9525	0.9520	0.9582	0.9547
			Women			
25-34	0.8799	0.8872	0.8846	0.8787	0.8782	0.8809
35-44	0.9148	0.9119	0.9014	0.9034	0.8892	0.9038
45-54	0.9038	0.9013	0.8937	0.8777	0.8546	0.8865
55-64	0.8862	0.8896	0.8842	0.8703	0.8560	0.8780
65-74	0.8620	0.8569	0.8523	0.8363	0.8307	0.8479
75-84	0.8803	0.8869	0.8824	0.8778	0.8622	0.8779
85+	0.9394	0.9399	0.9409	0.9463	0.9386	0.9410
Overall	0.9089	0.9082	0.9045	0.9006	0.8924	0.9029

Table K: Adjustment factors by age, sex and IMD quintile

3.11. Uncertainty analysis: parameter distributions, functions and sources

Table M records the type of distribution and associated functions for each of the input variables in the $IMPACT_{SEC}$ model. We implemented stochastic uncertainty analysis in Excel using Ersatz (version 1.0 available at http://www.epigear.com), an add-in that allows probabilistic bootstrapping in Excel [62]. Ersatz allows repeated random draws from specified distributions for input variables that are used to recalculate iteratively the model. It then calculates the 95% uncertainty intervals from the realised values of the output variable (deaths prevented or postponed). For the $IMPACT_{SEC}$ model, we calculated the uncertainty intervals based on 1000 draws taking the 95% uncertainty intervals as the 2.5^{th} and 97.5^{th} percentiles. Input variables taken from external sources (e.g. case fatality rates, beta coefficients and relative risk reductions) were randomly drawn from specified distributions but assumed constant across deprivation quintiles.

Input parameters	***Type of distribution and functions (Mean, Standard error)***	Source
Population		
Population counts and CHD deaths stratified by age, sex, and Index of Multiple Deprivation quintiles	• Population counts (no error) • Deaths expected in 2007 had CHD mortality rates in 2000 persisted (***Poisson distribution***)	Office for National Statistics
Risk factors		
Prevalence/mean estimates (pooled data; national estimates for 2000 and 2007)	• Continuous variables (Body Mass Index, SBP, total cholesterol, fruit and vegetable consumption): (***Normal distribution***: mean, SE of mean)	Health Survey for England
Beta coefficient: **SBP**	***Normal distribution*** (mean, SE of mean): M < 45 (-0.036,0.004); M 45-54 (-0.035,0.004) M 55-64 (-0.032,0.003); M 65-74 (-0.027,0.003) M 75-84 (-0.021,0.002); M 85+ (-0.016,0.002) F < 55 (-0.046, 0.005); F 55-64 (-0.035,0.004) F 65-74 (-0.032,0.003); F 75-84 (-0.026,0.003)	Prospective studies collaborative meta-analysis (2002) [53]. Parameters on the log scale.

	F 85+ (-0.019,0.002)	
Beta coefficient: **total cholesterol**	***Normal distribution*** (mean, SE of mean): M < 45 (-0.799,0.081); M 45-54 (-0.755,0.077) M 55-64 (-0.446,0.046); M 65-74 (-0.236,0.024) M 75-84 (-0.117,0.012); M 85+ (-0.083,0.009) F < 45 (-0.844,0.086); F 45-54 (-0.734,0.075) F 55-64 (-0.431,0.044); F 65-74 (-0.261,0.027) F 75-84 (-0.174,0.018); F 85+ (-0.051,0.005)	Prospective studies collaborative meta-analysis (2007) [54]. Parameters on the log-scale.
Aspirin Beta blockers ACE Inhibitors Statins Rehabilitation Warfarin	M & F (0.15,0.139) M & F (0.23,0.185) M & F (0.20,0.177) M & F (0.24,0.245) M & F (0.26,0.347) M & F (0.22,0.305)	ATC (2002) [35] Freemantle (1999) [29] Flather (2000) [40] Hulten (2006) [41] Taylor (2004) [43] Anand and Yusuf (1999) [42]
Primary prevention therapies: Statins		
Eligible patients: Population	Population counts (no error)	Office for National Statistics
Treatment uptake	% never having had angina or heart attack and currently taking lipid lowering drugs prescribed by a doctor: (***Beta distribution***: cases, sample-size minus cases)	Health Survey for England
Case fatality rate	Sample size (*n*) = never having had angina or heart attack and currently taking lipid lowering drugs in 2006: ***Beta distribution*** (cases = *n* × CFR estimate, non-cases = *n* – cases)	Wijeysundera et al (2010) [5]
Compliance	***Beta distribution*** (cases = *n* × assumed compliance, non-cases = *n* – cases)	Health Survey for England
Relative risk reduction: Statins	***Ersatz RR function*** (RRR, SE ln(RRR)): M & F (0.35,0.396)	Pignone (2000) [52]
Primary prevention therapies: Treatments for high blood pressure		
Eligible patients:	Population counts (no error)	Office for National Statistics

Population		
Treatment uptake	% never having had angina or heart attack and currently taking medication specifically prescribed to treat high blood pressure: (***Beta distribution***: cases, sample-size minus cases)	Health Survey for England
Case fatality rate	Sample size (n) = never having had angina or heart attack and currently taking medication to lower blood pressure in 2006: ***Beta distribution*** (cases = n × CFR estimate, non-cases = n – cases)	Wijeysundera et al (2010) [5]
Compliance	***Beta distribution*** (cases = n × assumed compliance, non-cases = n – cases)	Health Survey for England
Relative risk reduction: Treatments for high blood pressure	***Ersatz RR function*** (RRR, SE ln(RRR)): M & F (0.13,0.294)	Law (2003) [51]

Table L: Parameter distributions, functions and sources

4 Tables

DPPS through changes in the population						
	England	IMD quintile 1	IMD quintile 2	IMD quintile 3	IMD quintile 4	IMD quintile 5
		Affluent				Deprived
Mean	13253	2093	2666	2608	2742	3143
95% LL	8495	1187	1632	1577	1775	2302
95% UL	17371	2880	3551	3497	3590	3880
DPPS through changes in the treatments uptakes						
	England	IMD quintile 1	IMD quintile 2	IMD quintile 3	IMD quintile 4	IMD quintile 5
		Affluent				Deprived
Mean	7098	1411	1386	1713	1539	1049
95% LL	3479	656	665	800	716	500
95% UL	14195	3069	2811	3819	3141	2135

Table M: CHD deaths prevented or postponed through changes in population and treatment uptakes between 2000 and 2007 in England, stratified by deprivation quintiles.

DPPS through SBP reduction						
Overall						
	England	IMD quintile 1	IMD quintile 2	IMD quintile 3	IMD quintile 4	IMD quintile 5
		Affluent				Deprived
Mean	12960	2218	2579	2729	2736	2698
95% LL	8181	1295	1537	1690	1776	1868
95% UL	17463	3086	3560	3723	3649	3468
Population wide changes						
	England	IMD quintile 1	IMD quintile 2	IMD quintile 3	IMD quintile 4	IMD quintile 5
		Affluent				Deprived
Mean	11162	1861	2168	2321	2391	2421
95% LL	6500	978	1156	1322	1439	1612
95% UL	15093	2616	3024	3163	3190	3121
Anti-hypertension treatment						

	England	IMD quintile 1	IMD quintile 2	IMD quintile 3	IMD quintile 4	IMD quintile 5
		Affluent				Deprived
Mean	1798	357	411	408	345	277
95% LL	675	138	151	150	126	105
95% UL	3860	784	907	898	780	606

Table N: CHD DPPs through medication and population changes in SBP between 2000 and 2007 in England, stratified by deprivation quintiles

DPPS through Cholesterol reduction						
Overall						
	England	**IMD quintile 1**	**IMD quintile 2**	**IMD quintile 3**	**IMD quintile 4**	**IMD quintile 5**
		Affluent				**Deprived**
Mean	7391	1286	1473	1592	1545	1494
95% LL	3851	551	794	700	725	930
95% UL	14493	2900	2819	3669	3161	2579
Population wide changes						
	England	**IMD quintile 1**	**IMD quintile 2**	**IMD quintile 3**	**IMD quintile 4**	**IMD quintile 5**
		Affluent				**Deprived**
Mean	2091	232	498	287	351	722
95% LL	1020	43	282	56	129	496
95% UL	3148	419	709	516	572	944
Dyslipaedimia treatment						
	England	**IMD quintile 1**	**IMD quintile 2**	**IMD quintile 3**	**IMD quintile 4**	**IMD quintile 5**
		Affluent				**Deprived**
Mean	5300	1054	975	1305	1194	772
95% LL	2051	375	359	480	443	279
95% UL	12318	2679	2326	3369	2804	1869

Table O: CHD deaths prevented or postponed through medication and population changes in cholesterol between 2000 and 2007 in England, stratified by deprivation quintiles

5 Tables by gender

5.1. Men

DPPS through changes in the population						
	England	**IMD quintile 1**	**IMD quintile 2**	**IMD quintile 3**	**IMD quintile 4**	**IMD quintile 5**
		Affluent				**Deprived**
Mean	5872	1041	1015	1121	1247	1449
95% LL	3029	495	411	510	675	912
95% UL	8593	1557	1591	1709	1785	1960
DPPS through changes in the treatments uptakes						
	England	**IMD quintile 1**	**IMD quintile 2**	**IMD quintile 3**	**IMD quintile 4**	**IMD quintile 5**
		Affluent				**Deprived**
Mean	3017	474	763	751	596	434
95% LL	1211	187	291	261	218	157
95% UL	7005	1017	1867	2144	1470	1028

Table P: CHD deaths prevented or postponed through medication and population changes in SBP and Cholesterol between 2000 and 2007 in England, stratified by deprivation quintiles

DPPS through SBP reduction						
Overall						
	England	**IMD quintile 1**	**IMD quintile 2**	**IMD quintile 3**	**IMD quintile 4**	**IMD quintile 5**
		Affluent				**Deprived**
Mean	4812	806	941	996	1014	1054
95% LL	2011	265	320	390	463	540
95% UL	7625	1356	1573	1598	1557	1549
Population wide changes						
	England	**IMD quintile 1**	**IMD quintile 2**	**IMD quintile 3**	**IMD quintile 4**	**IMD quintile 5**
		Affluent				**Deprived**
Mean	4106	659	745	850	898	954
95% LL	1416	138	168	269	365	456
95% UL	6713	1165	1304	1414	1419	1442
Anti-hypertension treatment						
	England	**IMD quintile 1**	**IMD quintile 2**	**IMD quintile 3**	**IMD quintile 4**	**IMD quintile 5**
		Affluent				**Deprived**
Mean	705	147	196	146	116	100
95% LL	198	45	46	39	31	30
95% UL	1808	370	528	386	312	247

Table Q: CHD deaths prevented or postponed through medication and population changes in SBP between 2000 and 2007 in England, stratified by deprivation quintiles

DPPS through Cholesterol reduction						
Overall						
	England	**IMD quintile 1**	**IMD quintile 2**	**IMD quintile 3**	**IMD quintile 4**	**IMD quintile 5**
		Affluent				**Deprived**
Mean	4078	709	836	875	829	829
95% LL	2150	400	365	371	414	498
95% UL	8149	1246	1905	2242	1681	1407
Population wide changes						
	England	**IMD quintile 1**	**IMD quintile 2**	**IMD quintile 3**	**IMD quintile 4**	**IMD quintile 5**
		Affluent				**Deprived**
Mean	1766	381	270	271	349	495
95% LL	916	234	99	88	175	311
95% UL	2615	535	442	450	521	675
Statins treatment						
	England	**IMD quintile 1**	**IMD quintile 2**	**IMD quintile 3**	**IMD quintile 4**	**IMD quintile 5**
		Affluent				**Deprived**
Mean	2312	327	566	605	480	334
95% LL	684	85	155	159	130	83
95% UL	6184	861	1648	1992	1351	912

Table R: CHD deaths prevented or postponed through medication and population changes in cholesterol between 2000 and 2007 in England, stratified by deprivation quintiles

5.2. Women

DPPS through changes in the population						
	England	IMD quintile 1	IMD quintile 2	IMD quintile 3	IMD quintile 4	IMD quintile 5
		Affluent				Deprived
Mean	7380	1053	1652	1487	1495	1694
95% LL	3673	341	834	682	730	1062
95% UL	10669	1679	2370	2197	2175	2264
DPPS through changes in the treatments uptakes						
	England	**IMD quintile 1**	**IMD quintile 2**	**IMD quintile 3**	**IMD quintile 4**	**IMD quintile 5**
		Affluent				**Deprived**
Mean	4081	937	623	962	944	615
95% LL	1692	342	261	383	365	246
95% UL	8916	2402	1357	2250	2112	1494

Table S: CHD deaths prevented or postponed through medication and population changes in SBP and Cholesterol between 2000 and 2007 in England, stratified by deprivation quintiles

DPPS through SBP reduction						
Overall						
	England	**IMD quintile 1**	**IMD quintile 2**	**IMD quintile 3**	**IMD quintile 4**	**IMD quintile 5**
		Affluent				**Deprived**
Mean	8149	1412	1638	1733	1722	1644
95% LL	4422	696	822	917	955	1011
95% UL	11540	2064	2366	2475	2420	2218
Population wide changes						
	England	**IMD quintile 1**	**IMD quintile 2**	**IMD quintile 3**	**IMD quintile 4**	**IMD quintile 5**
		Affluent				**Deprived**
Mean	7056	1202	1424	1471	1492	1467
95% LL	3446	513	628	701	745	854
95% UL	10329	1816	2136	2176	2161	2018
Anti-hypertension treatment						
	England	**IMD quintile 1**	**IMD quintile 2**	**IMD quintile 3**	**IMD quintile 4**	**IMD quintile 5**
		Affluent				**Deprived**
Mean	1093	210	215	262	229	177
95% LL	319	63	64	75	65	53
95% UL	2624	510	520	641	575	433

Table T: CHD deaths prevented or postponed through medication and population changes in SBP between 2000 and 2007 in England, stratified by deprivation quintiles

DPPS through Cholesterol reduction						
Overall						
	England	**IMD quintile 1**	**IMD quintile 2**	**IMD quintile 3**	**IMD quintile 4**	**IMD quintile 5**
		Affluent				**Deprived**
Mean	3313	577	637	717	717	665
95% LL	1069	18	298	179	171	304
95% UL	8202	2065	1335	2005	1904	1562
Population wide changes						
	England	**IMD quintile 1**	**IMD quintile 2**	**IMD quintile 3**	**IMD quintile 4**	**IMD quintile 5**
		Affluent				**Deprived**
Mean	325	-149	228	16	2	227
95% LL	-315	-264	99	-123	-134	97
95% UL	996	-31	364	161	144	365
Statins treatment						
	England	**IMD quintile 1**	**IMD quintile 2**	**IMD quintile 3**	**IMD quintile 4**	**IMD quintile 5**
		Affluent				**Deprived**
Mean	2988	727	409	700	714	438
95% LL	922	190	115	197	199	123
95% UL	7822	2203	1095	2009	1905	1323

Table U: CHD deaths prevented or postponed through medication and population changes in cholesterol between 2000 and 2007 in England, stratified by deprivation quintiles

5.3. Percentage difference in men relative to women

DPPS through changes in the population						
	England	**IMD quintile 1**	**IMD quintile 2**	**IMD quintile 3**	**IMD quintile 4**	**IMD quintile 5**
		Affluent				**Deprived**
Mean	13%	-17%	33%	16%	8%	11%
95% LL	-74%	-222%	-35%	-80%	-87%	-49%

95% UL	61%	58%	75%	67%	58%	49%
DPPS through changes in the treatments uptakes						
	England	**IMD quintile 1**	**IMD quintile 2**	**IMD quintile 3**	**IMD quintile 4**	**IMD quintile 5**
		Affluent				**Deprived**
Mean	15%	40%	-43%	6%	26%	19%
95% LL	-101%	-49%	-262%	-165%	-91%	-105%
95% UL	74%	85%	56%	76%	80%	79%

Table V: Percentage difference of DPPs for men relative to women through medication and population changes in SBP and Cholesterol between 2000 and 2007 in England

DPPS through SBP reduction						
Overall						
	England	**IMD quintile 1**	**IMD quintile 2**	**IMD quintile 3**	**IMD quintile 4**	**IMD quintile 5**
		Affluent				**Deprived**
Mean	36%	37%	40%	38%	37%	33%
95% LL	-24%	-32%	-33%	-25%	-20%	-19%
95% UL	75%	80%	79%	77%	74%	68%
Population wide changes						
	England	**IMD quintile 1**	**IMD quintile 2**	**IMD quintile 3**	**IMD quintile 4**	**IMD quintile 5**
		Affluent				**Deprived**
Mean	34%	36%	44%	37%	34%	31%
95% LL	-38%	-47%	-37%	-41%	-37%	-29%
95% UL	80%	89%	88%	81%	76%	70%
Anti-hypertension treatment						
	England	**IMD quintile 1**	**IMD quintile 2**	**IMD quintile 3**	**IMD quintile 4**	**IMD quintile 5**
		Affluent				**Deprived**
Mean	19%	17%	-15%	29%	35%	32%
95% LL	-128%	-145%	-243%	-103%	-90%	-96%
95% UL	81%	79%	77%	85%	87%	84%

Table W: Percentage difference of DPPs for men relative to women through medication and population changes in SBP between 2000 and 2007 in England

DPPS through Cholesterol reduction						
Overall						
	England	**IMD quintile 1**	**IMD quintile 2**	**IMD quintile 3**	**IMD quintile 4**	**IMD quintile 5**
		Affluent				**Deprived**
Mean	-52%	-458%	-48%	-69%	-57%	-40%
95% LL	-273%	-1102%	-246%	-448%	-367%	-180%
95% UL	53%	78%	49%	61%	61%	48%
Population wide changes						
	England	**IMD quintile 1**	**IMD quintile 2**	**IMD quintile 3**	**IMD quintile 4**	**IMD quintile 5**
		Affluent				**Deprived**
Mean	-25%	402%	-35%	1065%	680%	-148%
95% LL	-6102%	215%	-211%	-6121%	-7144%	-436%
95% UL	6040%	1190%	59%	5990%	6646%	-15%
Statins treatment						
	England	**IMD quintile 1**	**IMD quintile 2**	**IMD quintile 3**	**IMD quintile 4**	**IMD quintile 5**
		Affluent				**Deprived**
Mean	5%	42%	-80%	-15%	14%	4%
95% LL	-173%	-84%	-465%	-288%	-160%	-184%
95% UL	79%	91%	65%	79%	84%	84%

Table X: Percentage difference of DPPs for men relative to women through medication and population changes in cholesterol between 2000 and 2007 in England

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