Technical appendix for the Scottish *IMPACT$_{SEC}$* model, 2000-2010

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List of abbreviations:

ACE Inhibitors	Angiotensin-converting enzyme inhibitors
AMI/MI	Acute myocardial infarction
AR	Additive risk-reduction
ARB	Angiotensin receptor blocker
BMI	Body mass index
CABG	Coronary artery bypass graft
CAD	Coronary artery disease
CFR	Case fatality rates
CHD	Coronary heart disease
CMF	Comparative mortality factor
CPR	Cardiopulmonary resuscitation
CR	Combined/cumulative risk-reduction
DG	Disease Group
DPP	Deaths prevented or postponed
GBD	Global burden of disease
GPRD	General practice research database
HES	Hospital episode statistics
HF	Heart failure
HSfE	Health survey for England
ICD	International classification of diseases
IMD	Index of multiple deprivation
ISD	Information Services Division
MINAP	Myocardial ischaemia national audit project
NHANES	National health and nutrition examination survey
NHS	National health service
NSTEACS	Non-ST elevation acute coronary syndrome
NSTEMI	Non-ST elevation myocardial infarction
ONS	Office for National Statistics
OPCS codes	Office of Population Censuses and Surveys classification of surgical operations and procedures (used in HES)
PARF	Population attributable risk fraction
PCI	Percutaneous coronary intervention
PCCIUR	Primary Care Clinical Informatics Unit
PG IIB/IIIA	Platelet glycoprotein IIB/IIIA inhibitors
PTCA	Percutaneous transluminal coronary angioplasty
RR	Relative risk
RRR	Relative risk reduction
SBP	Systolic blood pressure
SE	Standard error
SEC	Socio-economic circumstances
SHeS	Scottish Health Survey
SIMD	Scottish Index of Multiple Deprivation
SMR01	Scottish Morbidity Records database 01
STEMI	ST-elevation myocardial infarction
UA	Unstable angina
WHO	World Health Organization

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

1.1 INTRODUCTION

This technical appendix is based on the technical report for the IMPACT$_{SEC}$ model created using English data.[1] We have adapted their model to create the Scottish IMPACT$_{SEC}$ model. However, much of the theory and methods remain.

IMPACT is a deterministic, cell-based policy model. It uses epidemiological information to estimate the contributions of population-level risk factor changes (impacting mainly on incidence) and changes in the uptake of evidence-based treatments (impacting mainly on case fatality) on mortality decline between two points in time (the start-year and the end-year). The primary outcome measure of the model is the deaths prevented or postponed (DPPs).

The starting point for the model is to calculate the 'target' number of deaths the model needs to explain. This target number is obtained by using death counts recorded in the official registration system to calculate the difference between the actual observed Coronary Heart Disease (CHD) deaths recorded in the end-year and the deaths expected in the end-year had the CHD mortality rates remained the same as in the start-year (i.e. simple direct standardisation).

The calculation of the modelled estimate of DPPs rests on utilising two well-studied relationships: firstly, that between risk factor change and the relative reduction in CHD mortality; secondly, that between treatment uptake and reductions in case-fatality in patients with a specific form of CHD.

The model applies the relative risk reduction quantified in previous randomised controlled trials and meta-analyses to estimate the mortality reduction attributable to:

a) temporal change in risk factor prevalence (in those without diagnosed CHD) to calculate the DPPs 'explained' by specific risk factor trends;

b) net change over the period in the uptake of specific treatments in patients with each specific form of CHD to estimate DPPs 'explained' owing to improved 1-year case fatality rates. Great care is taken to avoid double counting the same individuals.

The mortality benefits from the risk factor reduction in the population, and the treatment benefits in patient groups are then summed. Thus summing uses a cumulative approach (rather than an additive approach), in order to avoid double-counting of benefits in the same individual. (This approach is detailed in Section 1.3).

This mortality sum represents the deaths prevented or postponed (DPPs) 'explained' by the model.

At the end of the modelling process, the total DPPs 'explained' by the model is then compared with the observed fall in deaths (the 'target' to be explained).

Model fit is therefore calculated as the difference between the observed deaths and model DPPs, and expressed as the percentage explained. This measures the extent to

which the model was successful in explaining the observed change in CHD mortality in the population.

A policy model like IMPACT thus stands in contrast to a typical multivariate regression model. A typical multivariate regression model represents a statistical approach to describing a single data-set, for instance generated by a single cohort or randomised controlled trial. In contrast, a policy model such as IMPACT seeks to integrate and synthesise best estimates from a variety of sources to reliably estimate the extent to which a range of factors, acting in combination, explain or predict an outcome. We did not obtain the parameters for this model by running regressions. Rather, the model incorporates the best coefficients from the largest meta-analysis or randomised controlled trials of the reduction in case fatality attributed to treatment or the independent effect sizes of a unit change in each risk factor on CHD mortality.

Examples of the calculation method used for estimating the DPPs due to treatment uptake (Example 1) and for continuous and binary risk factor change (Examples 2 and 3, respectively) are provided below. Earlier versions of the IMPACT mortality model have been previously applied to national data from Europe, United States, Ontario, New Zealand and China.[2-6] The methodology has previously been described in detail online and elsewhere.[3-5]

The IMPACT$_{SEC}$ model

We have now extended the IMPACT model to accommodate sub-national variation in CHD mortality trends by socioeconomic circumstances (IMPACT$_{SEC}$ model). The tables included in this supplementary appendix provide details about the sources and methods that were used in extending the IMPACT model to accommodate socioeconomic circumstances (IMPACT$_{SEC}$ model). We used the Scottish Index of Multiple Deprivation (SIMD) 2009 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 Scotland aged 25 years and over.

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

1.2.1 Changes in mortality rates from CHD, Scotland 2000 to 2010

Data sources used in examining the changes in CHD mortality rates over 2000 to 2010 are shown in Table A. Mortality rates from CHD were calculated using the underlying cause of death (2000: ICD9 410-414 and 429; 2010: ICD10 I20-I25). Both unadjusted and age-adjusted mortality rates were calculated. Rates are standardised to the European Standard Population aged 25+ years using direct standardisation.

1.2.2 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 2010 are shown in Table A. The expected number of CHD deaths in 2010 was calculated by multiplying the age-sex-SIMD quintile specific mortality rates from

CHD in 2000 by the population counts for 2010 in that age-sex-SIMD quintile stratum. Summing over all strata then yielded the expected number of deaths in 2010 had mortality rates remained unchanged. The difference between the number of expected and observed deaths from CHD represented the mortality fall, or the total number of deaths prevented or postponed (DPP), in 2010 relative to 2000. Population counts, CHD mortality rates, observed and expected numbers of deaths are shown in Table E.

1.2.3 Treatment component of IMPACT$_{SEC}$ model

The treatment component of the IMPACT$_{SEC}$ model included nine mutually exclusive CHD patient groups:

- Patients treated in hospital for acute myocardial infarction (ST-elevation myocardial infarction and non-ST elevation acute coronary syndrome)
- Patients admitted to hospital with unstable angina
- Community-dwelling patients who have survived a myocardial infarction since 1981
- Patients who have undergone a revascularisation procedure: Coronary Artery Bypass Grafting (CABG) (since 1981), or a Percutaneous Coronary Intervention (PCI) (since 1989).
- Community-dwelling patients with stable coronary artery disease
- Patients admitted to hospital with heart failure (associated with CHD)
- Community-dwelling patients with heart failure (associated with CHD)
- Hypercholesterolaemic subjects without CHD eligible for cholesterol lowering therapy such as statins
- Hypertensive individuals without CHD eligible for anti-hypertensive therapy

ST-segment and non-ST segment elevation myocardial infarction (STEMI and non-STEMI respectively) patients were examined separately as the management and outcomes of these entities differ markedly[7].

In order to minimise double counting, major efforts were made to ensure that patients counted in each CHD patient group were mutually exclusive. These approaches are detailed later, in Table N.

The data sources used to estimate the size of each treatment group (stratified by age-sex-SIMD quintile) are shown in Table A. For each group, we estimated the number of DPPs that were attributable to various treatments. A list of the treatments considered in the model and the data sources used to estimate the percentage of patients receiving treatments is shown in Table B.

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 SEC, then to multiply the estimated number of patients in 2010 by the proportion of these patients receiving a particular treatment, by the one-year case fatality rate, and by the relative reduction in the case fatality rate due to the administered treatment. Sources for treatment uptake are shown in Table B. Sources for estimates of treatment efficacy (relative risk reductions) are shown in Table F. 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 Table G. Linked hospital admission and death data were used to calculate historical case fatality rates in Scotland where possible. The year 1986 was chosen as baseline as it is before most of the major changes in therapy/diagnosis were brought in and gives the ability to retrospectively exclude pre-existing cases of CHD. Linked data permits individual cases to be followed for 0 to 365 days allowing calculation of rates for the following disease groups: AMI; ACS; and Heart failure in hospital. Further, case fatality rates were calculated using 1995 as the baseline, namely: Post MI and post revascularisation (no MI) (separately for CABG and PTCA). Previously published data[6] was used for the remaining disease groups where Scottish data was not available to calculate rates.

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.

Note that **Examples 1-5** are taken directly from the technical appendix of the English $IMPACT_{SEC}$ model[1] hence use English data and time points (start year 2000, end year 2007) in the calculations.

EXAMPLE 1: Estimation of DPPs from a specific treatment

Mortality fall in STEMI patients as a result of taking aspirin in men aged 55-64 in the most affluent quintile (in England)

For example, in England in 2007, about 1,410 men aged 55-64 in the most affluent quintile were hospitalised with myocardial infarction (ICD10: I21). 40% of these were assumed to be STEMI cases. Uptake of aspirin was estimated to be approximately 99%. Aspirin use reduces case fatality in patients with ST-segment elevation by approximately 23%. The underlying one-year case fatality rate in these men was approximately 6%. The DPPs for at least a year were therefore calculated as:

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

= (1,410 × 40%) × 99% × 23% × 6% ≈ 8 DPPs

This calculation was then repeated:

a) For each age-sex-Index of multiple deprivation (IMD) quintile group (70 in total).
b) Incorporating a Mant and Hicks adjustment[8] for multiple medications within each patient group (see Section 1.4.1).

1.2.4 Risk factor component of $IMPACT_{SEC}$ model

The second part of the $IMPACT_{SEC}$ model estimated the number of DPPs related to changes in cardiovascular risk factor levels in the population. The risk factors considered were cigarette smoking, total cholesterol, systolic blood pressure, body mass index, diabetes and physical inactivity. The Scottish Health Survey was used to calculate trends in the prevalence (or mean values) of each risk factor (Table C). Two approaches to calculating DPPs from changes in risk factors were used: the regression approach and change in the Population Attributable Risk Fraction (PARF). These are illustrated below.

Estimating DPPs from risk factor change – regression approach for continuous risk factors

In the regression approach – used for systolic blood pressure (SBP), total cholesterol and body mass index – the number of CHD deaths in 2000 (the start year) after adjusting for population change between 2000 and 2010 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 (Table I). 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 2010 by sex and SIMD quintile are shown in Table K.

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 (in England)

For example, in 2000, there were 227 CHD deaths among 573,291 women aged 55-64 years in the most affluent quintile in England. The population total had increased to 714,111 in 2007. Applying the CHD death rate from 2000 (39.6 per 1000) 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 2000 mortality rates 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-IMD quintile group.

Data sources for the number of CHD deaths are shown in Table A, the Scottish Health Survey (SHeS) was used to estimate risk factor trends (Table C), and sources for the regression (beta) coefficients used in these analyses are listed in Table I. 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 Table O.

Estimating DPPs from risk factor change – PARF approach for binary risk factors

The PARF approach was used for cigarette smoking, diabetes, and physical inactivity. PARF, which can be interpreted as the proportion by which the mortality rate from CHD would be reduced if the exposure were eliminated,[9] was calculated as:

PARF = [P × (RR - 1)] / [1 + P × (RR - 1)]

Where P is the prevalence of the risk factor and RR is the relative risk for CHD mortality associated with risk factor presence. A relative risk of 3.3 associated with smoking in Scotland, for example, expresses the ratio of risk of CHD mortality in smokers to that in non-smokers. DPPs were then estimated as the expected CHD deaths in 2010 (had 2000 mortality rates remained constant) multiplied by the difference in PARF for 2000 and 2010.

EXAMPLE 3: Estimation of DPPs from risk factor changes using the PARF method

Mortality increase due to increase in diabetes in men aged 65-74 in the most deprived quintile (in England)

For example, the prevalence of diabetes among men aged 65-74 years was 7% in 1998 and 15.7% in 2006. Assuming a relative risk of 1.86, the PARF at the national level for men aged 65-74 was 0.057 in 1998 and 0.119 in 2006.

Using estimates of diabetes prevalence pooled over 1998, 2003, and 2006 survey data (to maximise precision), and the same relative risk value of 1.86, a 'risk factor' gradient was calculated using the ratio of the PARF at the national level to that in each deprivation quintile (See Table O for details of the SEC gradient approach). The risk factor gradient in the PARF in the most deprived quintile was estimated to be 1.38

times higher than the national. The gradient of 1.38 was then applied to the national PARF values in the base and final year of the model (0.057 and 0.119 respectively) to give estimated PARFs of 0.079 (start year) and 0.164 (end year) for men aged 65-74 in the most deprived quintile. The DPPs attributable to the increase in diabetes prevalence was therefore:

DPPs = expected CHD deaths in 2007 (had 2000 mortality rates remained constant) × ($PARF_{2000}$ – $PARF_{2007}$)

DPPs = expected CHD deaths in 2007 (3,583) × (0.079 – 0.164) ≈ -305 DPPs

A negative sign for the DPPs denotes deaths increased or brought-forward due to the increase in diabetes prevalence. The calculation was then repeated for each age-sex-quintile group.

Relative risks estimated by expert working groups for the World Health Organization's Global Burden of Disease 2001 Study were used for smoking and physical activity.[10] Effect estimates were based on systematic reviews of cohort studies (adjusted for regression dilution bias) and meta-analyses of randomised controlled trials. Age-variation in the relative risks for diabetes were taken from the DECODE study.[11] These were then applied to the sex-variation in relative risks estimated by Huxley et al.[12] The published relative risk values for smoking, physical activity and diabetes are shown in Table J. These were adjusted in our study to: a) match the 10-year age bands used in $IMPACT_{SEC}$ and b) employ a dichotomous rather than trichotomous measure of physical activity. Full details on these adjustments are given in Table J.

1.3 CUMULATIVE RISK-REDUCTION: ADJUSTING DEATHS PREVENTED OR POSTPONED (DPPs) TO CALCULATE CUMULATIVE BENEFIT OF MULTIPLE RISK FACTOR CHANGES

1.3.1 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.[13-17]

We do not currently have sources that allow joint estimation of relative risks for combinations of risk factors in this Scottish population. However, several large cohort studies and meta-analyses have published independent risk reduction coefficients for each risk factor included in this study. These are detailed in Tables I and J for continuous and dichotomous risk factors, respectively. One approach commonly used is to calculate the cumulative risk-reduction.[18] 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) =

$1 - ((1-a) \times (1-b) \times (1-c) \times \ldots \times (1-n))$ [1]

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

$CR = 1 - ((1-RSBP) \times (1-Rsmoke) \times (1-Rdiabetes) \times \ldots \times (1-Rn))$

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

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

$AR = (RSBP) + (Rsmoke) + (Rdiabetes) + \ldots\ldots + (Rn)$ [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:

$R_{continuous} = 1 - \exp(\text{beta} \times \text{absolute mean risk factor change})$ [3]

Dichotomous risk factors:

$R_{dichotomous} = PARF \times (\Delta P/P)$ [4]

where $PARF = [P \times (RR - 1)] / [1 + P \times (RR - 1)]$

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 ten year period (2000-2010) 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.

Calculating aggregate change in risk factors over 2000 and 2010

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), ten years apart, 2000 and 2010. We therefore adapted formulas [3] and [4], substituting change over the ten year study period for the estimation of annual average change. We checked our resulting estimates of cumulative risk reduction calculated over ten years against uprating the annual average by a factor of ten. The two sets of estimates were found to be virtually identical.

Regression models to estimate risk factor change, 2000-2010

Formulas [3] and [4] require 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 Scottish Health Survey data, we obtained estimates of risk factor change for each risk factor over 2000-2010 by using the predicted values from regression models. Separate models were fitted by sex and seven ten-year age-bands (14 in total for each risk factor).

Estimates of absolute change in the mean levels of risk factors measured on a continuous scale (blood pressure, total cholesterol, and body mass index) were calculated by linear regression. 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 2010, by age and sex.

Estimates of change in prevalence estimates (smoking, diabetes and physical activity) were calculated using a generalised linear model with binomial distribution and a log link function. The outcome variable was binary (1 indicating risk factor presence; 0 absence) with calendar year as the explanatory variable. The absolute difference in predicted values for 2010 and 2000 (ΔP in formula [4]) divided by the 2000 value provided the estimate of relative change.

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.

Combining risk factors contributing positive and negative benefits to CHD mortality change

In previous CHD modelling studies[14, 15] adjusting for cumulative risk-reduction was straightforward as the trends in smoking, blood pressure and total cholesterol were mostly unidirectional: that is, risk factor levels were falling as were CHD mortality rates. However, in our current modelling study, mean BMI and the prevalence of diabetes increased over 2000-2010 while the four remaining risk factors showed favourable trends. In effect, the impact of risk factor change on CHD mortality was not uniformly beneficial: therefore, the proportional change in CHD mortality attributable to risk factor change was in some cases negative.

In order to avoid positive and negative R values cancelling each other out in the mathematical application of cumulative risk-reduction (formula [1] above), with the perverse effect of the cumulative benefits being apparently greater than the additive in some instances, we first converted all R values into absolute (i.e. sign-free) numbers. We did this on the understanding that the proportional change in CHD mortality associated with risk factor change was independent of the direction of change. This meant that although the R values were not themselves 'true' indicators of the total proportional reduction in CHD mortality, both the additive and cumulative R values were computed on a like-for-like basis. Hence, the ratio of cumulative to additive risk reduction (the adjustment factor) was an accurate reflection of the degree to which the additive benefits needed to be adjusted down.

Age-sex-SIMD specific adjustment factors (70 in total) were calculated by taking the ratio of cumulative to additive risk factor reduction. This involved five steps:

1. Regression equations were fitted to individual level survey data to derive the national predicted risk factor levels for the start and end years of the model. Regression models were fitted separately by sex and ten-year age-bands (from ages 25 to 85+). (See section above describing the regression models fitted on the Scottish Health Survey data to estimate aggregate risk factor change).

2. The national predicted values for 2000 and 2010 were then graduated for increasing deprivation, using the SEC gradient calculated for each risk factor, based on pooled Scottish Health Survey data (see Table O). Multiplying the national predicted values by the SEC gradient resulted in a set of 70 age-sex-SIMD specific estimates for 2000 and 2010, for each risk factor.

3. R values for continuous risk factors were then calculated using estimates of absolute change over 2000-2010 (formula [3]). R values for dichotomous risk factors were calculated by multiplying the estimated PARF in 2000 by the relative

change in prevalence (formula [4]). This resulted in 70 R values (age-sex-SIMD) for each risk factor. All R values were then converted into absolute numbers.

4. The absolute R values were then combined to calculate the additive (AR) and cumulative (CR) risk factor reductions (formulas [1] and [2] respectively). Age-sex-SIMD specific adjustment factors were then calculated using the ratio CR/AR.

5. Multiplying through the age-sex-SIMD specific additive DPPs in the model for each risk factor by the corresponding adjustment factor yielded the estimate of the cumulative benefit of risk factor change to CHD mortality decline over the ten year period, 2000 and 2010.

Adjustment factors by age-sex-SIMD

The adjustment factors (shown in Table D) fell within the range of 0.85 to 0.93. The largest adjustment (0.85) was applied to the DPPs for those resident in the most deprived areas (men aged 55-64 and women aged 45-74 in SIMD5). The adjustments were on average, the same for women and men (0.89); and were higher in IMDQ5 than in IMDQ1 (mean values 0.88 and 0.91, respectively). Hence the adjustment values indicated a larger downward adjustment to the additive DPPs in the most deprived areas relative to the most affluent.

1.4 Other methodological considerations

Other than calculations to take into account change in treatments and risk factors over time, several other adjustments had to be made. These include:

- adjusting the relative reduction in the case fatality rate for persons receiving multiple treatments (poly-pharmacy),
- establishing rules for avoiding double-counting individuals belonging to more than one patient group,
- Assigning emergency AMI patients to either STEMI or nSTEMI patient groups,
- Assigning PCI uptake to either STEMI or nSTEMI,
- overlap between pharmacological and non-pharmacological contribution to risk factor change,
- uncertainty analyses,
- measuring net effects of changes in treatment uptake,
- allocating areas to quintiles by socioeconomic circumstances.

These are discussed in turn below.

1.4.1 Accounting for poly-pharmacy

Persons with or at high risk of developing CHD may take a number of different medications. However, data from randomised clinical trials on efficacy of treatment combinations are sparse. Mant and Hicks suggested a method to estimate case fatality reduction by poly-pharmacy.[8] The adjustment is carried out in a step-by-step manner

as set out in the example below. First the total effect is calculated using an inappropriate additive model, which is then adjusted using effect size calculation with an appropriate multiplicative model.

Example 4: Estimation of reduced benefit if patient taking multiple medications (Mant and Hicks approach)

Adjustment for polypharmacy in secondary prevention post myocardial infarction in men aged 55-64 in the most affluent quintile (in England)

Taking the example of secondary prevention post myocardial infarction, good evidence (Table F) suggests that, for each intervention, the relative reduction in case fatality is approximately: aspirin 15%, beta-blockers 23%, ACE inhibitors (ACE I) 20%, statins 22%, warfarin 22%, and rehabilitation 26%. Our best estimates for uptake were respectively 69%, 59%, 68%, 83%, 3%, and 45%. Assuming a one-year case fatality rate of 0.013 for men aged 55-64 and a total of 15,068 men aged 55-64 residing in the most affluent quintile in 2007 the total DPPs, with no adjustment for poly-pharmacy, would be calculated as shown in the table below:

Secondary prevention post MI	**Numbers**	**Treatment uptake**	**Comp-liance**	**Relative risk reduction**	**One year case fatality**	**Unadjusted DPPs**
Treatment	**A**	**B**	**C**	**D**	**E**	**(A × B × C × D × E)**
Aspirin	15,068	0.69	70%	0.15	0.013	14
Beta blockers	15,068	0.59	70%	0.23	0.013	19
ACE Inhibitors	15,068	0.68	70%	0.20	0.013	19
Statins	15,068	0.83	50%	0.22	0.013	18
Warfarin	15,068	0.03	70%	0.22	0.013	1
Rehabilitation	15,068	0.45	65%	0.26	0.013	15
Total						**85**

The Mant and Hicks approach suggests that in individual patients receiving all these interventions, case fatality reduction is very unlikely to be simply additive. Instead, having considered the 15% case fatality reduction achieved by aspirin, the next medication, in this case a beta-blocker, can only reduce the residual case fatality (1-15%). Likewise, the subsequent addition of an ACE inhibitor can then only decrease the remaining case fatality, which will be 1 – [(1-0.15) × (1-0.23)]. The Mant and Hicks approach therefore suggests that a cumulative relative benefit can be estimated as follows:

Cumulative relative benefit = ***1 – [(1 – (uptake of drug A × relative reduction in case fatality rate for drug A)) × (1 – (uptake of drug B × relative reduction in case fatality rate for drug B)) × …. × (1 – (uptake of drug N × relative reduction in case fatality rate for drug N))]***

In considering appropriate treatments for post MI patients, applying relative risk reductions (RRR) for aspirin, beta-blockers, ACE I, statins, warfarin, and rehabilitation then gives the following cumulative relative benefit (using a weighted average of the age-sex specific uptake figures in each quintile):

$$=1 - [(1 - (\text{aspirin}_{\text{uptake}} \times \text{aspirin}_{\text{RRR}})) \times (1 - (\text{beta blockers}_{\text{uptake}} \times \text{beta blockers}_{\text{RRR}})) \times (1 - (\text{ACE I}_{\text{uptake}} \times \text{ACE I}_{\text{RRR}})) \times (1 - (\text{statins}_{\text{uptake}} \times \text{statins}_{\text{RRR}})) \times (1 - (\text{warfarin}_{\text{uptake}} \times \text{warfarin}_{\text{RRR}})) \times (1 - (\text{rehabilitation}_{\text{uptake}} \times \text{rehabilitation}_{\text{RRR}}))$$

$$= 1 - [(1 - (0.72 \times 0.15)) \times (1 - (0.54 \times 0.23)) \times (1 - (0.63 \times 0.20)) \times (1 - (0.78 \times 0.22)) \times (1 - (0.08 \times 0.22)) \times (1 - (0.45 \times 0.26))]$$

$$= 1 - [(0.89) \times (0.88) \times (0.87) \times (0.81) \times (0.98) \times (0.88)]$$

$$\approx 0.52 \text{ (i.e. a 52\% lower case fatality)}$$

This represented a 24% relative reduction 1-(0.52/0.68) on the simple additive value of 68%, resulting in 24% fewer DPPs out of an original total of 85 DPPs (leaving an adjusted total of 65):

Adjusted DPPs = unadjusted DPPs × (cumulative relative benefit / additive benefit)

Adjusted DPPs = 85 × (0.52/0.68) ≈ 65

All treatment DPPs quoted in the results tables refer to the adjusted DPPs.

1.4.2 Potential overlaps between patient groups: avoiding double counting

There are potential overlaps between CHD patient groups. For example, approximately 30% of myocardial infarction survivors have or will go on to develop heart failure within 12 months. Overlap adjustments between CHD patient groups were made to ensure that the final groups could be considered mutually exclusive. Patient overlaps for 2010 are shown in Figure N.1.

1.4.3 Assigning emergency AMI patients to either STEMI or NSTEMI patient groups

Specific data was not available to distinguish emergency AMI admissions as either STEMI or NSTEMI cases. In the previous use of the $\text{IMPACT}_{\text{SEC}}$ model in England[1] the assumption had been made that 40% of emergency AMI admission would be STEMI and 60% NSTEMI. This assumption was also used in relation to emergency AMI admissions during 2000 in this Scottish $\text{IMPACT}_{\text{SEC}}$ model.

For 2010 data it was possible to make a more informed assumption as to the ratio of STEMI/nSTEMI cases using SMR01 data for the year 2011. New rules introduced by ISD for coding SMR data came in to affect from October 2010. In brief it was dictated that:

1. Unstable angina should be coded as I20.0 (Unstable angina), exactly according to ICD10 rules and conventions.
2. ST elevation myocardial infarction (STEMI) and Non-ST elevation myocardial infarction (NSTEMI) should be coded using the existing structure of the ICD10 codes for MI by adding a 5th digit for use only with codes I21 (Acute myocardial infarction) and I22 (Subsequent myocardial infarction). This is summarised in the table below:

Fifth digit	Meaning of fifth digit for I21.- and I22.- ONLY
0	NSTEMI
1	STEMI
9	MI with no statement of ST elevation or non-elevation

All emergency AMI index events for the year 2011 (ICD code I21) were identified using the same rules as for 2010. In the table below the breakdown in emergency AMI according to the revised coding for the year 2011 is detailed below. Not all coders were using the new coding system. However, the ratio of STEMI/NSTEMI could be estimated; overall the proportion of AMI admissions coded as STEMI= 35%.

Fifth digit coding for 2011 emergency AMI admissions

Total emergency AMI	No fifth digit	MI_ND	NSTEMI	STEMI	STEMI plus NSTEMI	STEMI proportion
7497	2009	596	3158	1734	4892	0.35

The table below details age group and gender specific proportions of STEMI/NSTEMI patients estimated for 2011. These were then applied to the corresponding emergency AMI groups for 2010 to apportion the divide in cases.

Using just the AMIs coded for STEMI and NSTEMI to give age/gender splits for STEMI/NSTEMI in 2010 combine this with emergency AMIs

	Number of NSTEMI and STEMI (n)	Proportion NSTEMI	Proportion STEMI
All	4892	0.65	0.35
Men	3012	0.62	0.38
Women	1879	0.68	0.32
M25-34	18	0.06	0.94
M35-44	162	0.53	0.47
M45-54	561	0.51	0.49
M55-64	788	0.56	0.44
M65-74	678	0.68	0.32
M75-84	601	0.72	0.28
M85+	204	0.81	0.19

W25-34	4	0.50	0.50
W35-44	47	0.51	0.49
W45-54	177	0.63	0.37
W55-64	283	0.59	0.41
W65-74	430	0.66	0.34
W75-84	569	0.72	0.28
W85+	370	0.76	0.24

1.4.4 Assigning PCI uptake to either STEMI or NSTEMI

In the previous use of the $IMPACT_{SEC}$ model in England[1] the assumption was made that the uptake of PCI for AMI was exclusively for STEMI cases. The uptake of PCI for UA was also used as a proxy for the combined uptake of PCI by UA and nSTEMI cases (nSTEACS). This assumption was utilised for 2000 data in this Scottish $IMPACT_{SEC}$ model.

For the 2010 data it was decided that this assumption was no longer appropriate. By 2010 the use of PCI had increased dramatically in Scotland and is the treatment of choice (where appropriate) for all AMI cases (not just STEMI cases). SMR01 data for 2011 was used to estimate the proportional uptake of PCI by STEMI and NSTEMI cases to guide the apportioning of the PCI uptake by each disease group in 2010. This data was stratified by age group and gender.

Table below shows those coded as STEMI and NSTEMI 2011 the proportion with PCI:

	NSTEMI /STEMI	NSTEMI	STEMI	PCI NSTEMI /STEMI	PCI NSTEMI	PCI STEMI
All	4892	0.65	0.35	1288	0.16	0.84
Men	3012	0.62	0.38	923	0.17	0.83
Women	1879	0.68	0.32	365	0.14	0.86
M25-34	18	0.06	0.94	12	0.00	1.00
M35-44	162	0.53	0.47	75	0.19	0.81
M45-54	561	0.51	0.49	245	0.14	0.86
M55-64	788	0.56	0.44	290	0.16	0.84
M65-74	678	0.68	0.32	168	0.21	0.79
M75-84	601	0.72	0.28	118	0.18	0.82
M85+	204	0.81	0.19	15	0.13	0.87
W25-34	4	0.50	0.50	2	0.50	0.50
W35-44	47	0.51	0.49	16	0.06	0.94
W45-54	177	0.63	0.37	57	0.21	0.79
W55-64	283	0.59	0.41	82	0.09	0.91
W65-74	430	0.66	0.34	98	0.12	0.88
W75-84	569	0.72	0.28	89	0.18	0.82
W85+	370	0.76	0.24	21	0.10	0.90

1.4.5 Overlap between pharmacological and non-pharmacological contributions to risk factor DPPs

Risk factor improvements, such as lower blood pressure or 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.

1.4.6 Net effects

As all treatments were in use in 2000, the net benefit of an intervention in 2010 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 2010 uptake rates. This is illustrated in the example below.

EXAMPLE 5: Net effects for treatments

Calculating net effects for clopidogrel use in STEMI cases in men aged 75-84 in the most affluent quintile (in England)

With an estimated total of 1,440 men aged 75-84 in the most affluent quintile (of whom 40% were assumed to be STEMI cases), 89% uptake, a relative risk reduction of 3%, a one-year case fatality rate of 34%, and 100% compliance, the total number of DPPs in 2007 was calculated as:

Patient numbers × treatment uptake$_{2007}$ × relative mortality reduction × one year case fatality

= (1,440 × 40%) × **89**% × 3% × 34% ≈ 5 DPPs

Applying the uptake rate in 2000 (31%) gave a total of 2 DPPs:

Patient numbers × treatment uptake$_{2000}$ × relative mortality reduction × one year case fatality

= (1440 × 40%) × **31**% × 3% × 34% ≈ 2 DPPs

The net DPPs were therefore:

Net DPPs = DPPs using uptake$_{2007}$ – DPPs using uptake$_{2000}$
= 5 –2 = 3

The estimated changes in treatment uptake between 2000 and 2010 by deprivation quintile are shown in Table H.

In a small number of cases, "negative" DPPs were apparently generated reflecting a decrease in treatment uptake or numbers. For instance with CPR in hospital (fewer number of arrests requiring resuscitation) and thrombolysis treatments (a larger proportion receiving angioplasty instead of thrombolysis). These negatives were mostly trivial, and were zeroed to reflect the reality: harmful treatments were not being administered. This approach was applied only to disease group (DG) 1 (STEMI) in relation to in-hospital CPR and treatment using thrombolysis and disease group 2 (NSTEACS) in relation to in-hospital CPR and treatment using aspirin but no heparin. The effects of zeroing the negatives on the DPPs for DG1 and DG2 are illustrated in the tables below. It was considered unnecessary to correct the very minor negative DPPs associated with three treatments in the DG4 and DG5 community groups.

Original DPPs for disease groups one and two before zeroing of negative DPPS for selected treatments

	NET DPPs	SIMDQ1	SIMDQ2	SIMDQ3	SIMDQ4	SIMDQ5
INITIAL TREATMENTS FOR ACUTE MI (DG1) - STEMI						
Community CPR	2	0	1	0	1	1
Hospital CPR (STEMI)	-27	-3	-4	-6	-7	-7
Thrombolysis	-27	-4	-4	-5	-6	-7
Aspirin	4	1	1	1	1	1
Beta blockers	0	0	0	0	0	0
ACE inhibitors/ARB	0	0	0	0	0	0
PPCI	90	16	18	18	19	19
CABG	0	0	0	0	0	0
Clopidogrel	12	2	2	2	3	2
Sum (2010)	**54**	**12**	**12**	**9**	**11**	**10**
NSTEACS (DG2)						
Hospital CPR (NSTEMI)	-37	-5	-7	-8	-9	-9
Aspirin & heparin	40	5	8	7	8	11
Aspirin alone (without heparin)	-13	-1	-3	-2	-3	-4
PG IIA/IIIB	0	0	0	0	0	0
CABG surgery (within 7 days)	0	0	0	0	0	0
PTCA (within 7 days)	7	1	2	1	1	2
ACE inhibitors/ARB	5	1	1	1	1	1
Beta blockers	3	0	1	1	1	1
Clopidogrel	23	4	5	5	5	5
Sum (2010)	**27**	**4**	**6**	**5**	**5**	**7**

Treatments affected by zeroing of negative DPPS are shaded in grey

DPPs for disease groups one and two after zeroing of negative DPPS for selected treatments

	NET DPPs	SIMDQ1	SIMDQ2	SIMDQ3	SIMDQ4	SIMDQ5
INITIAL TREATMENTS FOR ACUTE MI (DG1) - STEMI						
Community CPR	2	0	1	0	1	1
Hospital CPR (STEMI)	0	0	0	0	0	0
Thrombolysis	0	0	0	0	0	0
Aspirin	4	1	1	1	1	1
Beta blockers	0	0	0	0	0	0
ACE inhibitors/ARB	0	0	0	0	0	0
PPCI	90	16	18	18	19	19
CABG	0	0	0	0	0	0
Clopidogrel	12	2	2	2	3	2
Sum (2010)	**108**	**19**	**21**	**21**	**23**	**24**
NSTEACS (DG2)						
Hospital CPR (NSTEMI)	0	0	0	0	0	0
Aspirin & heparin	40	5	8	7	8	11
Aspirin alone (without heparin)	0	0	0	0	0	0
PG IIA/IIIB	0	0	0	0	0	0
CABG surgery (within 7 days)	0	0	0	0	0	0
PTCA (within 7 days)	7	1	2	1	1	2
ACE inhibitors/ARB	5	1	1	1	1	1
Beta blockers	3	0	1	1	1	1
Clopidogrel	23	4	5	5	5	5
Sum (2010)	**78**	**10**	**16**	**15**	**17**	**20**

Treatments affected by zeroing of negative DPPS are shaded in grey

1.4.7 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 $IMPACT_{SEC}$ model, we calculated the uncertainty intervals based on 1000 draws – taking the 95% uncertainty intervals from the 2.5th and 97.5th 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.

1.4.8 Model fit

Overall, the model could not explain 19% of the total deaths prevented (i.e. a shortfall of about 1000 CHD deaths unexplained by the model). However, the percentage unexplained varied by age, sex and socio-economic circumstances. These are shown in Tables L.1- L.4 and Figure L.1.

1.4.9 Allocating areas to socioeconomic quintiles using Scottish Index of Multiple Deprivation, 2009

The Scottish Index of Multiple Deprivation (SIMD) identifies small area concentrations of multiple deprivation across all of Scotland and is based on seven domains, income; employment; health; education, skills and training; housing; geographical access to services; and crime. The overall SIMD 2009v2 utilises data based principally on 2008

with population data from 2007 [19]. The SIMD is presented at data zone level, enabling small pockets of deprivation to be identified. The data zones, which have a median population size of 769, are ranked from most deprived (1) to least deprived (6,505). The datazones were grouped into equal quintiles representing 20% of the population with quintile one (SIMDQ1) including the most affluent and quintile five (SIMDQ5) the most deprived areas. The result is a comprehensive picture of relative area deprivation across Scotland. SIMD is essentially identical / very similar to Index of multiple deprivation (IMD) successfully used in the English $IMPACT_{SEC}$ project.[1] Based on their postcode of residence, patients treated in hospital (e.g. SMR01) or in the community (e.g. PCCIUR) were matched via their area of residence to the corresponding deprivation quintile by the data providers to protect patient anonymity. The PCCIUR dataset does not have individual level SIMD information available therefore quintiles of individual 2001 Carstairs index were substituted.[20] SIMD quintiles were assigned to population and mortality data using look-up files based on datazone. Similarly anonymous look-up files for SIMD quintiles were provided by Scotcen[21] to enable assignment of SIMD quintiles to the Scottish Heath Survey datasets obtained from the University of Essex Research Repository. It was not possible to obtain information stratified by any measure of deprivation for the following datasets: 2008 Health Improvement Scotland Heart Failure audit and the 2010/2011 Health Improvement Scotland Cardiac Rehabilitation Audit.

The health domain of SIMD includes an indicator of the Comparative Mortality Factor (CMF) and so includes number of deaths in the period under examination. Describing deprivation by a measure that includes this domain may be thought of as tautological since the outcome we are analysing is CHD deaths. 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.[22] Conceptually, the SIMD 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'.

Table A. Population and patient data sources used in the IMPACT$_{SEC}$ model

Data by gender age and SIMD quintile unless stated

Information	Source
Population data	
Population: counts by age, sex and SIMD	National Records of Scotland (NRS)
Deaths: counts by age, sex and SIMD	(2000 and 2010: ICD10 I20-I25)
Number of patients admitted to hospital	
Myocardial infarction (MI) STEMI nSTEMI	Information Services Division (ISD) – linked SMR01[b] and death record dataset Emergency admissions with a primary diagnosis of MI (ICD10: I21) 2000: the ratio of MI admissions to STEMI and nSTEMI cases taken as 40/60[23] 2010: the age-gender specific ratios of STEMI to NSTEMI in 2011 were used to inform the split (see section 1.4.8)
Angina pectoris	ISD - linked SMR01[b] and death record dataset Emergency admissions with a primary diagnosis of angina pectoris (ICD10: I20)
Heart failure (non CHD excluded)	ISD - linked SMR01[b] and death record dataset Admissions with a primary diagnosis of heart failure (ICD10: I50); restrict to those with heart failure due to CHD (coded in prior record, or as a co-morbidity (ICD-10 I20-I25))
Number of patients undergoing revascularisation	
CABG	ISD - linked SMR01 and death record dataset OPCS Classification of Surgical Operations and Procedures (4th Revision) (OPCS-4) K40-K46 and (OPCS-3) 3043
PCI	ISD - linked SMR01 and death record dataset OPCS Classification of Surgical Operations and Procedures – Fourth Revision (OPCS-4) OPCS K49, K50.1, K508.8, K75 (No OPCS-3)
Patients in the community eligible for secondary prevention therapies	
Post MI (eligible for cardiac rehabilitation)	ISD - Linked SMR01[c] and death record dataset
Angina without MI[a]	Primary Care Clinical Informatics Unit (PCCIUR)
Heart failure[a]	Primary Care Clinical Informatics Unit (PCCIUR)
CABG/PCI survivors (eligible for cardiac rehabilitation)	ISD - Linked SMR01[c] and death record dataset

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*	Scottish Health Survey 1998, 2003, 2010 (2008, 2009 and 2010 combined)
Hypertension treatment *Prevalence of never having had angina or heart attack and currently taking medication specifically prescribed to treat high blood pressure*	Scottish Health Survey 1998, 2003, 2010 (2008, 2009 and 2010 combined)

[a] Individual Carstairs scores[20] used to assign deprivation quintiles in 2000 and 2010 as SIMD unavailable
[b] SMR01 linked dataset extracted in March 2013
[c] Data only available for 2004-2010

Table B. Data sources for treatment uptake levels

Medical treatments included in the model. All data stratified by gender, age group and SIMD quintile unless stated.

Information	Source
Medication use in hospital (ST-segment elevation myocardial infarction)	
Aspirin Beta Blockers ACE I or Angiotensin-II receptor antagonists (ARB) Thrombolysis Clopidogrel	MINAP 2003 to 2007[a]
Non-ST-segment elevation acute coronary syndrome (NSTEACS)	
Aspirin without heparin Aspirin & heparin Platelet glycoprotein IIB/IIIA inhibitors Beta Blockers ACE I/ARB Clopidogrel	MINAP 2003 to 2007[a]
Heart failure due to CHD	
Aspirin[b] Beta blockers ACE I/ARB Spironolactone	Health Improvement Scotland Audit HF[b]
In-hospital cardio-pulmonary resuscitation (CPR)	MINAP 2003 to 2007
CPR in the community	HeartStart (Scotland) Register annual data 2000 to 2007
Cardiac rehabilitation for MI & revascularisation survivors (2006-2010 survivors only)	2010-2011 (financial year): Health Improvement[c] Scotland Audit CR (ISD website) 2000: not available[d] *Estimates are for completion of rehabilitation program*
Medication use in the community: Post MI and revascularisation survivors, chronic stable coronary artery disease (CAD), heart failure	
Aspirin Beta blockers ACE I/ARB Statins Warfarin Spironolactone	Primary Care Clinical Informatics Unit (PCCIUR)[e]
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*	Scottish Health Survey 1998, 2003, 2010 (2008, 2009 and 2010 combined)
Anti-hypertensive medication **Hypertension treatment** *Prevalence of never having had angina or heart attack and currently taking medication specifically prescribed to treat high blood pressure*	Scottish Health Survey 1998, 2003, 2010 (2008, 2009 and 2010 combined)

[a] Data stratified by IMD, age and sex (English data)
[b] Assumed equal to HF with CHD rates in the community obtained from PCCIUR
[c] Data not stratified by deprivation quintile
[d] Estimate not available so based on ratio approach and literature
[e] Individual Carstairs scores[20] used to assign deprivation quintiles in 2000 as SIMD unavailable

Table C. Risk factors – variable definitions and source

The Scottish Health Survey (SHeS) is a cross-sectional, nationally representative survey reporting the health and health-related behaviours (with emphasis on cardiovascular disease) of people living in private households in Scotland.[24] Surveys have been conducted in 1995, 1998, 2003 and since 2008 they have been repeated yearly as part of a continuous survey until 2012. Samples are selected using a multi-stage stratified clustered probability sampling design. Data are collected during two household visits; first by an interviewer (face-to-face interviews) then by a nurse.

During the face-to-face interviews current cigarette smoking status, physical activity behaviour and self-reported diabetes are ascertained. Compliance to the physical activity recommendations ≥5 occasions/week of at least moderate activity (for a total of at least thirty minutes per day) is recorded. Contributing activities included those performed at home (housework, gardening, DIY etc) and at work, as well as sport, exercise and walking. Activities performed for longer than fifteen minutes contributed to the total. Self-reported diabetes is recorded only if a doctor had informed respondents of the diagnosis. This was irrespective of treatment and was excluded if associated with pregnancy (no blood samples were taken for glucose in the SHeS). The interviewers also obtained weight and height measurements. Bodyweight is measured to the nearest 100g using electronic scales, an estimate is requested from respondents that exceeded the scales' upper limit of 130kg. Height is measured to the nearest millimetre using a stadiometer.

During the nurse visit blood pressure measurements, details of prescription drug use for hypertension, details of lipid lowering drugs and non-fasting venous blood samples were taken. Blood pressure readings were taken three times using an automated device with the informant in a seated position, after a five-minute rest. Readings were taken from participants that had not eaten, smoked, drunk alcohol or taken vigorous exercise in the 30 minutes preceding measurement. The 1995 and 1998 surveys employed Dinamap 8100 monitors (Critikon, USA) while from 2003 Omron HEM 907 devices (Omron Healthcare, Japan) were used. Regression equations generated from a calibration study are available to derive predicted Omron readings from Dinamap readings. The same laboratory conducted all blood sample analyses (except 1995). Total cholesterol serum concentration was determined by a cholesterol oxidase assay.

We used all available surveys from 1998 to 2010 within gender stratified generalised linear models to produce point estimates for both 2000 and 2010 for the six risk factors. The 1995 survey was not used due to missing or non compatible variables, a more limited age range plus the time period focused on is 2000 to 2010 – 1995 is outside this and should not be allowed to have undue influence.

For the categorical risk factors (smoking, diabetes and physical activity) a generalised linear model with binomial distribution and a logit link function was employed. The outcome variable was binary (1 indicating risk factor presence; 0 absence) with calendar year and age group (10 year bands) as explanatory variables. Interaction

between year and age group were investigated as well as transformations of year (e.g. quadratic term for year). In the case of physical activity amongst women there was a significant interaction between year and age group and this was included in the prediction model. For the continuous risk factors (BMI, SBP and cholesterol) a generalised linear model with normal distribution and an identity link function was utilised. The dependent variable was the risk-factor level for each survey respondent; calendar year (i.e. year of survey) and age group (10 year bands) were the explanatory variables. There were significant interactions between age and year for all genders and risk factors so this was included in the model. Additionally for cholesterol a quadratic term for calendar year significantly improved the model for both genders and this was also included in the model.

The magnitude of risk factor change from 2000 to 2010 used for the calculation of DPPs (see Examples 2 and 3) was estimated using a 'fixed gradient' approach across deprivation quintiles to maximise precision. All surveys were pooled to enable stratification by age, sex and SIMD quintile (70 groups) to obtain the fixed socioeconomic gradient; for details on this approach see Table O.

SHeS data was accessed from the Essex archive. Anonymous look up files for SIMD quintiles were provided by Scotcen.

Risk factor	SHeS survey years	Description
Current cigarette smoking	1998, 2003, (2008, 2009, 2010)[a]	Self-reported status
SBP (mmHg)	1998, 2003, (2008, 2009, 2010)[a]	Mean of second and third readings of participants that had not eaten, smoked, drunk alcohol or taken vigorous exercise in the 30mins preceding measurement.
Body Mass Index	1998, 2003, (2008, 2009, 2010)[a]	Valid height and weight measurements
Total cholesterol (mmol/l)	1998, 2003, (2008, 2009, 2010)[a]	Those reporting taking lipid lowering drugs were included
Diabetes	1998, 2003, (2008, 2009, 2010)[a]	If a doctor had informed respondents of the diagnosis, irrespective of treatment and was excluded if associated with pregnancy.
Physical inactivity	1998, 2003, (2008, 2009, 2010)[a]	≥5 occasions/week of at least moderate activity (for a total of at least 30mins per day). Contributing activities included those performed at home (housework, gardening, DIY etc) and at work, as well as sport, exercise and walking. Activities performed for longer than fifteen minutes contributed to the total.

[a] 2008, 2009 and 2010 combined

Table D. Cumulative benefit: Adjustment factors by age, sex and SIMD quintile

The DPPs were adjusted down in an additive fashion over the six risk factors by using the ratio of cumulative to additive risk-reduction (section 1.3). The 70 age-sex-SIMD specific adjustment factors are shown below.

	Deprivation quintile					
	SIMDQ1	**SIMDQ2**	**SIMDQ3**	**SIMDQ4**	**SIMDQ5**	**Scotland**
Men:						
25-34	0.8775	0.8793	0.8604	0.8700	0.8691	0.8703
35-44	0.8845	0.8809	0.8766	0.8626	0.8748	0.8749
45-54	0.9171	0.9064	0.8993	0.8984	0.8877	0.9010
55-64	0.8902	0.8751	0.8688	0.8664	0.8542	0.8702
65-74	0.9098	0.9039	0.8992	0.8906	0.8887	0.8982
75-84	0.8902	0.8828	0.8865	0.8846	0.8764	0.8847
85+	0.9227	0.8974	0.9033	0.9209	0.9057	0.9094
Women:						
25-34	0.9077	0.9034	0.9028	0.8868	0.8877	0.8960
35-44	0.9323	0.9232	0.9085	0.9127	0.8990	0.9140
45-54	0.8958	0.8880	0.8663	0.8626	0.8535	0.8715
55-64	0.8950	0.8901	0.8716	0.8715	0.8543	0.8751
65-74	0.8773	0.8751	0.8630	0.8571	0.8493	0.8634
75-84	0.8869	0.8855	0.8866	0.8750	0.8678	0.8802
85+	0.9316	0.9329	0.9205	0.9215	0.9139	0.9233
Overall	0.9013	0.8946	0.8867	0.8843	0.8773	0.8749

Table E. CHD mortality rates 2000 and 2010 by sex and deprivation quintiles

	Year	Scotland	SIMD Q1	SIMD Q2	SIMD Q3	SIMD Q4	SIMD Q5
Male							
Population	**2000**	1645868	326354	322654	333889	336500	326471
	2010	1745130	352118	364751	361232	346602	320427
Observed CHD deaths	**2000**	6464	799	1013	1356	1519	1777
	2010	4529	623	785	909	1079	1133
Age-standardised rates (per 100,000)[a]	**2000**	363	252	293	364	393	494
	2010	210	139	169	197	253	313
Annual % fall[b]		5.3	5.8	5.4	5.9	4.3	4.5
Expected deaths[c]	**2010**	7603	1119	1348	1653	1684	1799
Target DPPs[d]	**2010**	3074	496	563	744	605	666
% of expected deaths prevented	**2010**	40.4	44.3	41.8	45.0	35.9	37.0
Female							
Population	**2000**	1870132	358808	355786	371914	390437	393187
	2010	1940414	383671	396873	394327	390188	375355
Observed CHD deaths	**2000**	5796	754	952	1207	1408	1475
	2010	3513	514	632	670	841	856
Age-standardised rates (per 100,000)[a]	**2000**	185	129	155	186	201	239
	2010	99	69	81	91	118	141
Annual % fall[b]		6.0	6.0	6.3	6.9	5.2	5.1
Expected deaths[c]	**2010**	6210	923	1128	1317	1423	1419
Target DPPs[d]	**2010**	2697	409	496	647	582	563
% of expected deaths prevented	**2010**	43.4	44.3	44.0	49.1	40.9	39.7
Total							
Population	**2000**	3516000	685162	678440	705803	726937	719658
	2010	3685544	735789	761624	755559	736790	695782
Observed CHD deaths	**2000**	12260	1553	1965	2563	2927	3252
	2010	8042	1137	1417	1579	1920	1989
Age-standardised rates (per 100,000)[a]	**2000**	262	181	215	263	283	349
	2010	148	100	120	137	177	217
Annual % fall[b]		5.5	5.8	5.7	6.3	4.6	4.6
Expected deaths[c]	**2010**	13813	2042	2476	2971	3107	3218
Total DPPs[d]	**2010**	5771	905	1059	1392	1187	1229
% of expected deaths prevented	**2010**	41.8	44.3	42.8	46.9	38.2	38.2

[a] Rates are standardised to the European Standard Population aged 25+ years
[b] Annual % fall = (1-(2010 rate/2000 rate)^(1/10))
[c] Expected deaths = CHD deaths expected in 2010 had 2000 CHD rates remained.
[d] DPPs, deaths prevented or postponed. DPPs = expected – observed deaths in 2010

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

Treatments	Relative risk reduction[a]	Comments	Source paper: First author (year) [ref list], notes
ST elevation myocardial infarction (STEMI):			
Thrombolysis	31% (95% CI: 14,45)	<55 years: Odds Ratio (OR)=0.692; Relative Risk Reduction (RRR)=30.8% (95% CI: 14,45) 55-64 years: OR=0.736; RRR=26.4% (95% CI: 17,40) 65-74 years: OR=0.752; RRR=24.8% (95% CI: 15,37) > 75 years: OR=0.844; RRR=15.6% (95% CI: 4,30)	Estess (2002)[25]
Aspirin	23% (95% CI: 15,30)	RRR=23% (95% CI: 15,30): outcome is vascular deaths	ISIS-2 (1988)[26]
Primary CABG surgery	39% (95% CI: 23,52)	OR=0.61 (95% CI: 0.48,0.77); RRR=39% (95% CI: 23,52) on page 565, 0-5 year mortality	Yusuf (1994)[27]
Primary PCI	30% (95% CI: 15,42)	OR=0.70 (95% CI: 0.58,0.85); RRR=30% (95% CI: 15,42) outcome compares primary angioplasty to thrombolytics.	Keeley (2003)[28]
Beta blockers	4% (95% CI: -8,15)	OR=0.96 (95% CI: 0.85,1.08); RRR=4% (95% CI: -8,15) on page 1732	Freemantle (1999)[29]
ACE inhibitors	7% (95% CI: 2,11)	OR=0.93 (95% CI: 0.89,0.98); RRR=7% (95% CI: 2,11) for 30 day mortality in myocardial infarction	ACE Inhibitor Myocardial Infarction Collaborative Group (1998)[30]
Clopidogrel	3% (95% CI: 1,6)	RRR=3% (95% CI: 1,6) for 30 day mortality in myocardial infarction	Chen (2005)[31] Sabatine (2005)[32]
Hospital CPR	33% (95% CI: 10,36)	Survival at 24 hours estimated to be 32%, discharge to home at 21%, and 1 year survival to be 15% overall.	Tunstall-Pedoe (1992)[33] Nadkarni (2006)[34]
Non-ST-segment elevation acute coronary syndrome (NSTEACS):			
Aspirin alone	15% (95% CI: 11,19)	OR=0.85 (95% CI: 0.49,0.95); RRR=15% (95% CI: 11,19). Outcome is vascular and nonvascular deaths on page 75. Assume appropriate for patients with NSTE-ACS.	Antithrombotic Trialists' Collaboration (2002)[35]

Aspirin & heparin	33% (95% CI: -2,56)	OR=0.67 (95% CI: 0.48,1.02); RRR=33% (95% CI: -2,56%) in Table 2. The study outcome is composite MI death and non-fatal MI; compares those on aspirin & heparin to aspirin only.	Oler (1996)[36]
Platelet glycoprotein IIB/IIA inhibitors	9% (95% CI: 2,16)	OR=0.91 (95% CI: 0.84,0.98); RRR=9% (95% CI: 2,16). Study looked at acute coronary syndrome without persistent ST elevation.	Boersma (2002)[37]
Early PCI	32% (95% CI: 5,51)	OR=0.68 (95% CI: 0.49,0.95); RRR=32% (95% CI: 5,51)	Fox (2005)[38]
Primary CABG surgery	39% (95% CI: 23,52)	OR=0.61 (95% CI: 0.48,0.77); RRR=39% (95% CI: 23,52) on page 565, 0-5 year mortality	Yusuf (1994)[27] Assumed similar as STEMI
Clopidogrel	7% (95% CI: 2,11)	RRR=7% (95% CI: 2,11)	Yusuf (2001)[39]
Beta blockers	4% (95% CI: -8,15)	OR=0.96 (95% CI: 0.85,1.08); RRR=4% (95% CI: -8,15) on page 1732	Freemantle (1999)[29] Assumed similar as STEMI
ACE inhibitors	7% (95% CI: 2,11)	OR=0.93 (95% CI: 0.89,0.98); RRR=7% (95% CI: 2,11) for 30 day mortality in myocardial infarction	ACE Inhibitor Myocardial Infarction Collaborative Group (1998)[30]
Secondary prevention post myocardial infarction / revascularisation:			
Aspirin	15% (95% CI: 11,19)	OR=0.85 (95% CI: 0.49,0.95); RRR=15% (95% CI: 11,19). Outcome is vascular and nonvascular deaths on page 75. This data seems to be appropriate to this outcome in CHD patients.	Antithrombotic Trialists' Collaboration (2002)[35]
Beta blockers	23% (95% CI: 15,31)	OR=0.77 (95% CI: 0.69,0.85); RRR=23% (95% CI: 15,31) on page 1734. Odds of death in long term trials.	Freemantle (1999)[29]
ACE inhibitors or Angiotensin-II receptor antagonists	20% (95% CI: 13,26)	OR=0.80 (95% CI: 0.74,0.87); RRR=20% (95% CI: 13,26) on page 1577, death up to four years [endpoint of study looking at those with heart failure or LV dysfunction].	Flather (2000)[40]
Statins	24% (95% CI: 10,26)	RRR=24% (95% CI: 10,26) Intensive statin therapy in acute coronary syndromes.	Hulten (2006)[41]
Warfarin	22% (95% CI: 13,31)	OR=0.78 (95% CI: 0.67,0.90); RRR=22% (95% CI: 10,33)	Anand and Yusuf (1999)[42]

Rehabilitation	26% (95% CI: 10,39)	OR=0.74 (95% CI: 0.61,0.90); RRR=26% (95% CI: 10,39) in Figure 1, page 685 Taylor reference	Taylor (2004)[43]
Chronic stable coronary artery disease:			
CABG surgery years 0-5	39% (95% CI:23,52)	OR = 0.61 (95% CI: 0.48-0.77), RRR 39% (95% CI: 23,52) on page 565, 5 year mortality	Yusuf (1994)[27]
CABG surgery years 6-10	32% (95% CI: 2,30)	OR = 0.83 (95% CI: 0.70-0.98), RRR 17% (95% CI: 2,30) on page 565, 10 year mortality. OR = 0.68 (95% CI: 0.56-0.83), RRR 32% (95% CI: 17,44) on page 565, 7 year mortality CABG compared to medical treatment	Yusuf (1994)[27]
Angioplasty	No effect		Boden (2007)[44]
Aspirin	15% (95% CI: 11,19)	OR=0.85 (95% CI: 0.49-0.95); RRR=15% (95% CI: 11,19). Outcome is vascular and nonvascular deaths on page 75.	Antithrombotic Trialists' Collaboration (2002)[35]
Statins	23% (95% CI: 10,26)	RRR=23% (95% CI 10,26) Standard dose statin therapy in coronary artery disease.	Wilt (2004)[45]
ACE inhibitors/ARB	17% (95% CI: 6,28)	RRR=17% (95% CI 6,28)	Al-Mallah (2006)[46]
Heart failure in patients requiring hospitalisation or in the community:			
ACE inhibitors	20% (95% CI: 13,26)	OR=0.80 (95% CI: 0.74,0.87); RRR=20% (95% CI: 13,26) on page 1577 [death up to four years was study endpoint for those with heart failure or LV dysfunction]	Flather (2000)[40]
Beta blockers	35% (95% CI: 26,43)	OR=0.65 (95% CI: 0.57,0.74); RRR=35% (95% CI: 26,43): all cause mortality	Shibata (2001)[47]
Spironolactone	30% (95% CI: 18,41) 31% (95% CI: 18,42)	OR=0.70 (95% CI: 0.59,0.82); RRR=30% (95% CI: 18,41) in those that had at least one cardiac related hospitalisation. OR=0.69 (95% CI: 0.58,0.82); RRR=31% (95% CI: 18,42) in	Pitt (1999)[48]

		entire study population consisting of those with community heart failure, page 711.	
Aspirin	15% (95% CI: 11,19)	OR=0.85 (95% CI: 0.49,0.95); RRR=15% (95% CI: 11,19). Outcome is vascular and nonvascular deaths on page 75.	Antithrombotic Trialists' Collaboration (2002)[35]
Statins	No effect		Kjekshus (2007)[49] Tavazzi (2008)[50]
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]

[a]Relative risk reduction (RRR) calculated as 1 – odds ratio

Table G. Case fatality rates for each patient group

Age and gender specific one year case-fatality rates were required for each patient group. Where possible these were estimated using the linked Scottish Morbidity Record (SMR01) and death record dataset provided by Information Services Division Scotland. It was possible to estimate Scottish specific case fatality rates for the following disease groups: DG1: STEMI; DG2: nSTEACS; DG6: Hospital HF with CHD; DG3: Post MI in community and DG4: Post revascularization in the community (no MI) split into CABG and PCI. Previously published data was utilised for the following disease groups DG5: chronic stable coronary artery disease; DG7: heart failure in the community; DG8: Statin medication for primary prevention and DG9: Anti-hypertensive medication for primary prevention.[6]

Historical/baseline one year case fatality rates were estimated for disease groups 1 (AMI), 2 (UA) and 6 (HF with CHD) using linked SMR01 data from 1986; before major changes in therapy/diagnosis. The linked data enabled individuals to be followed for 0 to 365 days after the index event. The use of data from 1986 enabled look back to 1981 in order to exclude pre-existing conditions. Index admissions (main diagnosis and first admission of year) during 1986 were assigned to the three mutually exclusive disease groups adhering to the hierarchy HF>AMI>UA. It was then identified what proportion of these patients died within 365 days (all-cause death). The following disease definitions were used to identify index admissions:
DG1: STEMI using emergency AMI (ICD9 410; ICD10 I21) as proxy for STEMI
DG2: nSTEACS using emergency UA (ICD9 4111 or 413_; ICD10 I21) as proxy for nSTEACS
DG6: Hospital HF with previous CHD since 1981 using HF (ICD9 4280 or 4281 or 4289 ICD10 I50) with a previous admission for CHD (ICD9 410 or 411 or 412 or 414; ICD10 I21 or I22 or I23 or I24) as well as previous CABG (OCPS3 3043).

One year case fatality rates were created for the DG3 and DG4 community groups using data from 1981 to 1995 from the linked SMR01 and death record dataset. This was selected as it allowed a longer period of look back plus angioplasty was not coded until 1989. Patients were assigned to disease groups using the following hierarchy: Post AMI> Post CABG >Post PCI. All patients with index events up to 31st December 1994 and alive on 1st January 1995 were identified and the proportion that died within 365 days determined. The following disease definitions were used to identify index admission:
DG3: Post MI in community using AMI (ICD9 410)
DG4: Post revascularisation in community (no MI) divided into CABG (pre 1989 OCPS3 3043 or post 1989 OPCS4 K40 or K41 or K42 or K43 or K44 or K45 or K46) and PCI (post 1989 K49 or K501 or K75).

Table G. Case fatality rates for each patient group

	Source: Information Services Division (ISD) – linked SMR01 and death record dataset						**Source:** Wijeysundera et.al (2010) [6]			
Patient group	**AMI**	**POST AMI**	**ACS (UA)**	**Post revascularisation**		**Heart failure in hospital associated with CHD**	**Chronic stable coronary artery disease**	**Heart failure in community**	**Hyper-tension**	**Hyper-cholesterolaemia**
				CABG	**PTCA**					
Interval	**1 year**	**1 year**	**1 year**	**1 year**		**1 year**	**1 year**	**1 year**	**1 year**	**1 year**
Men										
25-34	0.120	0.008	0.000	0.000	0.000	0.000	0.006	0.04	0.000	0.000
35-44	0.082	0.010	0.028	0.005	0.013	0.389	0.009	0.04	0.001	0.001
45-54	0.126	0.017	0.039	0.008	0.003	0.393	0.012	0.06	0.002	0.002
55-64	0.230	0.027	0.054	0.015	0.015	0.446	0.016	0.08	0.006	0.006
65-74	0.383	0.047	0.102	0.035	0.029	0.520	0.029	0.13	0.014	0.014
75-84	0.543	0.097	0.119	0.047	0.034	0.553	0.065	0.20	0.035	0.035
85+	0.782	0.152	0.091	0.000	0.000	0.620	0.163	0.32	0.094	0.094
Women										
25-34	0.250	0.022	0.000	0.000	0.000	0.000	0.007	0.05	0.000	0.000
35-44	0.121	0.007	0.000	0.000	0.000	0.143	0.007	0.05	0.001	0.001
45-54	0.129	0.015	0.013	0.000	0.011	0.313	0.010	0.05	0.002	0.002
55-64	0.226	0.022	0.039	0.015	0.005	0.393	0.014	0.08	0.004	0.004
65-74	0.375	0.042	0.068	0.019	0.022	0.476	0.025	0.12	0.014	0.014
75-84	0.530	0.076	0.146	0.037	0.071	0.582	0.054	0.17	0.035	0.035
85+	0.628	0.143	0.207	0.000	0.000	0.570	0.155	0.30	0.094	0.094

AMI – Acute Myocardial infarction; ACS – Acute coronary syndrome; UA – unstable angina; CHD – coronary heart disease; CABG – coronary artery bypass graft; PTCA – Percutaneous transluminal coronary angioplasty

Table H. Treatment uptake in 2000 and 2010[a]

	National			SIMD Q1			SIMD Q2			SIMD Q3			SIMD Q4			SIMD Q5		
	N	Uptake (%)		N	Uptake (%)		N	Uptake (%)		N	Uptake (%)		N	Uptake (%)		N	Uptake (%)	
		2000	2010		2000	2010		2000	2010		2000	2010		2000	2010		2000	2010
ST elevation myocardial infarction (STEMI):																		
Thrombolysis	2502	77.6	58.5	360	79.7	60.5	479	78.0	62.1	511	75.9	59.4	552	76.3	57.4	600	78.7	54.5
Aspirin	2502	93.6	96.6	360	93.7	97.0	479	94.6	96.9	511	93.0	96.1	552	93.1	96.4	600	93.8	96.8
B-Blocker	2502	71.7	72.8	360	75.2	72.9	479	72.6	71.9	511	71.4	72.0	552	69.7	72.1	600	71.4	74.7
ACE I/ARB	2502	77.5	78.3	360	79.8	78.4	479	79.0	77.4	511	75.9	77.5	552	75.5	77.0	600	78.5	80.9
Clopidogrel	2502	28.1	90.0	360	27.1	90.2	479	25.8	89.3	511	28.0	90.3	552	29.1	89.9	600	29.2	90.4
Primary PCI	2502	4.2	58.6	360	6.2	66.7	479	4.0	58.4	511	4.1	55.8	552	5.0	56.2	600	2.6	58.4
Primary CABG	2502	0.0	0.1	360	0.0	0.3	479	0.2	0.0	511	0.0	0.0	552	0.0	0.2	600	0.0	0.0
Hospital CPR	2502	11.2	5.8	360	9.8	5.8	479	11.4	6.1	511	11.7	5.5	552	11.7	5.9	600	11.1	5.6
Community CPR	1316	23.4	28.3	185	9.8	5.8	239	11.4	6.1	260	11.7	5.5	288	11.7	5.9	344	11.1	5.6
Non-ST-segment elevation acute coronary syndrome (NSTEACS):																		
Aspirin & heparin	9108	64.0	79.9	1251	67.4	79.7	1650	65.6	80.7	1867	67.0	80.1	2091	65.9	80.1	2249	58.0	78.9
Aspirin alone	9108	24.3	12.8	1251	21.4	13.6	1650	23.5	12.2	1867	21.4	12.6	2091	23.4	12.5	2249	28.8	13.1
Platelet glycoprotein IIB/IIIA inhibitors	9108	6.0	5.9	1251	9.6	6.3	1650	7.4	6.0	1867	6.3	5.3	2091	4.8	5.1	2249	4.6	7.0
ACE I/ARB	9108	66.2	73.5	1251	68.8	73.3	1650	64.3	72.6	1867	66.2	72.8	2091	64.5	72.8	2249	67.7	75.2
B-Blocker	9108	63.9	67.9	1251	66.9	68.3	1650	63.5	68.3	1867	64.2	67.1	2091	62.5	66.2	2249	63.9	69.5
Clopidogrel	9108	45.1	86.8	1251	44.0	87.3	1650	44.7	87.4	1867	43.0	87.1	2091	46.2	86.0	2249	46.4	86.5
CABG (< 6 weeks)	9108	0.4	0.4	1251	0.9	0.3	1650	0.4	0.6	1867	0.3	0.5	2091	0.4	0.3	2249	0.4	0.2
PCI (0-14 days)	9108	3.5	6.7	1251	5.6	7.9	1650	3.1	7.8	1867	4.2	6.2	2091	3.3	5.9	2249	2.6	6.4
Hospital CPR	4638	5.2	2.4	712	4.5	2.3	908	4.8	2.2	955	5.3	2.2	1029	5.5	2.7	1034	5.5	2.4
Secondary prevention post myocardial infarction:																		
Aspirin	60197	68.6	80.5	9282	67.4	80.0	10490	69.1	78.8	12023	67.3	78.8	13872	69.3	80.9	14530	69.2	83.3
B-Blocker	60197	45.7	65.8	9282	50.9	67.5	10490	45.5	63.3	12023	47.5	64.2	13872	44.0	65.3	14530	43.1	68.6
ACE I/ARB	60197	26.5	68.0	9282	26.4	68.3	10490	29.2	67.1	12023	26.6	64.5	13872	26.7	69.2	14530	24.6	70.2
Statin	60197	41.7	86.6	9282	43.4	84.9	10490	44.2	84.6	12023	40.9	85.7	13872	41.6	87.0	14530	39.8	89.5
Warfarin	60197	4.7	6.0	9282	5.3	6.5	10490	5.9	6.0	12023	4.9	6.9	13872	4.2	5.3	14530	4.0	5.7
Rehabilitation	60197	17.1	42.1	9282	17.0	41.7	10490	17.0	41.9	12023	17.0	42.1	13872	17.1	42.0	14530	17.3	42.8
Secondary prevention post revascularisation:																		
Aspirin	40295	75.6	79.2	7538	72.5	75.1	7539	81.4	80.6	8128	70.3	78.5	8691	77.1	78.0	8399	76.8	83.8
B-Blocker	40295	45.3	62.0	7538	48.5	60.3	7539	48.4	61.8	8128	47.1	62.4	8691	39.1	59.7	8399	44.9	65.9
ACE I/ARB	40295	20.7	59.5	7538	21.8	56.9	7539	22.0	53.9	8128	16.3	60.3	8691	24.1	65.3	8399	19.4	60.2
Statin	40295	62.4	90.9	7538	67.3	89.5	7539	62.6	88.5	8128	57.4	90.3	8691	63.8	92.3	8399	61.2	93.4
Warfarin	40295	8.5	7.3	7538	6.0	8.3	7539	6.8	7.6	8128	11.2	8.1	8691	9.8	7.7	8399	8.1	5.0
Rehabilitation (PTCA)	11099	7.5	12.4	2029	7.5	12.6	2141	7.5	12.4	2297	7.5	12.3	2344	7.5	12.4	2288	7.5	12.2
Rehabilitation (CABG)	7113	42.5	41.9	1391	43.1	41.9	1414	42.6	42.4	1460	42.6	41.7	1519	42.5	42.0	1329	42.0	41.3
Chronic stable coronary artery disease:																		
Aspirin	72394	59.6	73.6	11705	57.7	71.4	13457	60.3	72.0	16889	57.4	72.2	15283	61.2	75.0	15061	60.7	77.2
Statins	72394	28.7	78.6	11705	31.1	77.6	13457	27.6	76.3	16889	30.2	78.4	15283	28.9	81.7	15061	26.8	78.4
ACE I/ARB	72394	15.3	45.2	11705	16.8	45.2	13457	15.7	45.1	16889	14.6	41.7	15283	15.7	47.9	15061	14.8	46.4
CABG surgery (last 5 years)	72394	11.8	9.8	11705	16.0	11.9	13457	11.9	10.5	16889	10.2	8.6	15283	11.4	9.9	15061	11.4	8.8
Heart failure in patients requiring hospitalisation:																		
ACE I/ARB	3644	51.4	64.3	502	50.1	62.6	619	50.1	62.7	764	51.5	64.4	844	51.8	64.7	915	52.7	65.8
B-Blocker	3644	31.9	45.6	502	31.0	44.2	619	31.1	44.4	764	32.0	45.7	844	32.2	46.0	915	32.7	46.7
Spironolactone	3644	21.0	26.2	502	20.5	25.6	619	20.3	25.4	764	21.1	26.4	844	21.2	26.6	915	21.2	26.5
Aspirin	3644	71.9	79.9	502	70.8	80.7	619	74.9	77.1	764	68.6	78.8	844	72.7	80.1	915	72.4	82.3
Heart failure in the community:																		
ACE I/ARB	16224	69.7	81.4	2243	72.6	79.7	2826	72.5	79.4	3271	61.5	79.3	3523	70.0	79.7	4362	72.7	86.5
B-Blocker	16224	30.9	65.8	2243	34.3	57.3	2826	28.2	60.0	3271	32.8	66.9	3523	28.2	65.5	4362	32.1	73.3
Spironolactone	16224	7.7	11.7	2243	6.2	7.8	2826	10.4	14.5	3271	6.6	12.7	3523	6.5	16.4	4362	8.2	7.4
Aspirin	16224	74.3	75.1	2243	71.9	75.4	2826	71.8	76.9	3271	71.2	71.6	3523	77.8	73.7	4362	77.0	77.7

Primary prevention therapies:																	
Anti-hypertension	3685544	12.2	18.3	735789	9.4	15.6	761624	12.4	19.3	755559	12.2	17.8	736790	12.9	18.8	695782	14.0	19.9
Statins	3685544	2.7	15.1	735789	2.2	13.2	761624	2.8	15.8	755559	2.8	15.3	736790	2.6	14.3	695782	3.2	17.0

[a] For sources see Table A

Table I. Beta coefficients for major 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 randomized controlled trials, results stratified by age and sex, with 95% confidence intervals
Limitations:	Some publication bias still possible

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 randomized controlled trials, RCT values consistent with observational data, results stratified by age and sex, with 95% confidence intervals					
Limitations:	Some publication bias still possible					

Body Mass Index (BMI)	**Age groups (years)**				
	<44	**45-59**	**60-69**	**70-79**	**80+**
James et.al (2004):					
Hazard ratio	0.89	0.91	0.95	0.96	0.97
Risk reduction[a] per 1 kg/m^2	0.11	0.09	0.05	0.04	0.03
Age gradient (45-59 as reference)	1.22	**1.00**	0.56	0.44	0.33
Bogers (2006):					
Relative risks, CHD deaths per 5 BMI units (kg/m^2)		**1.16**			
Relative risks per 1 kg/m^2 applying age gradients from James et.al	1.04	1.03	1.02	1.01	1.01
Log coefficients	**0.0363**	**0.0297**	**0.0165**	**0.0132**	**0.0099**
Minimum	*0.0255*	*0.0209*	*0.0116*	*0.0093*	*0.0070*
Maximum	*0.0466*	*0.0381*	*0.0212*	*0.0169*	*0.0127*
Source:	Bogers et al (2006)[55], James et al (2004)[56]				
Units:	Percentage change in CHD mortality per 1 kg/m^2 change in BMI				
Strengths:	Large number of studies included. Adjusted for blood pressure, total cholesterol, and physical activity. 95% confidence intervals included.				
Limitations:	Observational data; age gradient applied from James study				

[a] Risk reduction = 1 – hazard ratio

Table J. Relative risk for CHD mortality: smoking, diabetes and physical inactivity

Calculation of Relative Risk estimates for dichotomous risk factors in the IMPACT$_{SEC}$ model

Relative risks (RRs) estimated by expert working groups for the World Health Organization's (WHO) Global Burden of Disease (GBD) 2001 Study were used for smoking and physical activity[10] Effect estimates were based on systematic reviews of cohort studies (adjusted for regression dilution bias) and meta-analyses of randomised controlled trials. Age-variation in the relative risks for diabetes were taken from the DECODE study.[11] These were then applied to the sex-variation in relative risks estimated by Huxley et al.[12] The set of RRs used in the IMPACT$_{SEC}$ model for the three binary risk factors with 95% Confidence Intervals (in parentheses) are shown below. RRs were assumed constant across deprivation quintiles.

	Smoking	Physical inactivity	Diabetes
Male 25-34	5.51 (2.47-12.25)	1.50 (1.35-1.67)	4.33 (3.47-5.20)
Male 35-44	5.51 (2.47-12.25)	1.50 (1.35-1.67)	3.22 (2.58-3.86)
Male 45-54	3.04 (2.66-3.48)	1.50 (1.35-1.67)	2.14 (1.71-2.57)
Male 55-64	2.51 (2.22-2.84)	1.50 (1.35-1.67)	1.99 (1.59-2.39)
Male 65-74	1.69 (1.52-1.89)	1.44 (1.30-1.61)	1.86 (1.49-2.23)
Male 75-84	1.31 (1.11-1.56)	1.32 (1.19-1.47)	1.71 (1.37-2.05)
Male 85+	1.05 (0.78-1.43)	1.23 (1.11-1.37)	1.71 (1.37-2.05)
Female 25-34	2.26 (0.83-6.14)	1.50 (1.35-1.68)	7.55 (6.04-9.06)
Female 35-44	2.26 (0.83-6.14)	1.50 (1.35-1.68)	5.63 (4.51-6.76)
Female 45-54	3.78 (3.10-4.62)	1.50 (1.35-1.68)	3.81 (3.05-4.57)
Female 55-64	3.21 (2.70-3.82)	1.50 (1.35-1.68)	3.12 (2.50-3.74)
Female 65-74	2.17 (1.89-2.47)	1.45 (1.30-1.61)	2.55 (2.04-3.06)
Female 75-84	1.58 (1.33-1.88)	1.33 (1.20-1.47)	2.36 (1.89-2.83)
Female 85+	1.38 (1.08-1.77)	1.24 (1.13-1.37)	2.36 (1.89-2.83)

In Section J.1 we list the published RRs for each of the three risk factors; in Section J.2 we detail how these were modified to fit to the age-sex distributions used in the IMPACT$_{SEC}$ model.

J.1 Published relative risks

1 Current smoking

Relative risk of mortality from Ischaemic Heart Disease (ICD9: 410-414) for current smokers relative to non-smokers (95% CIs in parentheses), from the American Cancer Society's Cancer Prevention Study (CPS-II)

Age	Male	Female
30-44	5.51 (2.47-12.25)	2.26 (0.83-6.14)
45-59	3.04 (2.66-3.48)	3.78 (3.10-4.62)
60-69	1.88 (1.70-2.08)	2.53 (2.22-2.87)
70-79	1.44 (1.27-1.63)	1.68 (1.46-1.93)
≥ 80 years	1.05 (0.78-1.43)	1.38 (1.08-1.77)

Notes: CPS-II is an ongoing prospective study of mortality in 1.2 million Americans aged 30 years or more when they completed a questionnaire on tobacco and alcohol use, diet, and multiple other factors affecting health and mortality in 1982. RRs were estimated from Cox proportional-hazard models, with non-smokers as the reference group (RR=1.0 for non-smokers). Risks were adjusted for age, race, education, marital status, "blue collar" employment in most recent or current job, weekly consumption of vegetables and citrus fruit, vitamin (A, C, and E) use, alcohol use, aspirin use, body mass index, exercise, dietary fat consumption and for hypertension and diabetes (both at baseline). Analyses of the hazards associated with smoking were based on the first six years of follow-up (1982 through 1988).

Source: Ezzati et al (2005)[57]

2 Physical inactivity

Relative risk of Ischaemic Heart Disease (ICD10: I20-I25) from physical (in)activity levels from WHO GBD Study (95% CIs in parentheses), relative to those considered physically active

Age	Inactive level	Insufficiently active level
15-69	1.71 (1.58-1.85)	1.44 (1.28-1.62)
70-79	1.50 (1.38-1.61)	1.31 (1.17-1.48)
80+ years	1.30 (1.21-1.41)	1.20 (1.07-1.35)

Notes: Physical (in)activity in the WHO GBD study was treated as a categorical variable with three categories: **Level 1**: Inactive: 'doing no or very little physical activity at work, at home, for transport, or during discretionary time'. **Level 2**: Insufficiently active: 'doing some physical activity but less than 150 minutes of moderate-intensity physical activity or 60 minutes of vigorous-intensity physical activity a week accumulated across work, home, transport or discretionary domains'. **Level 3**: Sufficiently active (unexposed): 'at least 150 minutes of moderate-intensity physical activity or 60 minutes of vigorous-intensity physical activity a week accumulated across work, home, transport or discretionary domains', which

approximately corresponds to current recommendations in many countries. RR estimates were adjusted for confounding variables, measurement error associated with self-report, and attenuated over age (25% of the excess risk for the 70-79 year age-group and 50% of the excess risk for the oldest age group, 80+), but not adjusted for blood pressure and cholesterol.

Sources: Bull et al (2004)[58]; Joubert et al (2007)[59]

3 Diabetes

A meta-analysis of 22 prospective cohort studies by Huxley et al[12] estimated that the relative risk for CHD due to diabetes was 1.99 (95% CI: 1.69-2.35) in men and 3.12 (2.34-4.17) in women. These estimates were derived from studies that provided multiple risk factor adjusted coefficients. This systematic review included Asia-Pacific studies with larger RR values compared to Western studies, although the difference was not statistically significant. To obtain age-specific relative risk estimates, we used the age-gradients in relative risk for **total** mortality for diabetic persons compared to non-diabetics taken from the DECODE study as detailed below.

Estimates of relative risk for total mortality due to diabetes (DECODE study)

Age	Males	Females
20-29	3.66	6.05
30-39	3.38	5.41
40-49	1.85	3.14
50-59	1.63	2.64
60-69	1.60	2.04
70-79	1.39	1.79

Notes: Undertaken in 1997, the Diabetes Epidemiology: Collaborative Analysis of Diagnostic Criteria in Europe (DECODE) study built a dataset that included the baseline values needed to determine the presence of the metabolic syndrome using a modification of the WHO definition for 11 European study cohorts, and follow-up data on all-cause and cardiovascular disease mortality[60].

Source: Roglic and Unwin (2010)[11]

J.2 Adjusting the published RR values

The published relative risk values outlined in the previous section were adjusted to conform to the age distributions and binary classification of risk used in the $IMPACT_{SEC}$ study. Table J above shows the final, adjusted RR values used in our model to estimate the Population Attributable Risk Fractions. Below we detail how the adjustments to the published RR values were calculated.

Weighted averages using the European Standard Population

We adjusted the RRs for each binary risk factor to match the ten-year age-bands used in our study. A population-weighted approach, using weights from the European

Union (EU) reference population, was used to estimate the RRs for each of the 7 age-bands. We used the EU standard reference population for two reasons: first, for consistency. The EU standard was used as the reference population distribution in all $IMPACT_{SEC}$ and related studies to calculate directly-standardised rates. Secondly, using the EU reference population aids comparability. The ensuing age-weighted rates can easily be used in studies in other European countries with a similar population structure and results compared against each other or with other health statistics (e.g. mortality rates) standardised using the same reference population.

1 Adjustment to published RRs for current smoking

The population-weighted adjustment approach is illustrated below using the RRs for current smoking in men as an example. For example, the RR value used in our model for males aged 55-64 was 2.51. This is roughly, but not exactly, halfway between the CPS-II estimates of 3.04 and 1.88 for males aged 55-59 and 60-64 with population weights of 0.545 and 0.455, respectively. The same calculations using a population weighted approach were performed using the CPS-II 95% confidence intervals to estimate the standard error of the RRs to use as input to the Ersatz Relative Risk function (See Table M).

Age bands for $IMPACT_{SEC}$	**5 year age-bands**	**EU population**	**EU population weight**	**CPS-II RR**	**$IMPACT_{SEC}$ RR**
M 25-34	**M 25-29**	7000	0.5	5.51	5.51
	M 30-34	7000	0.5	5.51	
M 35-44	**M 35-39**	7000	0.5	5.51	5.51
	M 40-44	7000	0.5	5.51	
M 45-54	**M 45-49**	7000	0.5	3.04	3.04
	M 50-54	7000	0.5	3.04	
M 55-64	**M 55-59**	6000	0.545	3.04	2.51
	M 60-64	5000	0.455	1.88	
M 65-74	**M 65-69**	4000	0.571	1.88	1.69
	M 70-74	3000	0.429	1.44	
M 75-84	**M 75-79**	2000	0.667	1.44	1.31
	M 80-84	1000	0.333	1.05	
M 85+		1000	1	1.05	1.05

2 Adjustment to published RRs for physical activity

We adjusted the published RRs for physical activity to employ a dichotomous rather than trichotomous measure (i.e. combining the GBD 'insufficiently active' and 'inactive' categories into a single inactive group). We used a weighted average approach using as weights the GBD estimates of exposure to physical inactivity in the EUR-A subregion (Table 10.10 in Bull et al, 2004)[58]. The physical activity exposure levels (%) with the corresponding RR value (RR=1 for the Level 3 'sufficiently active' group) shown in parentheses are detailed below.

Physical activity exposure levels (%) in the GBD EUR-A region[a] with accompanying RRs

Exposure category	Age-group (years) 15-29	30-44	45-59	60-69	70-79	≥ 80 years
Men:						
Level 3: Recommended	35 (1)	29 (1)	30 (1)	30 (1)	30 (1)	32 (1)
Level 2: Insufficient	52 (1.44)	57 (1.44)	55 (1.44)	52 (1.44)	50 (1.31)	47 (1.20)
Level 1: Inactive	13 (1.71)	15 (1.71)	16 (1.71)	18 (1.71)	20 (1.50)	21 (1.30)
Levels 1 and 2 (combined RR)	*1.49*	*1.50*	*1.50*	*1.51*	*1.36*	*1.23*
Women:						
Level 3: Recommended	37 (1)	31 (1)	31 (1)	33 (1)	31 (1)	30 (1)
Level 2: Insufficient	47 (1.44)	51 (1.44)	51 (1.44)	45 (1.44)	45 (1.31)	42 (1.20)
Level 1: Inactive	17 (1.71)	18 (1.71)	18 (1.71)	22 (1.71)	24 (1.50)	28 (1.30)
Levels 1 and 2 (combined RR)	*1.51*	*1.51*	*1.51*	*1.53*	*1.38*	*1.24*

Notes: For example, using the GBD estimates of exposure and RRs, the combined RR for males aged 45-59 equalled 1.50:

RR (combining insufficient and inactive):
$((0.55\times1.44)+(0.16\times1.71))/(0.55+0.16) = 1.50$

[a] Countries in the EUR-A GBD subregion: Andorra, Austria, Belgium, Croatia, Czech Republic, Denmark, Finland, France, Germany, Greece, Iceland, Ireland, Israel, Italy, Luxembourg, Malta, Monaco, Netherlands, Norway, Portugal, San Marino, Slovenia, Spain, Sweden, Switzerland, United Kingdom

Source: Bull et al (2004)[58]

Due to negligible differences in the combined RRs across the youngest age categories we used a relative risk of 1.50 for men and women aged 25-69. Having used the GBD data to obtain a set of RRs for a **binary** physical activity variable in each of three broad age-groups (25-69, 70-79, 80+) we then used the population-weighted average approach, using weights from the EU population, to estimate the combined RRs for the seven ten-year age-bands used in $IMPACT_{SEC}$. This is illustrated below for males. The same sets of calculations using a population weighted approach were performed using the GBD 95% confidence intervals to estimate the standard error of the RRs to use as input into the Ersatz Relative Risk function (See Table M).

Age bands for $IMPACT_{SEC}$	5 year age-bands	EU population	EU population weight	Combined inactive RR	$IMPACT_{SEC}$ RR
M 25-34	**M 25-29**	7000	0.5	1.50	1.50
	M 30-34	7000	0.5	1.50	
M 35-44	**M 35-39**	7000	0.5	1.50	1.50
	M 40-44	7000	0.5	1.50	
M 45-54	**M 45-49**	7000	0.5	1.50	1.50
	M 50-54	7000	0.5	1.50	
M 55-64	**M 55-59**	6000	0.545	1.50	1.50
	M 60-64	5000	0.455	1.50	
M 65-74	**M 65-69**	4000	0.571	1.50	1.44
	M 70-74	3000	0.429	1.36	
M 75-84	**M 75-79**	2000	0.667	1.36	1.32
	M 80-84	1000	0.333	1.23	
M 85+		1000	1	1.23	1.23

3 Adjustment to published RRs for diabetes

Unlike the relative risk estimates for smoking and physical activity, the meta-analysis of 22 prospective cohort studies by Huxley et al[12] provided just overall estimates of RR for diabetes by gender. From previous studies we know that the relative risks associated with diabetes are higher for women and decline with age. To obtain age variation in the diabetes RRs, we used the age-gradient in the RR estimates for total mortality taken from the DECODE study.[11] As diabetes is a proximate risk factor for cardiovascular disease, and cardiovascular disease comprises about half of total mortality[61], we have assumed that the relative age pattern of diabetes-related CHD mortality will be similar. We made the reasonable assumption that the mean age across the prospective studies examined in the meta-analysis by Huxley et al[12] was age 55-64 years. Hence the age-adjusted values were anchored to this age group for both sexes.

To estimate the relative risks for diabetes, we first used the DECODE study estimates to compute the age gradient in RRs, indexed on the value for the 55-64 age-group. The resulting value for each age group was then multiplied by the overall RR for men and women (1.99 and 3.12, respectively) taken from the study by Huxley et al[12] to give the age-specific RR of CHD mortality for diabetes. For ages 80 and over (for which published RRs were not found), we have assumed that the RR remained the same as for those aged 70-79. Detailed below is the worked example for males. Estimates of the 95% confidence intervals were not provided for the RRs taken from the DECODE study.[11] Hence, similar to previous IMPACT models, we used ± 20% of the point estimate as an approximation of the 95% confidence interval. We then used this interval to derive the standard error of the RR to use as an input parameter in the Ersatz uncertainty analysis. This value was equal to 0.103 - a value lying reasonably close to the average of the standard errors around the sex-specific estimates from Huxley et al.[12]

Age-bands for $IMPACT_{SEC}$	5 year age bands	EU pop	EU pop weight	RR from DECODE study	Weighted RRs from DECODE	Age variation from DECODE[a]	$IMPACT_{SEC}$ RRs[b]
M 25-34	**M 25-29**	7000	0.5	3.66	3.5	2.18	4.33
	M 30-34	7000	0.5	3.38			
M 35-44	**M 35-39**	7000	0.5	3.38	2.6	1.62	3.22
	M 40-44	7000	0.5	1.85			
M 45-54	**M 45-49**	7000	0.5	1.85	1.7	1.08	2.14
	M 50-54	7000	0.5	1.63			
M 55-64	**M 55-59**	6000	0.545	1.63	1.6	**1.00**	**1.99**
	M 60-64	5000	0.455	1.60			
M 65-74	**M 65-69**	4000	0.571	1.60	1.5	0.93	1.86
	M 70-74	3000	0.429	1.39			
M 75-84	**M 75-79**	2000	0.667	1.39	1.4	0.86	1.71
	M 80-84	1000	0.333	1.39			
M 85+		1000	1	1.39	1.4	0.86	1.71

Notes:

[a] 55-64 age-group taken as the reference

[b] $IMPACT_{SEC}$ RR calculated as sex-specific RR from Huxley et al (2006)[12] (men:1.99; women:3.12) multiplied by age-variation in EU weighted RRs taken from DECODE study[11]

Table K. Observed risk factor levels in 2000 and 2010 by sex and deprivation quintiles

	Scotland		SIMDQ1		SIMDQ2		SIMDQ3		SIMDQ4		SIMDQ5	
	2000	**2010**	**2000**	**2010**	**2000**	**2010**	**2000**	**2010**	**2000**	**2010**	**2000**	**2010**
Smoking prevalence, %												
Male	30.3	26.0	19.9	17.1	25.1	21.6	30.2	25.9	34.3	29.4	39.0	33.5
Female	28.9	23.7	17.7	14.5	22.3	18.3	28.6	23.5	32.8	27.0	39.0	32.0
Diabetes prevalence, %												
Male	4.2	7.3	3.1	5.3	4.1	7.0	4.5	7.8	4.6	7.9	4.9	8.4
Female	3.4	5.3	2.3	3.5	2.4	3.6	3.8	5.8	3.9	6.0	4.7	7.3
Physical inactivity, %												
Male	66.3	58.9	66.7	59.2	65.4	58.1	64.9	57.8	66.0	58.6	68.1	60.3
Female	74.6	68.4	71.9	65.9	73.7	67.5	74.1	68.0	75.8	69.6	77.0	70.5
Systolic blood pressure, mmHg												
Male	133.1	132.2	132.6	131.6	133.7	132.8	133.4	132.4	132.6	131.7	133.5	132.7
Female	130.1	126.9	128.8	125.7	129.6	126.5	130.4	127.3	130.9	127.6	131.1	128.0
Cholesterol, mmol/L												
Male	5.6	5.2	5.7	5.3	5.6	5.2	5.6	5.2	5.5	5.1	5.5	5.1
Female	5.7	5.4	5.8	5.5	5.7	5.4	5.8	5.5	5.7	5.4	5.6	5.4
Body mass index, kg/m^2												
Male	27.3	28.2	27.1	28.0	27.3	28.3	27.3	28.2	27.3	28.3	27.2	28.1
Female	27.1	27.9	26.1	26.9	26.9	27.8	27.1	27.9	27.6	28.4	27.8	28.6

Tables L. Gender specific coronary heart disease deaths prevented or postponed between 2000 and 2010

Table L.1 Coronary heart disease deaths prevented or postponed (DPPs) amongst men between 2000 and 2010 as percentage of men specific total DPPs to be explained, stratified by deprivation quintile

		Men					
Treatments by Patient Groups; Risk Factors	**Scotland**	**Most Affluent**	**SIMDQ2**	**SIMDQ3**	**SIMDQ4**	**Most Deprived**	**P-Value**
Treatments							
STEMI*	2.2	2.5	2.4	1.7	2.5	2.2	0.89
NSTEACS*	1.3	1.0	1.5	1.0	1.4	1.5	0.53
Secondary prevention post MI*	11.2	12.1	10.5	9.7	12.2	11.9	0.67
Secondary prevention post revasc*	2.9	3.0	2.4	3.2	3.2	2.8	0.90
Chronic stable CAD	5.1	5.6	5.9	4.4	6.0	4.0	0.27
Heart failure in hospital*	1.6	1.8	1.4	1.4	2.0	1.8	0.71
Heart failure in community	6.0	3.9	5.1	5.1	7.5	8.1	<0.001
Hypertension treatment	3.1	3.8	3.4	2.2	3.1	3.2	0.56
Hyperlipidaemia treatment (statins)	11.4	12.3	10.7	11.9	12.8	9.1	0.28
Total treatments[a]	**44.8**	**46.0**	**43.3**	**40.6**	**50.7**	**44.6**	**0.43**
Risk factors							
Smoking	3.5	1.3	2.2	2.9	4.6	5.9	<0.0001
Diabetes	-8.5	-5.0	-8.5	-7.5	-9.5	-11.4	<0.001
Physical activity	2.4	1.8	2.0	2.1	2.7	3.0	0.12
Systolic blood pressure, mmHg	31.2	31.8	31.6	29.2	34.5	29.7	0.81
Total cholesterol, mmol/l	15.0	11.0	14.8	11.8	16.7	20.0	<0.0001
BMI	-4.0	-3.4	-3.8	-3.6	-4.6	-4.6	0.16
Total Risk Factors[a]	**39.5**	**37.5**	**38.4**	**34.8**	**44.3**	**42.7**	**0.009**
DPPs explained by model[a]	**84.3**	**83.6**	**81.7**	**75.4**	**95.1**	**87.3**	
DPPs not explained by model[a]	**15.7**	**16.4**	**18.3**	**24.6**	**4.9**	**12.7**	
DPP counts							
DPPs explained by model[b]	***2595***	***414***	***460***	***562***	***576***	***581***	
T - Due to treatment uptake[b]	*1380*	*228*	*244*	*302*	*307*	*297*	
R- Due to risk factor change[b]	*1215*	*186*	*216*	*259*	*269*	*284*	
DPPs unexplained by model[b]	*480*	*81*	*103*	*183*	*30*	*85*	
Total DPPs[b]	***3075***	***496***	***563***	***744***	***605***	***666***	

[a]Sub-totals (in rows).
[b]DPPs for **Scotland** (column 2) and **Total DPPs** (last row) have been rounded to nearest 5.
Abbreviations: CAD, coronary artery disease; SIMD, Scottish index of multiple deprivation; NSTEACS, non-ST elevation acute coronary syndrome; MI, myocardial infarction; revasc,
revascularisation; STEMI, ST elevation myocardial infarction.

Table L.2 Coronary heart disease deaths prevented or postponed (DPPs) amongst women between 2000 and 2010 as percentage of women specific total DPPs to be explained, stratified by deprivation quintile

		Women					
Treatments by Patient Groups; Risk Factors	**Scotland**	**Most Affluent**	**SIMDQ2**	**SIMDQ3**	**SIMDQ4**	**Most Deprived**	**P-Value**
Treatments							
STEMI*	1.5	1.7	1.7	1.2	1.5	1.8	0.92
NSTEACS*	1.4	1.3	1.5	1.2	1.4	1.7	0.51
Secondary prevention post MI*	6.7	6.7	5.6	5.4	7.6	8.2	0.11
Secondary prevention post revasc*	1.2	1.2	1.3	0.8	1.4	1.5	0.66
Chronic stable CAD	8.1	9.1	8.3	7.2	8.0	8.6	0.83
Heart failure in hospital*	1.3	0.8	1.1	1.2	1.2	2.0	0.10
Heart failure in community	3.0	2.4	2.1	3.2	3.4	3.9	0.07
Hypertension treatment	2.2	2.4	2.7	2.0	1.8	2.1	0.43
Hyperlipidaemia treatment (statins)	15.6	19.2	22.1	14.5	10.4	13.7	<0.0001
Total treatments[a]	**41.0**	**44.8**	**46.4**	**36.6**	**36.6**	**43.4**	**0.10**
Risk factors							
Smoking	3.7	1.8	2.5	3.1	4.3	6.4	<0.0001
Diabetes	-7.9	-5.6	-5.5	-6.8	-9.4	-11.6	<0.0001
Physical activity	1.0	0.8	0.9	0.9	1.1	1.4	0.25
Systolic blood pressure, mmHg	43.4	44.4	43.7	37.7	46.4	46.0	0.30
Total cholesterol, mmol/l	1.9	-2.9	-5.2	1.2	7.8	6.5	<0.001
BMI	-4.2	-4.6	-4.5	-3.7	-4.4	-4.0	0.74
Total Risk Factors[a]	**37.9**	**33.8**	**31.8**	**32.4**	**45.9**	**44.6**	**<0.0001**
DPPs explained by model	**78.9**	**78.6**	**78.1**	**69.0**	**82.5**	**88.0**	
DPPs not explained by model	**21.1**	**21.4**	**21.9**	**31.0**	**17.5**	**12.0**	
DPP counts							
DPPs explained by model[b]	***2130***	***322***	***388***	***447***	***480***	***495***	
T - Due to treatment uptake[b]	*1105*	*183*	*230*	*237*	*213*	*244*	
R- Due to risk factor change[b]	*1025*	*138*	*158*	*209*	*267*	*251*	
DPPs unexplained by model[b]	*570*	*88*	*108*	*201*	*102*	*68*	
Total DPPs[b]	***2700***	***409***	***496***	***647***	***582***	***563***	

[a]Sub-totals (in rows).
[b]DPPs for **Scotland** (column 2) and **Total DPPs** (last row) have been rounded to nearest 5.
Abbreviations: CAD, coronary artery disease; SIMD, Scottish index of multiple deprivation; NSTEACS, non-ST elevation acute coronary syndrome; MI, myocardial infarction; revasc,
revascularisation; STEMI, ST elevation myocardial infarction.

Tables M. Model fit by age, sex and deprivation quintiles

Table M.1 Total CHD deaths prevented or postponed (DPPs) by age, sex and deprivation quintiles (*expected deaths had 2000 rates persisted – observed deaths in 2010)*

	National	Q1	Q2	Q3	Q4	Q5
Males	3074	496	563	744	605	666
Females	2697	409	496	647	582	563
Male 25-34	3	0	1	-2	0	4
Male 35-44	16	5	5	0	-6	13
Male 45-54	144	15	24	41	20	44
Male 55-64	489	52	74	110	139	114
Male 65-74	976	124	199	276	159	218
Male 75-84	1080	180	194	259	234	213
Male 85+	366	119	66	61	59	60
Female 25-34	-2	-1	0	-2	0	1
Female 35-44	4	-2	2	3	-4	5
Female 45-54	41	6	8	6	19	3
Female 55-64	209	7	39	38	45	80
Female 65-74	545	75	95	154	95	126
Female 75-84	1130	165	202	263	287	214
Female 85+	771	160	150	185	140	135
Total	**5771**	**905**	**1059**	**1392**	**1187**	**1229**

Table M.2 DPPs explained by model by age, sex and deprivation quintiles

	National	Q1	Q2	Q3	Q4	Q5
Males	2588	417	459	561	574	578
Females	2099	318	381	440	473	486
Male 25-34	3	0	0	0	1	2
Male 35-44	-4	-1	0	-1	0	-2
Male 45-54	119	13	18	20	26	41
Male 55-64	307	34	49	67	75	82
Male 65-74	539	74	98	117	117	132
Male 75-84	1041	171	185	231	233	220
Male 85+	583	125	109	125	121	103
Female 25-34	0	0	0	0	0	0
Female 35-44	0	0	0	0	0	0
Female 45-54	2	3	5	10	10	3
Female 55-64	8	17	17	23	31	17
Female 65-74	46	59	82	85	110	59
Female 75-84	139	169	206	220	215	169
Female 85+	123	133	130	134	119	133
Total	**4687**	**735**	**840**	**1001**	**1047**	**1064**

Notes: DPPs explained after adjustment for poly-pharmacy and cumulative risk factor reduction

Table M.3 Model fit[a] by age, sex and deprivation quintiles

	National	Q1	Q2	Q3	Q4	Q5
Males	84%	84%	82%	75%	95%	87%
Females	78%	78%	77%	68%	81%	86%
Male 25-34	113%	100%	24%	1%	890%	45%
Male 35-44	26%	14%	8%	251%	5%	15%
Male 45-54	83%	86%	78%	50%	128%	93%
Male 55-64	63%	65%	67%	61%	54%	72%
Male 65-74	55%	60%	49%	43%	74%	61%
Male 75-84	96%	95%	95%	89%	100%	103%
Male 85+	159%	105%	164%	206%	206%	170%
Female 25-34	24%	0%	100%	0%	151%	29%
Female 35-44	22%	2%	6%	5%	5%	6%
Female 45-54	75%	37%	38%	89%	54%	375%
Female 55-64	46%	113%	44%	44%	51%	39%
Female 65-74	70%	61%	62%	53%	90%	87%
Female 75-84	84%	85%	83%	78%	77%	101%
Female 85+	83%	77%	89%	70%	95%	89%
Total	81%	81%	79%	72%	88%	87%

[a]Model fit = absolute % of the total DPPs explained by the model:
% Model fit = ABSOLUTE (1- ((total DPPs – model DPPs)/total DPPs)) × 100

Table M.4 Overall model fit by deprivation quintiles: comparing modelled deaths prevented or postponed (DPPs) against observed fall in CHD deaths, and 95% uncertainty intervals (UI)

	Target DPPs	Explained DPPs	*Lower UI (95%)*	*Upper UI (95%)*	Explained (%)	*Lower UI (%)*	*Upper UI (%)*
SIMDQ1	905	736	*545*	*927*	81.3	*60.2*	*102.5*
SIMDQ2	1059	847	*623*	*1071*	80.0	*58.8*	*101.1*
SIMDQ3	1392	1006	*734*	*1279*	72.3	*52.8*	*91.9*
SIMDQ4	1187	1053	*841*	*1264*	88.7	*70.9*	*106.5*
SIMDQ5	1229	1075	*856*	*1294*	87.5	*69.7*	*105.3*
Scotland	**5771**	**4717**	***3700***	***5735***	**81.7**	***64.1***	***99.4***

Figure M.1 Model fit by age, gender and deprivation quintiles

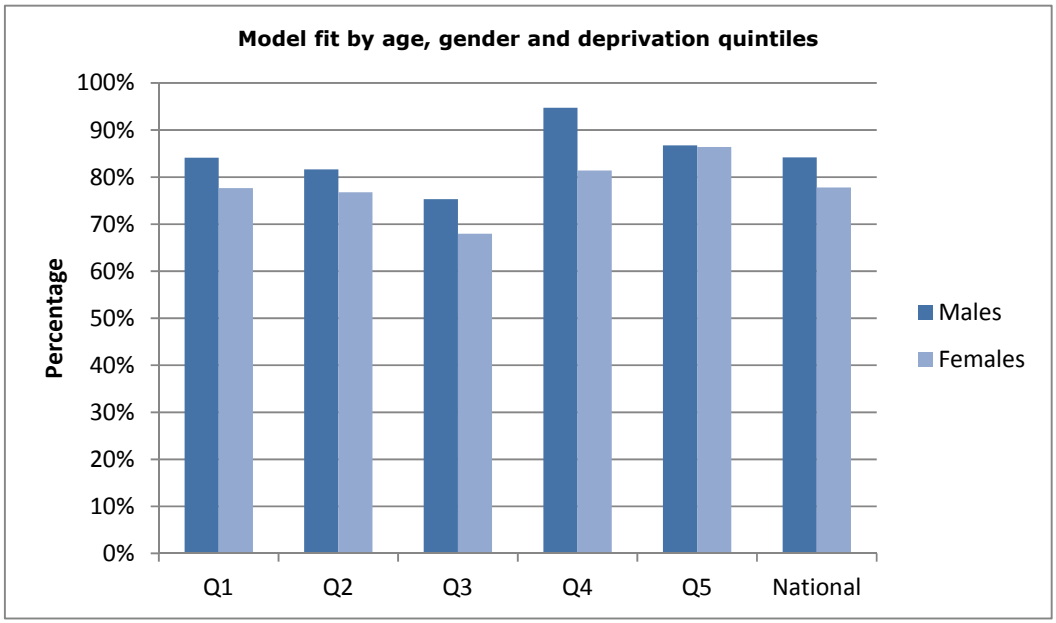


Table N. Uncertainty analysis: parameter distributions, functions and sources

Table N 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 2.5th and 97.5th 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. Worked examples using Ersatz to estimate uncertainty intervals for net treatment DPPs and DPPs attributable to risk factor change are shown below Table N.

Input parameters	***Type of distribution and functions (Mean, Standard error)***	Source
Population		
Population counts and CHD deaths stratified by age, sex, and Scottish Index of Multiple Deprivation quintiles	• Population counts (no error) • Deaths expected in 2010 had CHD mortality rates in 2000 persisted (***Poisson distribution***)	National Records Scotland
Risk factors		
Prevalence/mean estimates (pooled data; national estimates for 2000 and 2010)	• Prevalence estimates (smoking, physical activity, diabetes): (***Beta distribution***: cases, sample-size minus cases) • Continuous variables (Body Mass Index, SBP, total cholesterol): (***Normal distribution***: mean, SE of mean)	Scottish Health Survey
RR: **smoking**	***Ersatz RR function*** (RR, SE ln(RR)): RRs and 95% CIs shown in Table J.	Ezzati et al (2005)[57]
RR: **physical activity**	***Ersatz RR function*** (RR, SE ln(RR)): RRs and 95% CIs shown in Table J.	Bull et al (2004)[58]
RR: **diabetes**	***Ersatz RR function*** (RR, SE ln(RR)): RRs and 95% CIs shown in Table J.	Roglic and Unwin (2010)[11]; Huxley et al (2006)[12]
Beta coefficient: **Body Mass Index**	***Normal distribution*** (mean, SE of mean): M & F < 45 (0.036,0.005); M & F 45-54 (0.030, 0.004) M & F 55-64 (0.023,0.003); M & F 65-74 (0.015, 0.002) M & F 75-84 (0.012,0.002); M & F 85+ (0.010, 0.001)	Bogers et al (2006)[55], James et al (2004)[56]. Parameters on the log scale.
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)	Prospective studies collaborative meta-analysis (2002)[53]. Parameters on the log scale.

	F 65-74 (-0.032,0.003); F 75-84 (-0.026,0.003) 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.
ST elevation myocardial infarction (STEMI)		
Eligible patients: Emergency admissions with a primary diagnosis of myocardial infarction. (Ratio STEMI/nSTEMI in 2010 informed by ratio in 2011 from SMR01. Ratio STEMI/nSTEMI in 2000 as 40/60)	***Poisson distribution*** (admissions)	Linked Scottish Morbidity Records (SMR01)
Case fatality rate	Sample size (*n*) = emergency admissions for AMI in 1986 from SMR01 ***Beta distribution*** (cases= fatal cases within 1 year , non-cases=non fatal cases within 1 year)	Linked Scottish Morbidity Records (SMR01) for 1986
Treatment uptake	• *Medications and in-hospital CPR:* ***Beta distribution*** (cases = STEMI admissions from MINAP × medication uptake, non-cases = STEMI admissions – cases) • *PCI and CABG*: ***Beta distribution*** (cases = MI admissions from SMR01 × PCI/CABG uptake, non-cases = MI admissions – cases)	English MINAP for treatment uptake (2003 and 2007 for start and end year respectively); SMR01 for number of admissions (2000 and 2010 for start and end year respectively)
Relative risk reduction:	***Ersatz RR function*** (RRR, SE ln(RRR)):	
In-hospital CPR	M & F (33%,0.103): absolute risk reduction	Tunstall-Pedoe (1992) [33]
Thrombolysis Aspirin Beta-blockers Primary PCI Primary CABG surgery ACE Inhibitors	M & F (0.31,0.298) M & F (0.23,0.177) M & F (0.04,0.691): assumed lower limit of 1% M & F (0.30,0.587) M & F (0.39,0.293) M & F (0.07,0.435)	Estess (2002)[25] ISIS-2 (1988)[26] Freemantle (1999) [29] Keeley (2003)[28] Yusuf (1994)[27] ACE-I MI Collaborative Group (1998) [30]
Clopidogrel	M & F (0.03,0.457)	Chen (2003)[31] Sabatine (2005)[32]
Non-ST segment elevation acute coronary syndrome (NSTEACS)		
Eligible patients: Emergency admissions with a primary diagnosis of myocardial infarction (Ratio STEMI/nSTEMI in 2010 informed by ratio in 2011 from SMR01. Ratio STEMI/nSTEMI in 2000 as	***Poisson distribution*** (nSTEMI + unstable angina admissions)	Linked Scottish Morbidity Records (SMR01)

40/60) or primary diagnosis of unstable angina		
Case fatality rate	Sample size (*n*) = emergency admissions for unstable angina in 1986 from SMR01 ***Beta distribution*** (cases = fatal cases within 1 year, non-cases = non fatal cases within 1 year)	Linked Scottish Morbidity Records (SMR01)
Treatment uptake	• *Medications and in-hospital CPR:* ***Beta distribution*** (cases = NSTEACS admissions × medication uptake, non-cases = NSTEACS admissions – cases) • *PCI and CABG*: ***Beta distribution*** (cases = unstable angina admissions from SMR01 × PCI/CABG uptake, non-cases = unstable angina admissions – cases)	English MINAP (2003 and 2010 for start and end year respectively); SMR01 (2000 and 2010 for start and end year respectively)
Relative risk reduction:	***Ersatz RR function*** (RRR, SE ln(RRR)):	
In-hospital CPR	M & F (33%,0.103): absolute risk reduction	Tunstall-Pedoe (1992)[33]
Aspirin & heparin Primary CABG surgery Early PCI Beta blockers Clopidogrel ACE Inhibitors	M & F (0.33,0.470) M & F (0.39,0.293) M & F (0.32,0.592) M & F (0.04,0.691): assumed lower limit of 1% M & F (0.07,0.435) M & F (0.07,0.435)	Oler (1996)[36] Yusuf (1994)[27] Fox (2005)[38] Freemantle (1999)[29] Yusuf (2001)[39] ACE-I MI Collaborative Group (1998)[30]
Aspirin alone	M & F (0.15,0.139)	Antithrombotic Trialists' Collaboration ATC (2002)[35]
Platelet glycoprotein IIB/IIIA inhibitors	M & F (0.09,0.530)	Boersma (2002)[37]
Secondary prevention post myocardial infarction (MI)		
Eligible patients: Ever having had a myocardial infarction since 1981	***Poisson distribution*** (admissions since 1981 from SMR01, excluding AMI admissions in 2010 and HF admissions since 1981, minus assumed overlap with community Heart Failure)	Linked Scottish Morbidity Records (SMR01)
Case fatality rate	Sample size (*n*) = admissions since 1981 alive on 1st January 1995 ***Beta distribution*** (cases = fatal cases within 1 year, non-cases = non-fatal cases within 1 year)	Linked Scottish Morbidity Records (SMR01)
Treatment uptake	***Beta distribution*** (cases = *n* × medication uptake, non-cases = *n* – cases)	Primary Care Clinical Informatics Unit Research (PCCIUR) (2000 and 2010 for start and end year respectively)
Compliance	Sample size (*n1*) = ever having had MI in PCCIUR in 2010 with record of medication use: ***Beta distribution*** (cases = *n1* × assumed compliance, non-cases = *n1* – cases)	
Relative risk reduction:	***Ersatz RR function*** (RRR, SE ln(RRR)):	
Aspirin Beta blockers ACE Inhibitors Statins 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 (0.22,0.305)	ATC (2002)[35] Freemantle (1999)[29] Flather (2000)[40] Hulten (2006)[41] Anand and Yusuf (1999)[42]

Secondary prevention post revascularisation		
Eligible patients: Ever having had a revascularisation (excluding admissions for MI)	• ***Poisson distribution*** (CABG procedures from 1981 and PTCA procedures from 1989 excluding MI and HF admissions) • ***Rehabilitation (mortality benefits within last 6 years only): Poisson distribution*** (CABG/PTCA procedures from 1st January 2005 to 31st December 2010 excluding HF and MI admissions)	Linked Scottish Morbidity Records (SMR01)
Case fatality rate	Sample size (*n*) = ever having had revascularisation since 1981 alive on 1st January 1995 (separately for CABG and PTCA) ***Beta distribution*** (cases = fatal cases in 1 year, non-cases = non-fatal cases in 1 year)	Linked Scottish Morbidity Records (SMR01)
Treatment uptake	***Beta distribution*** (cases = *n* × medication uptake, non-cases = *n* – cases)	PCCIUR (2000 and 2010 for start and end year respectively)
Compliance	Sample size (*n1*) = ever having had revascularisation in PCCIUR in 2010 with record of medication use: ***Beta distribution*** (cases = *n1* × assumed compliance, non-cases = *n1* – cases)	
Relative risk reduction:	***Ersatz RR function*** (RRR, SE ln(RRR)):	
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]
Chronic stable coronary artery disease		
Eligible patients: Ever having had chronic stable artery disease but no myocardial infarction, revascularisation or heart failure (prior to 1/1/2010)	***Poisson distribution*** (Population in 2007 × (angina but no MI, HF or revascularisation prevalence obtained from PCCIUR) minus emergency admissions for unstable angina	Primary Care Clinical Informatics Unit Research (PCCIUR)
Case fatality rate	Sample size (*n*) = ever having had angina but no MI in PCCIUR in 2010: ***Beta distribution*** (cases = *n* × CFR estimate, non-cases = *n* – cases)	Wijeysundera et al (2010)[6]
Treatment uptake	***Beta distribution*** (cases = *n* × medication uptake, non-cases = *n* – cases)	PCCIUR (2000 and 2010 for start and end year respectively)
Compliance	Sample size (*n1*) = ever having had angina but no MI in PCCIUR in 2010 with record of medication use ***Beta distribution*** (cases = *n1* × assumed compliance, non-cases = *n1* – cases)	
Relative risk reduction: Statins Aspirin	***Ersatz RR function*** (RRR, SE ln(RRR)): M & F (0.23,0.244) M & F (0.15,0.139)	 Wilt (2004)[45] ATC (2002)[35]

ACE Inhibitors	M & F (0.17,0.177)	Al-Mallah (2006)[46]
CABG for chronic stable coronary artery disease (0-6 years)		
Eligible patients: Ever having had chronic stable artery disease but no myocardial infarction, revascularisation or heart failure (prior to 1/1/2010)	***Poisson distribution*** (estimated count of patients with stable coronary artery disease (described above) in 2010 × (estimated uptake of CABG)): • ***2010***: Uptake of CABG: (number of CABG procedures from 1st Jan 2005 to 31st Dec 2010)/eligible patients in 2010 • ***2000***: Uptake of CABG: (number of CABG procedures from 1st Jan 1995 to 31st Dec 2000)/eligible patients in 2000	Linked Scottish Morbidity Records (SMR01)
Case fatality rate	As described in the post-revascularisation group	
Treatment uptake and compliance	Fixed at 100%	
Relative risk reduction: CABG (0-5 years)	***Ersatz RR function*** (RRR, SE ln(RRR)): M & F (0.39,0.293)	Yusuf (1994)[27]
Heart failure in patients requiring hospitalization		
Eligible patients: Admissions with a primary diagnosis of heart failure associated with CHD admissions	***Poisson distribution*** (admissions)	Linked Scottish Morbidity Records (SMR01)
Case fatality rate	Sample size (*n*) = admissions for HF associated with CHD admission in 1986 ***Beta distribution*** (cases = fatal cases within 1 year, non-cases = non-fatal cases within 1 year)	Linked Scottish Morbidity Records (SMR01)
Treatment uptake	• Aspirin: as described in the heart failure in community group Other medications: Sample size (*n1*) = HF admissions from HIS audit: • ***Beta distribution*** (cases = *n1* × medication uptake, non-cases = *n1* – cases)	Heath Improvement Scotland (HIS) Audit (2008). 2008 rates taken as 2010 values. Rates assumed 20% lower in 2000 (30% lower for Beta blockers).
Compliance	Sample size (*n2*) = HF admissions from HIS audit with record of medication use: ***Beta distribution*** (cases = *n2* × assumed compliance, non-cases = *n2* – cases)	Heath Improvement Scotland (HIS) Audit (2008)
Relative risk reduction: Aspirin ACE Inhibitors Beta blockers Spironolactone	***Ersatz RR function*** (RRR, SE ln(RRR)): M & F (0.15,0.139) M & F (0.20,0.177) M & F (0.35,0.128) M & F (0.30,0.128)	 ATC (2002)[35] Flather (2000)[40] Shibata (2001)[47] Pitt (1999)[48]
Heart failure in the community		
Eligible patients: Ever having had heart failure associated with CHD (prior to 1/1/2010)	***Poisson distribution*** (Population in 2010 × HF prevalence obtained from PCCIUR) minus HF hospital admissions)	Primary Care Clinical Informatics Unit Research (PCCIUR)

Case fatality rate	Sample size (*n*) = ever having had HF in PCCIUR in 2010: ***Beta distribution*** (cases = *n* × CFR estimate, non-cases = *n* – cases)	Wijeysundera et al (2010)[6]
Treatment uptake	***Beta distribution*** (cases = *n* × medication uptake, non-cases = *n* – cases)	PCCIUR (2000 and 2010 for start and end year respectively)
Compliance	Sample size (*n1*) = ever having had HF associated with CHD in PCCIUR in 2010 with record of medication use: ***Beta distribution*** (cases = *n1* × assumed compliance, non-cases = *n1* – cases)	
Relative risk reduction: Aspirin ACE Inhibitors Beta blockers Spironolactone	***Ersatz RR function*** (RRR, SE ln(RRR)): M & F (0.15,0.139) M & F (0.20,0.177) M & F (0.35,0.128) M & F (0.31,0.216)	 ATC (2002)[35] Flather (2000)[40] Shibata (2001)[47] Pitt (1999)[48]
Primary prevention therapies: Statins		
Eligible patients: Population	Population counts (no error)	National Records Scotland
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)	Scottish Health Survey
Case fatality rate	Sample size (*n*) = never having had angina or heart attack and currently taking lipid lowering drugs in 2010: ***Beta distribution*** (cases = *n* × CFR estimate, non-cases = *n* – cases)	Wijeysundera et al (2010)[6]
Compliance	***Beta distribution*** (cases = *n* × assumed compliance, non-cases = *n* – cases)	Scottish Health Survey
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	Population counts (no error)	National Records Scotland
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)	Scottish Health Survey
Case fatality rate	Sample size (*n*) = never having had angina or heart attack and currently taking medication to lower blood pressure in 2010: ***Beta distribution*** (cases = *n* × CFR estimate, non-cases = *n* – cases)	Wijeysundera et al (2010)[6]
Compliance	***Beta distribution*** (cases = *n* × assumed compliance, non-cases = *n* – cases)	Scottish Health Survey
Relative risk reduction: Treatments for high blood pressure	***Ersatz RR function*** (RRR, SE ln(RRR)): M & F (0.13,0.294)	Law (2003)[51]

WORKED EXAMPLES USING ERSATZ FOR UNCERTAINTY ANALYSIS

Below we illustrate our use of Ersatz for uncertainty analysis using males aged 75-84 in the most deprived quintile in England (~ means "distributed as").

Note that **Examples 1-3** are taken directly from the technical appendix of the English $IMPACT_{SEC}$ model[1] hence use English data and time points (start year 2000, end year 2007) in the calculations.

1 Uncertainty analysis for treatments

The net effects of aspirin in the secondary prevention post MI (within the last five years) group was calculated as follows:

DPPs (2007) = patient numbers × treatment uptake$_{2007}$ × compliance × relative mortality reduction × 1-year case fatality

= (12 226) × 0.75 × 0.70 × 0.15 × 0.067 ≈ 65

DPPs (2000) = patient numbers × treatment uptake$_{2000}$ × compliance × relative mortality reduction × 1-year case fatality

= (12 226) × 0.59 × 0.70 × 0.15 × 0.067 ≈ 51

Net DPPs were therefore calculated as = **$DPPs_{2007}$ – $DPPs_{2000}$** ≈ 65 – 51 ≈ 14

Table M above shows the probability distributions and associated Ersatz functions used for each input variable in the DPP calculations. For secondary prevention post MI we used Poisson (patient numbers); beta (treatment uptake, compliance, and case fatality rate) and the Ersatz RR function (relative risk reduction in the 1-year case fatality rate owing to treatment). More specifically, for males aged 75-84 in IMDQ5, the input values for the uncertainty analysis were as follows:

- Patient numbers ~ Poisson (population in 2007 × post-MI prevalence) minus overlap with the heart failure in the community group ~ Poisson (12 226)
- Treatment uptake in 2007 and 2000 ~ Beta (cases, non-cases)

If we let *n* denote ever having had MI in 2007 then cases = (*n* × uptake of aspirin) and non-cases = (*n* – cases). Cases = (587 × 0.75) = 440; non-cases = (587-440) = 147. Treatment uptake in 2007 was therefore ~ Beta (440,147). Likewise, treatment uptake in 2000 was ~ Beta (247,169).

- Compliance ~ Beta (cases, non-cases)

If we let *n1* denote ever having had MI in 2007 *and* with record of medication use in 2007 then cases = (*n1* × assumed compliance (0.70)) and non-cases = (*n1* – cases). Cases = (440 × 0.70) = 308; non-cases = (440-308) = 132. Compliance therefore ~ Beta (308,132)

- Relative risk reduction (RRR) ~ Ersatz RR function (RRR, SE ln(RRR))

where SE and ln denote standard error and natural logarithm, respectively. RRR was 1-odds ratio for aspirin use in the community taken from ATC (2002) = 1-0.85 = 0.15; with 95% Confidence Interval (0.11,0.19).[35] Using the 95% CIs, the SE of ln(RR) was calculated as:

ln(0.19)-ln(0.11)/(1.96×2) = 0.139

Relative risk reduction for aspirin use was therefore ~ Ersatz RR function (0.15,0.139)

- Case fatality rate ~ Beta (cases, non-cases)

Parameter uncertainty around case fatality rates was calculated at the national level and assumed constant across all IMD quintiles. If we let *n* denote ever having had MI in 2007 in England then cases = (*n* × assumed CFR (0.067)) and non-cases = (*n* – cases). Using the GPRD data for males aged 75-84 and assumed CFRs,[6] cases = (5348 × 0.067) = 358; non-cases = (5348-358) = 4990. Case fatality for the post-MI group was therefore ~ Beta (358, 4990).

Putting all this together, 10 runs in Ersatz gave the following estimates of each input variable randomly drawn from the relevant probability distributions from which we calculate the net DPPs for aspirin use in male post myocardial infarction survivors aged 75-84 in IMDQ5:

Ten runs in Ersatz to calculate net DPPs for aspirin use in males aged 75-84 in IMDQ5 in England(post-MI in last 5 years)

Run	Numbers	$Uptake_{2007}$	Compliance	Relative risk reduction	Case fatality rate	$Uptake_{2000}$	Net DPPs†
	Probability distributions						
	Poisson	Beta	Beta	RR	Beta	Beta	
	Col A	Col B	Col C	Col D	Col E	Col F	
1	12 272	0.737	0.681	0.166	0.068	0.591	13.7
2	12 297	0.759	0.653	0.184	0.069	0.581	18.3
3	12 225	0.741	0.687	0.145	0.076	0.607	12.3
4	12 428	0.736	0.697	0.166	0.069	0.587	14.6
5	12 252	0.712	0.778	0.189	0.065	0.580	15.5
6	12 141	0.782	0.727	0.175	0.068	0.588	20.4
7	12 154	0.777	0.715	0.135	0.066	0.592	14.4

8	12 397	0.734	0.698	0.151	0.069	0.591	12.9
9	12 220	0.723	0.727	0.153	0.070	0.558	15.6
10	12 427	0.772	0.684	0.186	0.065	0.593	18.5
Point estimate	**12 226**	**0.75**	**0.70**	**0.15**	**0.067**	**0.59**	**14**

† Net DPPs = (A×B×C×D×E) - (A×F×C×D×E)

Uncertainty intervals for treatment contribution DPPs
In each Ersatz run, net DPPs were calculated for all age-sex-IMD groups and were then summed for each medication within each of the 9 mutually exclusive CHD patient groups. Each of the nine treatment DPP totals was then multiplied by a correction for poly-pharmacy (which varied across patient groups but took the same value in each of the 1000 Ersatz runs). An estimate of the total treatment contribution to model DPPs was obtained by summing the nine patient group totals.

95% uncertainty intervals from the set of 1000 runs (2.5^{th} and 97.5^{th} percentiles) were extracted for the nine treatment totals plus the overall estimate of treatment contribution DPPs.

2 Uncertainty analysis for change in binary risk factors

The DPPs attributable to change in smoking prevalence in England over 2000-2007 was calculated as follows:

DPPs = expected CHD deaths in 2007 (had mortality rates in 2000 remained constant) × ($PARF_{2000}$ – $PARF_{2007}$)

where PARF = [P × (RR-1)] / [1 + P × (RR-1)]; P is the prevalence of the risk factor and RR is the relative risk for CHD mortality associated with risk factor presence. For the three binary risk factors (smoking, diabetes, and physical activity) we used the following probability distributions: Poisson (expected deaths); beta (risk factor prevalence) and the Ersatz RR function (relative risk reduction owing to elimination of exposure). More specifically, for males aged 75-84 in IMDQ5, the input values for the uncertainty analysis were as follows:

- Expected CHD deaths in 2007 ~ Poisson (population in 2007 × CHD mortality rates in 2000) ~ Poisson (4236)
- Estimates of smoking prevalence ~ Beta (cases, non-cases)

If we let *n* denote the number of Health Survey for England male respondents aged 75-84 in IMDQ5 over all years from 2000 to 2007 (i.e. pooled data) then cases = (*n* × estimate of smoking prevalence) and non-cases = (*n* – cases). Cases = (439 × 0.160) = 70; non-cases = (439-70) = 369. Smoking prevalence over 2000-2007 therefore ~ Beta (70,369). The same method was used for a pooled estimate of smoking prevalence at the national level. Smoking prevalence over 2000-2007 in England for males aged 75-84 ~ Beta (283,2710)

National estimates of smoking prevalence were calculated in the start and final years of the model (2000 and 2007). Smoking prevalence in England for males aged 75-84 in 2000 ~ Beta (22,225); smoking prevalence in England for males aged 75-84 in 2007 ~ Beta (26,216)

- Increased relative risk attributable to smoking ~ Ersatz RR function (RR, SE ln(RR))

where RR was taken from the CPS-II study but modified to fit into the ten-year age bands used for $IMPACT_{SEC}$.[57] For males aged 75-84, RR for smoking = 1.31 with 95% CI (1.11,1.56). Using the 95% CI the SE of ln(RR) was calculated as follows:

ln(1.56)-ln(1.11)/(1.96×2) = 0.088

The relative risk for smoking in males aged 75-84 was therefore ~ Ersatz RR function (1.31, 0.088)

Putting all this together, ten runs in Ersatz gave the following estimates of each input variable randomly drawn from the relevant probability distributions from which we calculate DPPs from the change in smoking prevalence over 2000-2007 in males aged 75-84 in IMDQ5:

Ten runs in Ersatz to calculate DPPs for change in smoking prevalence over 2000-2007 in males aged 75-84 in IMDQ5 in England

Run	Expected deaths	Pooled % $smoke_{IMD}$	Pooled % $smoke_{Eng}$	Relative risk	% smoke in 2000_{Eng}	% smoke in 2007_{Eng}	DPPs[a]
	Probability distributions						
	Poisson	Beta	Beta	RR	Beta	Beta	
	Col A	Col B	Col C	Col D	Col E	Col F	
1	4258	0.141	0.103	1.072	0.095	0.127	-13.3
2	4207	0.175	0.092	1.231	0.082	0.101	-33.2
3	4294	0.169	0.097	1.461	0.089	0.096	-23.5
4	4130	0.161	0.092	1.377	0.080	0.118	-94.5
5	4294	0.154	0.093	1.169	0.108	0.083	28.7
6	4259	0.169	0.100	1.337	0.067	0.112	-101.4
7	4251	0.205	0.098	1.094	0.069	0.131	-50.4
8	4290	0.169	0.106	1.371	0.095	0.092	6.3
9	4310	0.135	0.094	1.299	0.079	0.093	-25.1
10	4402	0.151	0.090	1.158	0.050	0.100	-56.2
Point estimate	**4236**	**0.160**	**0.095**	**1.31**	**0.089**	**0.108**	**-38**

[a] Intermediate steps in calculating DPPs as follows:
PARF using pooled data (IMD) = (B × (D-1))/(B × (D-1)+1);
PARF using pooled data (England) = (C × (D-1))/(C × (D-1)+1).
SEC gradient calculated as the ratio of these two quantities.
PARF in 2000 (England) = (E × (D-1))/(E × (D-1)+1);
PARF in 2007 (England) = (F × (D-1))/(F × (D-1)+1)

DPPs = A × ((PARF in 2000 (England) × SEC gradient) - ((PARF in 2007 (England) × SEC gradient)

Uncertainty intervals for binary risk factor DPPs
Within each run, DPPs were calculated for all age-sex-IMD groups and were then summed within each of the three binary risk factors. 95% uncertainty intervals from the set of 1000 runs (2.5^{th} and 97.5^{th} percentiles) were extracted for each risk factor total. The 95% uncertainty intervals were then scaled down using an overall correction for cumulative risk reduction (See Section 1.3 and Table D).

3 Uncertainty analysis for change in continuous risk factors

DPPs attributable to change in mean levels of systolic blood pressure (SBP) in England over 2000-2007 were calculated as follows:

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

For continuous risk factors (SBP, total cholesterol, fruit and vegetable consumption, and BMI) we used the Poisson (expected deaths) and Normal probability distributions (mean risk factor levels and the beta coefficients quantifying the change in CHD mortality resulting from a one-unit absolute change in risk factor level between 2000 and 2007). The input values for the uncertainty analysis were as follows:

- Expected deaths ~ Poisson (population in 2007 × CHD mortality rates in 2000) ~ Poisson (4236)
- Estimates of SBP levels ~ Normal (mean, SE mean)

For males aged 75-84 in IMDQ5 mean SBP levels using all Health Survey for England data over the time period 2000 to 2007 ~ Normal (mean = 143.1 mmHg, SE = 1.51). The SE was estimated in Stata Version 11.1 to account for the complex survey design. Likewise, for males aged 75-84 in England mean SBP levels over 2000-2007 ~ Normal (mean = 141.0, SE = 0.49). The SEC gradient in mean SBP was computed as the ratio of these two quantities.

National estimates for 2000 and 2007 were used to estimate absolute change in SBP over the seven year period. In 2000, mean SBP for males aged 75-84 in England was ~ Normal (mean = 141.9, SE = 1.39); for 2007 mean SBP ~ Normal (mean = 135.8, SE = 1.48).

- Beta coefficients ~ Normal (mean, SE)

where the beta coefficient for SBP (on the logarithmic scale) taken from the PSC study for males aged 75-84 was -0.0212 with 95% CI (-0.0170,-0.0255) [53]. Using the 95% CIs the SE of the beta coefficient was calculated as follows:

(-0.0170) - (-0.0255)/(1.96×2) = 0.0022

The beta coefficient for SBP for males aged 75-84 in IMDQ5 was therefore ~ Normal (mean = -0.0212, SE = 0.0022).

Putting all this together, ten runs in Ersatz gave the following estimates of each input variable drawn from the relevant probability distributions from which we calculated DPPs from the absolute change in mean SBP over 2000-2007 in males aged 75-84 in IMDQ5:

Ten runs in Ersatz to calculate DPPs for change in mean SBP levels over 2000-2007 in males aged 75-84 in IMDQ5 in England

Run	Expected deaths	Pooled SBP_{IMD}	Pooled $SBP_{England}$	Beta	SBP in 2000_{Eng}	SBP in 2007_{Eng}	DPPs[a]
	Probability distributions						
	Poisson	Normal	Normal	Normal	Beta	Beta	
	Col A	Col B	Col C	Col D	Col E	Col F	
1	4168	142.7	141.8	-0.022	138.0	133.9	366.1
2	4149	146.2	142.1	-0.018	142.8	136.3	476.0
3	4075	143.5	141.7	-0.021	143.0	134.0	697.5
4	4225	144.2	140.6	-0.019	139.8	136.7	256.8
5	4240	142.8	140.7	-0.021	140.4	137.0	301.5
6	4194	143.8	141.8	-0.021	140.8	134.9	502.2
7	4234	144.1	140.5	-0.025	144.4	134.0	1012.8
8	4126	142.0	141.9	-0.023	141.3	132.2	778.0
9	4291	145.3	141.7	-0.019	140.2	135.2	389.1
10	4264	141.5	140.8	-0.025	138.4	137.6	84.0
Point estimate	**4236**	**143.1**	**141.0**	**-0.0212**	**141.9**	**135.8**	**524**

[a] Intermediate steps in calculating DPPs as follows:
SEC gradient calculated as B/C.
Absolute change in mean SBP calculated as (E × SEC gradient) – (F × SEC gradient)

DPPs = (1-exp(D × (absolute change in mean SBP))) × A

Uncertainty intervals for continuous risk factor DPPs
Within each run, DPPs were calculated for all age-sex-IMD groups and were then summed within each of the four continuous risk factors. For systolic blood pressure and total cholesterol we then subtracted the DPPs calculated in the treatment (primary prevention) component of the model from the DPPs calculated in the risk factor component (See Section 1.4.6). 95% uncertainty intervals were then calculated from the set of 1000 runs (taken from the 2.5^{th} and 97.5^{th} percentiles) for the four continuous risk factor DPP totals. These were then scaled down using an overall correction for cumulative risk reduction.

Uncertainty intervals for total risk factor contribution DPPs
Within each run, the total risk factor contribution to model DPPs was obtained by summation of six risk factor DPPs totals (within each age-sex-IMD group). A 95%

uncertainty interval for the overall risk factor contribution was obtained from the set of 1000 runs by taking the 2.5th and 97.5th percentiles. These lower and upper limits were then scaled down using the correction for cumulative risk reduction.

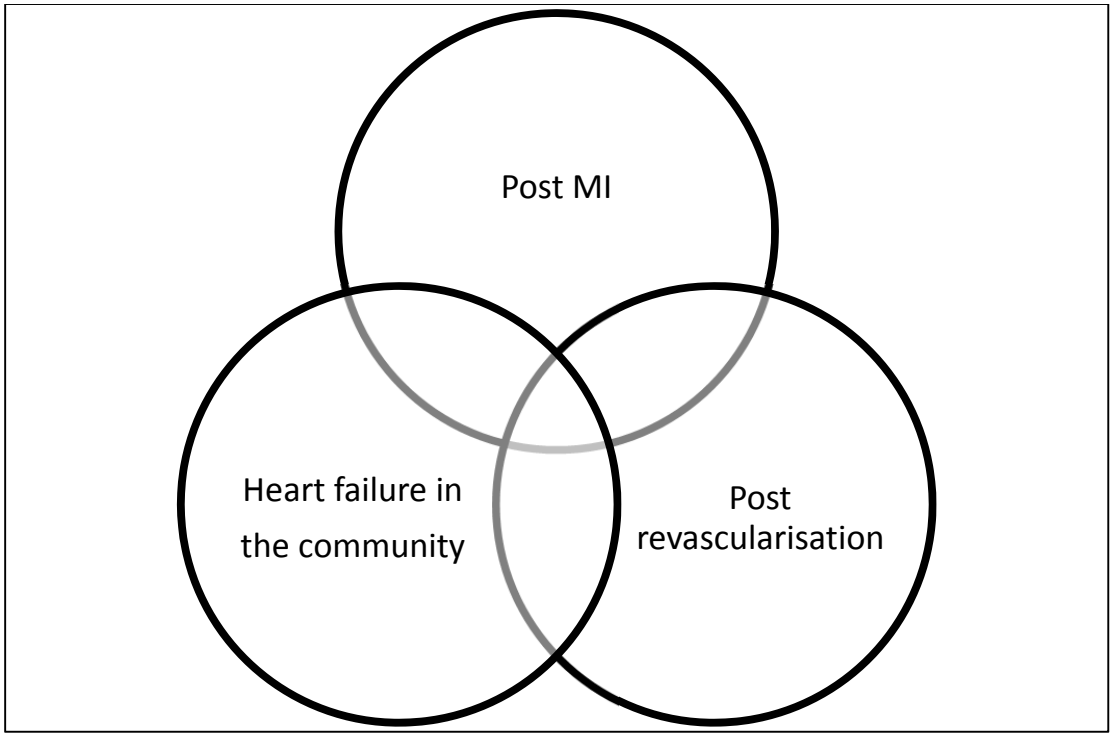
Uncertainty intervals for total model DPPs (changes in treatment uptake and risk factors)

Within each run, we also calculated an estimate of the total model DPPs by summation of the treatment contribution DPPs and the risk factor contribution DPPs *after* adjustment for cumulative risk reduction. The standard deviation of the estimated total model DPPs over the set of 1000 runs was extracted for England and each deprivation quintile. The 95% uncertainty intervals for total model DPPs were then obtained as follows:

Lower limit = estimate – (1.96 × standard deviation)
Upper limit = estimate + (1.96 × standard deviation)

Table O. Assumptions and overlap adjustments used in the IMPACT$_{SEC}$ model

Potential overlaps between patient groups with chronic CHD



Therefore, to avoid double counting, potential overlaps between different groups of patients were identified and appropriate adjustments made by subtracting one group from another. For instance, we can subtract the number of severe heart failure patients treated in hospital from the total number of heart failure patients in the community (because community heart failure patients could be admitted to hospital on one or more occasions). As far as possible the linked Scottish Morbidity Records (SMR01) and death record dataset has been used to assign individual patients to only one of the nine disease states; thus avoiding overlaps. Additionally patients within the PCCIUR dataset were assigned to mutually exclusive groups. In both the SMR01 and the PCCIUR a hierarchy of allocation based on case-fatality was created to assign an individual patient (existing in multiple patient groups) to just one patient group (the one with the highest case fatality). The hierarchy structure used is shown in Figure O.1.

Where this process is not possible then assumptions on overlap adjustment were made showing how potential overlaps were accounted for; these are shown in the table below. Patient overlaps for the final year of the model are shown in Figure O.2.

Table O.1 Main assumptions and overlap adjustments used in the IMPACT$_{SEC}$ model

Treatment category	Assumptions and overlap adjustments	Justification
Post-AMI	Assume 25% already counted in the heart failure in community group. This was reduced from 30% as all patients with HF admissions since 1981 had been excluded from this group	Weir (2006)[63]
Angina in the community	Start with the total numbers with angina in the community (without MI, HF or revascularisation) based on PCCIUR prevalence from mutually exclusive groups. Then deduct persons already treated for unstable angina in hospital	Capewell (2000)[2]
Heart failure in the community	Based on PCCIUR prevalence of patients with HF associated with CHD from mutually exclusive groups. Then deduct persons treated for severe heart failure in the hospital (already counted)	
Fall in population blood pressure	Estimate the number of DPPs by hypertension treatment. Then subtract this from the total DPPs attributed to the secular fall in population blood pressure	Capewell (1999)[3] Capewell (2000)[2]
Fall in population total cholesterol	Estimate the number of DPPs by cholesterol lowering medication. Then subtract this from the total DPPs attributed to the secular fall in population cholesterol	

AMI denotes acute myocardial infarction, CHD coronary heart disease, DPPs deaths prevented or postponed, PCCIUR Primary Clinical Care Informatics Unit Research.

Figure O.1 Assignment of patients and overlaps for Scottish IMPACT$_{SEC}$ (2010)

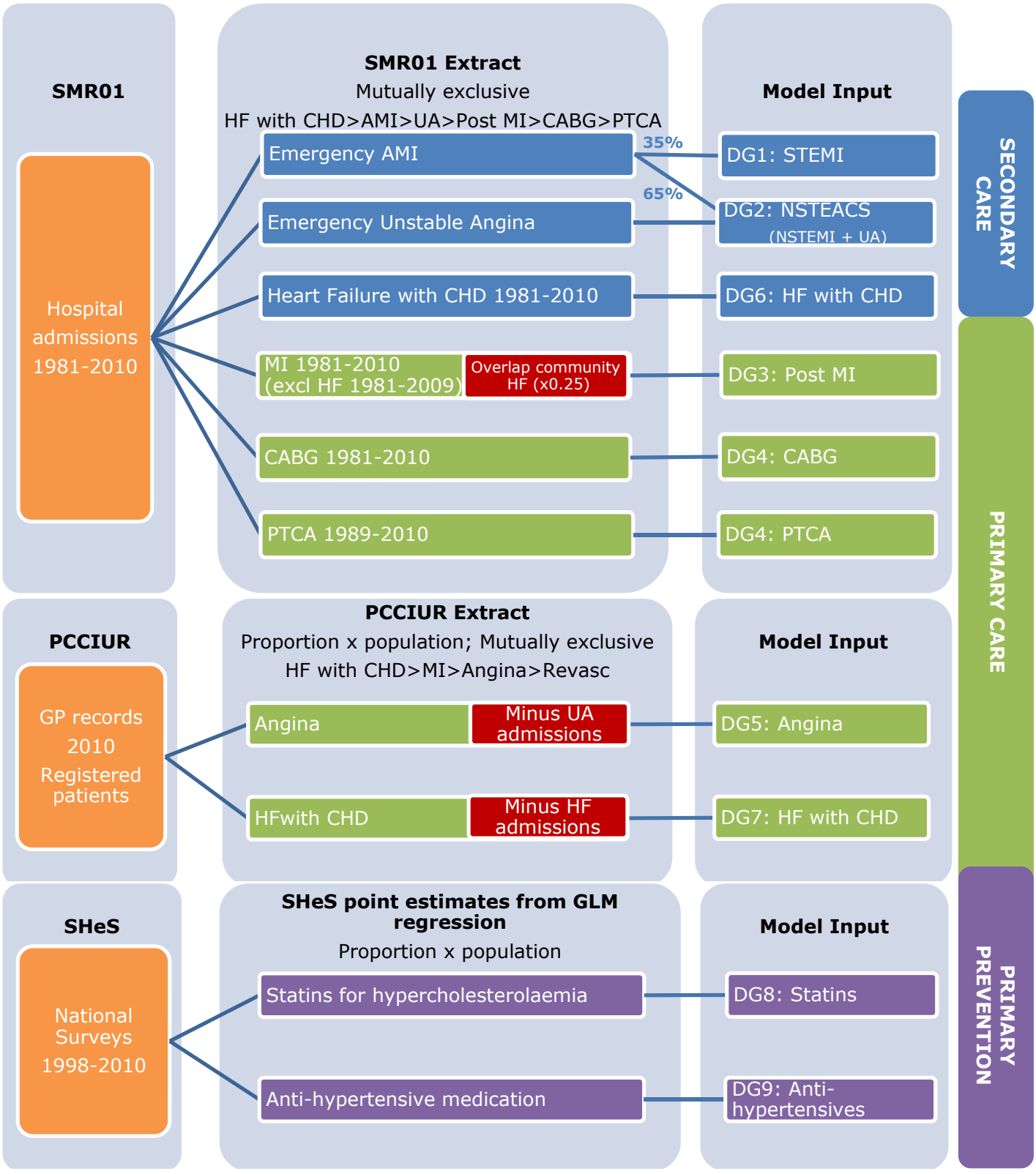
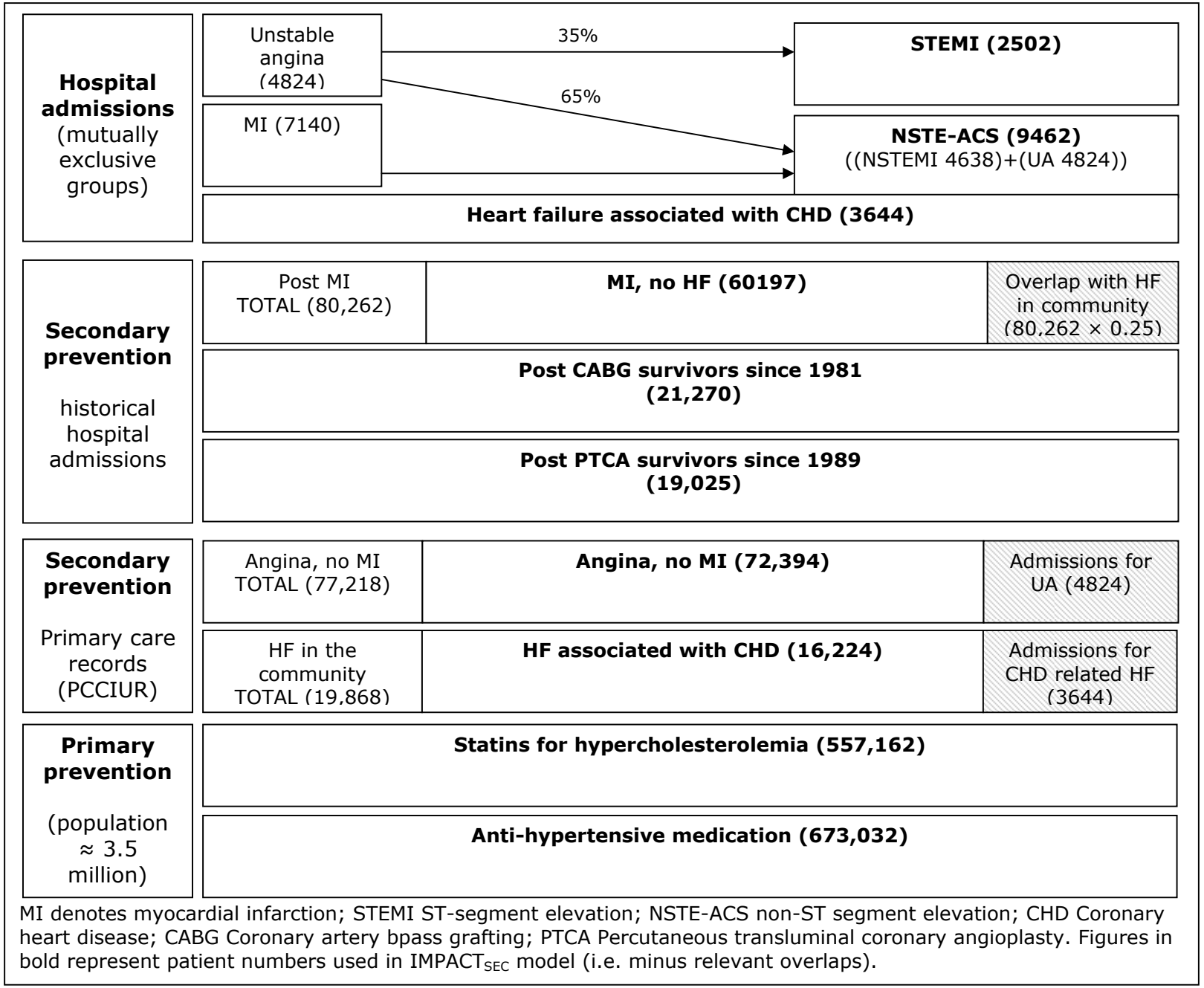


Figure O.2 Patient overlaps for IMPACT$_{SEC}$ with patient numbers for 2010



MI denotes myocardial infarction; STEMI ST-segment elevation; NSTE-ACS non-ST segment elevation; CHD Coronary heart disease; CABG Coronary artery bpass grafting; PTCA Percutaneous transluminal coronary angioplasty. Figures in bold represent patient numbers used in IMPACT$_{SEC}$ model (i.e. minus relevant overlaps).

Table P. 'Fixed gradients' for measuring risk factor change between two time points for deprivation quintiles

The sample size of the Scottish Health Survey (SHeS), roughly 6 to 8000 adults in each age-sex group aged 25 years and over, was not large enough to provide accurate/precise estimates of risk factor levels, and hence rates of change over time by age, sex, and deprivation quintiles (70 groups in total). Therefore, data from all surveys were pooled and a 'fixed gradient approach' was used for estimating risk factor change as key inputs into the regression and PARF deaths prevented or postponed calculations, as used in the English $IMPACT_{SEC}$ model[1].

The fixed gradient approach was 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 14 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 approach has the advantage of reducing the number of data breaks to a maximum of 14 (age by sex) for any single SHeS year and instead of discarding the survey information in the intermediate years, used the whole data series to improve and stabilise the 70 estimates. The disadvantage was that the assumption of a fixed gradient for each age-by-sex group remaining constant over time may not hold (e.g. the difference in risk factor level between a deprivation quintile and the national rate may be considerably larger in 2000 than in 2010). It was concluded that substantial relative changes over such a short period were possible but unlikely.

An illustrative example using data from the English $IMPACT_{SEC}$ model,[1] using the population-attributable risk fraction (PARF), is set out below.

EXAMPLE: Fixed gradient for change in smoking prevalence in men aged 45-54 in England

Step 1

Using the pooled 2000-7 HSfE data the national estimate of current smoking was 25.7% for men aged 45-54. Estimates by deprivation quintile ranged from 14.0% for men in the most affluent quintile (IMDQ1) to 46.5% in the most deprived (IMDQ5). The relative risk (RR) of smoking taken from the CPS-II study was 3.04[57]. Using the smoking prevalence (P) and the RR (assumed the same across deprivation quintiles) we calculated the PARF for England as a whole and each deprivation quintile using the formula:

$$PARF = [P \times (RR - 1)] / [1 + P \times (RR - 1)]$$

Applying step 1: Calculate the PARF gradient using 2000-7 pooled survey data

Men 45-54	England 2000-7	IMDQ1 2000-7	IMDQ2 2000-7	IMDQ3 2000-7	IMDQ4 2000-7	IMDQ5 2000-7
Proportion smokers (P)	0.2569	0.1398	0.1949	0.2668	0.2882	0.4652
RR	3.04	3.04	3.04	3.04	3.04	3.04
PARF	0.3427	0.2258	0.2819	0.3510	0.3671	0.4846
Gradient in PARF	1	0.659	0.823	1.024	1.071	1.414

The PARF calculated using pooled data at the national level was then set notionally to one, and the corresponding values for each deprivation quintile re-indexed to be below or above one. For example, the pooled gradient in the PARF for men aged 45-54 in Q1 was estimated to be 0.2258/0.3427 = 0.659.

Step 2

Using the HSfE data for the start and final year of the model we then derived the national PARF for 14 age-by-sex groups. The national PARF for men aged 45-54 based on prevalence (P) of 28.3% and RR of 3.04 in 2000 was 0.3662; a prevalence of 25.1% in 2007 gave a PARF of 0.3385.

Applying step 2: Calculate the national PARF in base and final year

Men 45-54	England 2000	England 2007
Proportion smokers (P)	0.2832	0.2508
RR	3.04	3.04
PARF	0.3662	0.3385

Step 3

The fixed gradient (Step 1) was then applied to the national PARF (Step 2) to produce estimates of the PARF for each deprivation quintile, separately for the base and final years of the model. For example, for men aged 45-54 in Q1 the 2000 estimate of the PARF was equal to 0.3662 (national PARF) multiplied by the gradient (0.659), to give an estimate of 0.2413. The 2007 estimate was equal to 0.3385 (national PARF) multiplied by the fixed gradient (0.659), to give an estimate of 0.2230.

Applying step 3: Estimate the PARF by deprivation quintiles for single years 2000 and 2007 using fixed gradient

Men 45-54	England 2000-7	IMDQ1 2000-7	IMDQ2 2000-7	IMDQ3 2000-7	IMDQ4 2000-7	IMDQ5 2000-7
PARF 2000	0.3662	0.2413	0.3012	0.3751	0.3923	0.5179
PARF 2007	0.3385	0.2230	0.2784	0.3467	0.3626	0.4787

Step 4: Calculating the DPPs

The formula for calculating DPPs using the change in PARF approach was as follows:

Expected CHD deaths in 2007 (had mortality rates in 2000 remained constant) × difference between the PARF in 2000 and 2007

Expected CHD deaths in 2007 × ($PARF_{2000}$ – $PARF_{2007}$)

Applying step 4: Estimate the DPPs due to change in PARF between 2000 and 2007

Men 45-54	**England 2000-7**	**IMDQ1 2000-7**	**IMDQ2 2000-7**	**IMDQ3 2000-7**	**IMDQ4 2000-7**	**IMDQ5 2000-7**
CHD mortality rate (2000)[a]	0.9131	0.5434	0.6644	0.8177	1.1173	1.6448
Population (2007)	3284291	736444	700676	660481	611424	575266
Aded deaths (2007)	3035	400	466	540	683	946
PARF 2000	0.3662	0.2413	0.3012	0.3751	0.3923	0.5179
PARF 2007	0.3385	0.2230	0.2784	0.3467	0.3626	0.4787
DPPs in 2007	**91**[b]	**7**	**11**	**15**	**20**	**37**

[a] Rate per 1000
[b] The total DPPs for England was based on the sum of the DPPs across the deprivation quintiles.

The 'fixed gradient' approach has the advantage of reducing the number of data breaks to a maximum of 14 (age by sex) for any single year and instead of discarding the survey information in the intermediate years, as other methods do, used the whole data series to improve and stabilise the 70 estimates. The disadvantage was that the assumption of a fixed gradient for each age-by-sex group remaining constant over time may not hold (e.g. the difference in risk factor level between a deprivation quintile and the national rate may be considerably larger in 2000 than in 2007). Furthermore, we concluded that substantial relative changes over such a short period were possible but unlikely.

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