Appendix 1. Example of mortality fall due to reduction in smoking in men aged 45-54

In Scotland, smoking prevalence in men aged 45-54 was 33% in 1994 and in the 'trends' analysis was assumed to fall to 21% by 2010, this would represent an absolute reduction of 12%, and a relative reduction of 35**%.**

Pooling of populations from the MONICA studies produced a beta (β, regression) coefficient value of **0.51.** (That is to say for every percent fall in relative smoking prevalence, the population coronary heart disease mortality would be expected to fall by 0.51%). The coronary heart disease deaths prevented or postponed as a consequence of a fall in smoking prevalence between 1994 and 2010 were then calculated as:
coronary heart disease deaths in that group in 1994 x risk factor decline x beta coefficient:

492 x 27.5% x 0.51 = 89 deaths prevented or postponed.

This calculation was then repeated
a) for maximum and minimum feasible values for each variable in that age group
b) for men and women in every others age group, and
c) for each risk factor.

In the results, maximum and minimum estimates were widest around blood pressure, reflecting the differing regression coefficients from MONICA, cohort studies, and meta-analyses [1] (appendix 2).[2][3][4]

Appendix 2. Methodological Issues: β coefficients and interactions between risk factors and treatments

β coefficients describing the relationship between risk factor declines and population CHD mortality

There are a range of different coefficients or relative risks describing the relationship between the three major risk factors and coronary heart disease mortality. These vary somewhat in magnitude (see table below).

Estimated β coefficients from multiple regression for the relationship between changes in population mean risk factors and changes in coronary heart disease mortality or events (men under 65 only - not adjusted for regression dilution bias)

	Estimated β Coefficients		
Study	**Smoking**	**Cholesterol**	**Blood Pressure (diastolic)**
MONICA, 2000[1]	0.73	1.31	0.53
Vartianen *et al.* 1994[5]	0.63	2	1.67
Sigfusson 1991[6]	0.51	2.22	1.06
Dobson *et al.* 1996[7]	0.4	1.15	1.26
Collins/MacMahon, 1990[3][4]			2.08
Seven Countries[2][8]		2.1	2.09
Law *et al.* 1994[9]		2.46	
Our 'best' estimates	0.51	2.0	1.06

Footnote: Vartiainen *et al* [5] and Sigfusson *et al* [10] are individual populations (Finland and Iceland respectively) from the MONICA study. Dobson *et al.* 1996[11] estimates are based on a subset of data from the MONICA study. Hence it should be pointed out that these estimates are not independent of each other. The major outcome in the MONICA 2000[1] study was coronary event rate, as opposed to coronary heart disease mortality from the other MONICA studies.

In many respects, it could be argued that the MONICA coefficients are most appropriate, as only the MONICA study has considered the impact of changes in risk factors on changes in coronary heart disease mortality at a population level. However, the MONICA coefficients have been repeatedly criticised for 'ecological bias' and may underestimate the relationship

between changes in risk factors and population trends in coronary heart disease mortality. This is because:

1) those who do not respond to risk factor surveys may be at higher risk than attendees, and a decreasing response rate to MONICA surveys was observed over the course of the study.[1]
2) the major outcome from the MONICA study was all coronary events, not just coronary heart disease mortality, which may be expected to slightly dilute the β coefficients obtained.
3) MONICA coefficients do not account for possible regression dilution bias; adjusted coefficients may be as much as 60% higher.[9]
4) The principal MONICA estimates made no allowance for a possible lag time between changes in the risk factor levels and changes in population coronary heart disease mortality.[1]

These MONICA coefficients are generally lower than from other sources,[2][8] even constituent MONICA populations.[5][10][11] The MONICA coefficients have thus been used in our model as minimum estimates using the data for males only. In many cases, the number of events among females were too small to obtain reliable estimates, and the smoking coefficient appeared particularly anomalous. However, these global MONICA coefficients were mostly within the range of those estimated from individual populations in the MONICA study, with the possible exception of blood pressure.

Coefficients derived from meta-analyses and the large cohort studies were regarded in our model as maximums[2][3][4][9] Maximum estimates were taken from Law *et al* for cholesterol,[9] and Seven Countries for blood pressure,[2][8] and best estimates were taken from the MONICA study in Iceland for blood pressure and smoking,[10] and Finland for

cholesterol.[5] The coefficients were reduced among older age groups to reflect good epidemiological evidence suggesting that relative risk is attenuated by age.[9][12]

These 'maximum' coefficients may be overestimates being based on cohort analyses which consider only the incremental effects of a risk factor on coronary heart disease mortality. These estimates are unlikely to be fully reversible when a population reduces its risk factor levels. Arguably, these may still be conservative, lacking the adjustment for regression dilution bias[2][13][14] recommended by some authors[2][9][13][14] but not all.[15]

Independence Issues

All these β coefficients were obtained from multiple regression analyses, hence the interaction between the major risk factors should have been accounted for. However, these β coefficients may still overestimate because most models, of necessity, entered data into the model on only a limited range of risk factors. For the MONICA study, these are smoking (yes or no), systolic blood pressure, total cholesterol, and body mass index.[1] There are many other important risk factors for coronary heart disease, including diet (such as consumption of fish oils and anti-oxidants), physical activity, affluence, employment and education. Some may be highly correlated with the four risk factors measured. It is likely, therefore, that the calculated coefficients contain the effects of some of these changes at a population level, as well as those in the measured risk factor.

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