Appendix 1: Calculating the combined effect of meeting all risk factor targets
For the combined risk factor target scenario the population impact fractions (PIFs) for coronary heart disease (CHD) and stroke were calculated multiplicatively from the individual PIFs for physical activity (PA), body mass index (BMI), blood pressure (BP), diabetes, alcohol and tobacco.

\[ PIF_{\text{Combined}} = 1 - (1 - PIF_{BP}) \times (1 - PIF_{Diab}) \times (1 - PIF_{PA}) \times (1 - PIF_{BMI}) \times (1 - PIF_{Alc}) \times (1 - PIF_{Tab}) \]

Figure 1 shows our conceptual model of the relationships between the risk factor targets and CHD, and Table 1 summarises the methods for calculation of the individual PIFs via the different pathways shown in Table 1. Notes below the table provide further detail on methods used to prevent double-counting of effects.

Figure 1 The modelled relationships between the WHO risk factor targets and CHD (NB. an identical process was used to estimate the combined risk factor effect on stroke.)

<table>
<thead>
<tr>
<th>PIF</th>
<th>Calculations</th>
<th>Sources</th>
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</table>
| PIF\text{BP} | 1. Calculate the full PA target effect on BP (i.e. directly and via BMI)  
2. Calculate the remaining BMI target effect on BP (i.e. the BMI effect excluding PA – see Note 1 below)  
3. Calculate the Salt target effect on BP  
4. Sum the effects on BP from steps 1 to 3, and calculate the CHD/Stroke PIF  
5. Calculate the CHD/Stroke PIF for the Hypertension target effect \( PIF_{\text{BP}} = \text{the biggest of the PIFs calculated in steps 4 and 5} \) | Cornelissen et al[1]  
Neter et al[2]  
He et al[3]  
Prospective Studies Collaboration[4] |
| PIF\text{Diab} | 1. Calculate the full PA target effect on Diabetes (i.e. directly and via BMI), using RR adjusted for BMI | Wahid et al Under review  
Prospective Studies Collaboration[5] |
2. Calculate the remaining BMI target effect on Diabetes (i.e. the BMI effect excluding PA – see Note 1 below), using RR adjusted for PA (using adjustment estimate)  
3. Sum the effects on Diabetes from steps 1 and 2, and calculate the CHD/Stroke PIF  
4. Calculate the CHD/Stroke PIF for the Diabetes target effect  
   \( PIF_{\text{Diab}} \) = the biggest of the PIFs calculated in steps 4 and 5  

| \( PIF_{\text{Pa}} \) (excluding effects via BP and Diabetes) | \( PIF_{\text{Pa}} \) = PIF calculated for the direct PA using RR CHD/Stroke estimates (see Note 2 below) |
| \( PIF_{\text{BMI}} \) (excluding effects via BP and Diabetes) | \( PIF_{\text{BMI}} \) = PIF calculated for the direct BMI using RR CHD/Stroke estimates (see Note 2 below) |
| \( PIF_{\text{Alc}} \) | \( PIF_{\text{Alc}} \) = PIF calculated using RR CHD/Stroke estimates from meta-analyses |
| \( PIF_{\text{Tob}} \) | \( PIF_{\text{Tob}} \) = PIF calculated using RR CHD/Stroke estimates from meta-analyses |

Note 1 – calculating the PA target effect on BMI  
To prevent double-counting of effects of changes in physical activity and BMI in the combined scenario, we estimated the change in BMI that could be attributed to the physical activity changes. Change in body weight was estimated using energy balance equations described by Hall et al[14], assuming change in fat free mass remains constant as a proportion of change in body weight[15].  

Resting energy expenditure, a component of the energy balance calculations, was estimated from regression models derived by Mifflin et al[16] from a subset of healthy subjects enrolled in a diet and heart disease study. Physical activity levels, also a component of the energy balance calculations, were estimated from the total MET hours spent in all activities over the day. We used FAO[17] estimates of energy costs for sleeping, personal care (dressing, showering), eating, cooking and sitting/sedentary activities (e.g. office work, selling produce, tending shop). Energy costs of time spent in all other activities, such as sports and fitness activities, occupational lifting, active travel and home activities (e.g. housework) were determined from responses to physical activity survey questions in the Health Survey for England[9] and the Physical Activity Compendium[18]. We assumed that the increase in physical activity from reaching the WHO target, if it was to be sustained in the population, would need to result from a reduction in time spent sitting/sedentary rather than in time spent on sleeping, personal care, eating or cooking.  

We calculated change in body weight from meeting the physical activity target by solving the energy balance equations using least squares and the generalised reduced gradient nonlinear method of optimisation in Excel. We then calculated change in BMI using height data from the Health Survey for England. From this we could distinguish the remaining BMI effect (i.e. the proportion of the BMI target effect that is not attributable to achieving the PA target).
Note 2 – calculating RRs for pathways not mediated by BP or Diabetes

To calculate the $PIF_{PA}$ and $PIF_{BMI}$ components of the combined PIF equation, we needed to know relative risks of CHD and Stroke associated with changes in PA and BMI that would not be mediated by either diabetes or BP (since the mediated contributions would already be counted in the $PIF_{Diab}$ and $PIF_{BP}$ calculations). Since we did not have published estimates of these RRs, we derived them using an optimisation process in Excel, assuming that the fractions of the disease attributable to the risk factor via the direct and indirect pathways would have to sum to the total attributable fraction.

This process is illustrated in Figure 2, with physical activity as the risk factor, diabetes as the intermediate variable and CHD as the disease (pathway A is the unknown). Using optimisation, we determined what the relative risks for CHD (pathway A) would need to be so that the total fraction of CHD attributable to PA (pathway C) would be equal to the sum of the contributions from PA directly (pathway A) and from PA via diabetes (pathway B).

The optimisation was performed twice. First we used the PA-CHD RR (Wahid et al meta-analysis, adjusted for BMI), the diabetes prevalence (HSE) and CHD mortality (GBD 2010) to derive a PA-CHD RR that is not mediated by diabetes (but may be mediated by BP). Second, we used the ‘partly-mediated’ RR output from the first step, along with the BP distribution (HSE) and CHD mortality (GBD 2010) to derive a PA-CHD RR that is not mediated by either diabetes or BP. This was the RR used in the calculation of the $PIF_{PA}$ for the combined analyses.

The same methods were used to solve for the relative risks of stroke; and the whole process was repeated with BMI as the risk factor, using BMI RR estimates of CHD and stroke (for pathway C) from the Prospective Studies Collaboration[5].

Figure 2 Conceptual diagram of the pathways between risk factor (physical activity), intermediate variable (diabetes) and disease (CHD) in the optimisation process.
References


