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ABSTRACT

Objective – Model the impact of targets for obesity, diabetes, raised blood pressure, tobacco use, salt intake, physical inactivity and harmful alcohol use, as outlined in the Global Non-Communicable Disease Action Plan 2013-2020, on mortality and morbidity in the UK population.

Design – Dynamic population modelling study

Setting – UK population

Participants - NA

Main outcome measures – Mortality and morbidity (Years Lived with Disability) from non-communicable diseases (NCDs) that are averted or delayed. Probability of achieving a 25% reduction in premature mortality from NCDs by 2025 (current WHO target) and a 33% reduction by 2030 (proposed target).

Results – The UK could achieve the 2025 and 2030 targets with only a little additional preventive effort compared to current practice. Achieving all seven risk targets could avert a total of 300,000 deaths (95% uncertainty interval: 250,000 to 350,000) and 1.3 million Years Lived with Disability (1.2 million to 1.4 million) from NCDs by 2025, with the majority of health gains due to reduced mortality and morbidity from heart disease and stroke, and reduced morbidity from diabetes. Potential reductions in morbidity from depression and in morbidity and mortality from dementia at older ages are also substantial.

Conclusions - The global premature mortality targets are a potentially achievable goal for countries such as the UK that can capitalise on many decades of effort in prevention and treatment. High morbidity diseases and diseases in later life are not addressed in the Global NCD Action Plan and targets, but must also be considered a priority for prevention in the UK where the population is ageing and the costs of health and social care are rising.

ARTICLE SUMMARY

Strengths and limitations of the study:

- The study combined functional demographic modelling of population forecasting, logistic regression modelling of 'business-as-usual' trends in NCD rates and NCD risk factors, and dynamic modelling of population health outcomes.

- We simulated the future changes in NCD mortality and morbidity that would occur: (1) with 'business-as-usual'; (2) if the UK could achieve the World Health Organization's risk factor reduction targets; and (3) if all NCD burden could be addressed.

- We also estimated the probability that the UK would meet the current WHO target of a 25% reduction in premature mortality by 2025 and the new target of a 30% reduction by 2030.

- Integrating projections of risk factor and disease trends with a population demographic model that stochastically forecasts trends in mortality, fertility and migration, is an important advance on existing global modelling methods.

- Future work will focus on integrating the health models with other big systems models, such as the AgMIP models [1], which focus on food security under climate change.

INTRODUCTION

Non-communicable diseases (NCDs) have been recognised as a major challenge for all nations in the 21st century, affecting people of all ages, gender, race and income level[2]. It is a burden that is in large part preventable; closely linked to a range of risky behaviours, including tobacco use, unhealthy diet, physical inactivity and harmful use of alcohol; risks that are themselves closely related to the societies and environments in which we live. In response to the United Nations declaration on addressing prevention and control of NCDs[2], the World Health Organization (WHO) developed a Global NCD Action Plan 2013-2020[3], which outlines global targets for improving prevalence of NCD risk factors (obesity, diabetes, raised blood pressure, tobacco use, salt intake, physical inactivity and harmful use of alcohol) with an overarching goal of achieving a 25% reduction in premature mortality from the four main NCDs (cardiovascular diseases, chronic respiratory diseases, cancers and diabetes) by the year 2025. Global modelling of the risk factor impacts on NCDs shows that premature mortality from the four main NCDs could be reduced globally by 22% in men and 19% in women, between 2010 and 2025, if the targets could be achieved[4].

It is the responsibility of individual countries to initiate actions to achieve the targets, and regularly measure and review national progress[5]. However, it is not clear to what extent the NCD and risk factor targets should guide priorities for action or to what extent progress will reflect a nation's improvement in health. While the four main NCDs are responsible for 87% of all NCD deaths worldwide, they only contribute to 57% of the ill health burden from NCDs[6]. There are also indications that targets for reducing tobacco use could be more ambitious[4]. These concerns are to some extent reflected in the new set of 'Sustainable Development Goals' (SDGs) and targets for 2030 that were adopted by United Nations world leaders in September 2015. The new health-related NCD goals aim to 'promote mental health and well-being' and to strengthen implementation of the WHO Framework Convention on Tobacco Control, alongside a revision of the premature

mortality goal to a one-third reduction by 2030. In response to the SDGs, the WHO has signalled its intent to expand work on prevention of NCDs in 2016-17[7].

More information is needed about the impact of achieving the WHO risk factor targets on morbidity from NCDs and about the impact on a broad range of NCDs including mental health and neurological disorders. In a study funded by the Richmond Group of Charities[8], PROMISE, we have examined the implications of the WHO risk factor targets for priority setting in the UK. We modelled the impact of meeting the risk factor targets on morbidity and mortality from a wide range of NCDs, and examined whether the UK is likely to achieve a 25% reduction in premature mortality by 2025. In addition, in order to estimate how much of the potentially preventable portion of NCD burden could be addressed by the WHO targets, we evaluated an 'ideal risk reduction' scenario in which everyone in the UK achieves a normal weight, is physically active, non-smoking, without diabetes or raised blood pressure, has an ideal salt intake and does not drink alcohol at harmful levels. In this paper, we report on the results of this study, and consider the implications for setting future targets for risk reduction.

METHODS

We developed a dynamic model for simulating the effect of annual changes in risk factors on annual burden of non-communicable diseases in the UK. The modelling was carried out in two parts. First, we used historical data on risk factors in England to project trends in salt consumption, physical activity, alcohol consumption, smoking, body mass index, diabetes and blood pressure forward to 2025, and then used these trends to estimate the proportional impact on NCDs of achieving the 25x25 targets. Second, we developed a population and mortality forecast model which estimated business-as-usual projections of NCD morbidity and mortality to 2025. This was then used as the baseline to apply the proportional changes in disease, which were calculated in the first model to estimate the impact of achieving the WHO 25x25 targets and the ideal risk reduction on NCD mortality and morbidity.

Risk factor projections model

Historical risk factor data were obtained from the Health Survey for England series[9]. This survey is conducted annually and collects data on a representative sample of community-living adults in England. Annual sample sizes are approximately 11,000 adults aged 18 and over. Data are collected on health behaviour (including diet, smoking, alcohol consumption and physical activity) using a standard questionnaire delivered and recorded by a trained interviewer. Anthropometric data, including body mass index and blood pressure, are recorded by a trained nurse. For the PROMISE project, we compiled a dataset (Stata Version 11) with data on the seven WHO targets from all surveys conducted between 1995 and 2012.

All risk factor projections were stratified by sex and broad age group (18 to 35; 36 to 55; 56+). For each stratum, following a method used for the UK Foresight 'Modelling future trends in obesity and their impact on health' project[10], we modelled the relationship between prevalence of the risk factor (p) and time (**t**) using the following equation (where *a* and *b* are model parameters):

$$p(\mathbf{t}) = \frac{1}{2}\big(1 + \tanh(a + b\mathbf{t})\big)$$

This relationship is convenient for modelling future projections, as it results in smooth changes over time that are constrained between minimum and maximum values of 0 and 100%. For each risk factor, we derived variables from the Health Survey for England dataset to match the risk factor definitions used for the WHO targets[11], and then used logistic regression to fit the above equation, with survey year providing the time variable. We then projected prevalence forward to 2025, assuming the equations hold until this time. Table 1 provides further details regarding projections for each of the seven risk factors.

Relative risks for the relationship between risk factors and diseases were taken from meta-analyses of prospective studies (Table 2). In most cases, these were restricted to meta-analyses of cohort studies, but in some cases meta-analyses that combined results from cohort studies and prospective

case control studies (i.e. nested in cohort studies) were also included. With the exception of salt, the relationship between the risk factors and disease outcomes was modelled directly, and preference was given to relative risks that were adjusted for the most of the other risk factors. The effect of salt on blood pressure levels was modelled using a meta-analysis of salt reduction trials[12], and then the subsequent impact of blood pressure on disease was modelled as described above.

The evidence relating a link between the risk factors and both dementia and depression is less established than for the other disease outcomes. In some cases the mechanisms are unclear[13], or previous results investigating the relationship have been highly heterogeneous[14]. Meta-analyses of the relationship between risk factors and depression and dementia are often not based on analyses adjusted for other risk factors, increasing the risk of confounding[15]. For this reason, we present two sets of modelled results, for analyses that both include and do not include depression and dementia as outcomes.

Evaluating population impact fractions (PIFs)

The WHO targets and the ideal risk reduction scenarios for salt consumption, physical activity, alcohol consumption, smoking, body mass index, diabetes and blood pressure are described in Table 2. Our implementation of the WHO targets depended on whether the risk reductions were relative reductions (e.g. a 30% reduction in smoking) or absolute reductions (e.g. halt the rise in obesity). For relative reductions in the prevalence of a risk factor (smoking, blood pressure, alcohol, physical inactivity), the reduction was applied to the projected prevalence in every year between 2010 and 2025. For absolute reductions in the prevalence of a risk factor (obesity, diabetes), the target prevalence was assumed to be the actual prevalence in 2010. For relative reductions in a mean consumption of a risk factor (salt), the reduction was applied in every year between 2010 and 2025, and the standard deviation of the distribution for each age-sex stratum was assumed to remain constant (i.e. the entire distribution was shifted). The ideal risk reduction scenarios were based on definitions in the Global Burden of Disease study[16].

Table 1 Methods for the projection of risk factors.

Risk factor	WHO definition	HSE years used	Comments
Overweight and obesity	Overweight: adults with BMI between 25 and 30. Obese: adults with BMI greater than 30.	All years between 1995 and 2012.	Five BMI categories were projected: ≤20; 20-≤25; 25-<30; 30-≤35; >35. The relationship between prevalence of each BMI category and survey year was modelled separately. Projections combined proportionately, in order to ensure the sum of all BMI categories was exactly 100% in any year.
Smoking	Prevalence of adult population currently using any tobacco product.	All years between 1995 and 2012.	The prevalence of current smoking and never smoking were projected. The prevalence of former smoking was assumed to be 100% - prevalence of never and current smokers.
Diabetes	Prevalence of raised blood glucose, or medication for raised glucose.	1998; 2003; 2006; 2009; 2010; 2011; 2012	We used prevalence of doctor-diagnosed diabetes. The WHO definition could not be used due to lack of representative data in England.
Blood pressure	Prevalence of adult population with SBP≥140mmHg or DBP≥90mmHg.	All years between 1995 and 2012.	Prevalence of raised blood pressure projected. To estimate health impact of raised blood pressure, relative risks are based on median SBP of age-sex-raised blood pressure groups in HSE2012.
Alcohol	Prevalence of heavy episodic drinking (consuming ≥60g alcohol on a single occasion at least monthly)	All years between 1998 and 2012.	Three alcohol categories were projected: abstainers (≤1g alcohol per week); non-harmful drinkers; harmful drinkers. Projections were combined proportionately, in order to ensure the sum of all alcohol categories was exactly 100% in any year. Relationships between alcohol and disease outcomes were based on difference in weekly alcohol consumption between alcohol groups, estimated using the HSE2012. A dummy variable was included in regression analyses to isolate the impact of changes in alcohol measurement in the HSE in 2006.
Physical inactivity	Prevalence of physical inactivity (less than 150 minutes of moderate-intensity activity per week, or equivalent).	1997; 1998; 2003; 2004; 2006; 2008; 2012	Three physical activity categories were projected: sedentary (≤0.2METh/d); not sedentary, but inactive; active. Logistic regression models estimated the trend in the prevalence of first two groups combined, and we separated between these two groups based on proportion of adults in HSE2012. The prevalence of activity was assumed to be 100% - prevalence of inactivity. Data between 1997 and 2012 were available on a consistent measure of inactivity, but only HSE2012 measured inactivity equivalent to the WHO definition. Regression models were based on the consistent measure of inactivity then adjusted according to the difference in the two measures recorded in HSE2012. The risk relationship between physical activity and disease outcomes based on difference in amount of physical activity (METh/d) between physical activity categories, estimated using HSE2012 data.
Salt (mediated by blood pressure)	Mean population intake of salt.	2008; 2009; 2010; 2011*	National Diet and Nutrition Survey urinary analyses data used to assess trends by age-sex groups. No trends apparent, so projections assume no change from current mean consumption levels. Mean and standard deviations used to generate normal distributions of salt consumption, which were converted into salt-related blood pressure using the prevalence of normotensives and hypertensives derived from the blood pressure projections, and parameters drawn from meta-analyses of salt reduction trials.

NB. HSE: Health Survey for England. BMI: Body Mass Index. SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure.
* Note that salt estimates are taken from urinary analyses in the National Diet and Nutrition Survey.

Table 2 WHO risk factor definitions, target levels and modelled disease outcomes.

Risk factor	Risk definitions and targets	Modelled NCD outcomes
Overweight and obesity	Overweight: adults with BMI between 25 and 30. Obese: adults with BMI greater than 30. WHO target: Halt the rise in obesity. Ideal target: Everyone normal weight (BMI 20-25; median 22)	CHD[37]; Stroke[37]; Diabetes[37]; Cirrhosis[37]; Colorectal cancer[37]; Kidney cancer[37]; Breast cancer[37]; Pancreas cancer[38]; Liver cancer[37]; Hypertensive heart disease[37]; Kidney disease[37]; Depression[39]; Dementia[40]
Smoking	Prevalence of adult population currently using any tobacco product. WHO target: 30% relative reduction. Ideal target: No current or past use of tobacco	COPD[41]; CHD[41]; Stroke[41]; Diabetes[42]; Lung cancer[43]; Oesophagus cancer[43]; Larynx cancer[43]; Stomach cancer[43]; Liver cancer[44]; Pancreas cancer[43]; Kidney cancer[43]; Cervix cancer[43]; Bladder cancer[43]; Depression[45]; Dementia[46]
Diabetes	Prevalence of doctor-diagnosed diabetes. WHO target: Halt the rise in diabetes. Ideal target: No prevalence of diabetes	CHD[47]; Stroke[48]; Depression[49]; Dementia[50]
Blood pressure	Prevalence of adult population with SBP≥140mmHg or DBP≥90mmHg. WHO target: 25% relative reduction in raised blood pressure. Ideal target: No prevalence of raised blood pressure	CHD[51]; Stroke[51]
Alcohol	Prevalence of heavy episodic drinking (consuming ≥60g alcohol on a single occasion at least monthly) and per capita consumption. WHO target: 10% relative reduction. Ideal target: No consumption of alcohol	CHD[52]; Stroke[53]; Hypertensive heart disease[52]; Diabetes[54]; Cirrhosis[55]; Liver cancer[56]; Mouth cancer[56]; Colorectal cancer[56]; Breast cancer[56]; Oesophagus cancer[56]
Physical inactivity	Prevalence of physical inactivity (less than 150 minutes of moderate-intensity activity per week, or equivalent). WHO target: 10% relative reduction. Ideal target: Everyone physically active	CHD*; Stroke*; Diabetes*; Breast cancer[30]; Colorectal cancer[30]; Depression[57]; Dementia[58]
Salt (mediated by blood pressure)	Mean population intake of salt. WHO target: 30% relative reduction. Ideal target: Mean intake of 1000mg/day	CHD[12, 51]; Stroke[12, 51]

NB. CHD: Coronary Heart Disease; COPD: Chronic Obstructive Pulmonary Disease. * Wahid et al. In press, Journal of American Heart Association.

Using the disease projections and the relative risk estimates, we calculated PIFs for each disease-risk

factor relationship, in each age-sex stratum, in every year between 2010 and 2025. PIFs estimate the

proportion of disease in a population that is removed under a counterfactual scenario (in this case,

in the scenario where the WHO targets or ideal levels are achieved). We calculated PIFs using the

following equation, where there are k risk factor categories, p_i is the proportion of the population in

risk factor category i in the estimate year based on projections, p'_i is the proportion of the

population in risk factor category *i* in the estimate year based on achieving the WHO or ideal risk reduction target, and RR_i is the relative risk for the disease in risk factor category *i*:

$$PIF = \frac{\sum_{i=1}^{k} p_i RR_i - \sum_{i=1}^{k} p'_i RR_i}{\sum_{i=1}^{k} p_i RR_i}$$

We present results separately for each risk factor (i.e. when only the single risk factor target is achieved) and in combination (i.e. if all risk factor targets are achieved). For the combined scenario, we multiplicatively combined PIFs for blood pressure, diabetes, physical activity, BMI, alcohol and tobacco, adjusting for double-counting where there are interdependencies in risks (e.g. physical activity affects CHD directly and via changes in BMI; BMI affects CHD directly and via changes in blood pressure). These methods for avoiding double counting are described in further detail in Appendix 1. Where risk factors were both mediating variables and the subject of WHO targets (blood pressure and diabetes), we took the larger of the effects. For example, we calculated the combined effects of meeting physical activity, BMI and salt targets on BP (assuming they are independent i.e. additive), we then calculated the effect of the hypertension target on BP, and took only the larger of these two effects. Similarly, we calculated the combined effect of meeting physical activity and BMI targets on diabetes, estimated the effect of the diabetes target on diabetes prevalence, and took only the larger of the two effects.

We calculated 95% uncertainty intervals for all PIFs, based on lognormal distributions for the relative risks and normal distributions for other variables as reported in the literature (e.g. effect of salt on blood pressure), using Monte Carlo analysis[17].

Disease projections model

The PIFs were applied to projected disease rates in a UK population and mortality forecast model in order to estimate disease outcomes of meeting WHO targets. The model was built in R (version 3.1.2) using packages *demography* and *systemfit*.

The UK population was forecast out to 2025 based on historical demographic patterns. We used data from the period 1938 to 2010, obtaining population and mortality from the Human Mortality Database[18], fertility from the Human Fertility Database[19], and deriving net migration for the same time period, from these data. These demographic rates were smoothed using penalised regression splines. We then fitted functional demographic models[20] to mortality, fertility and migration rates from 1938 to 2010, and used these models to forecast future rates out to 2030. Finally, we simulated the population over time to 2030, using bootstrapping to estimate uncertainty in the population from the errors in the mortality, fertility and migration models.

For projecting disease-specific mortality, we developed regression models using methods described by Salomon and Murray[21] that ensure that disease-specific mortality projections are consistent with the projected all-cause mortality envelope. We obtained cause-specific mortality data from the WHO database[22], focusing on deaths coded using the most recent version of the International Classification of Diseases (ICD-10). ICD-10 was only adopted in the UK in 2001, which limited the analyses to only 10 years of past data points. Including deaths coded using the preceding ICD-9 version, increased the years of available data back to 1980, but although we applied translations from ICD-9 to ICD-10[23], there remained visible anomalies in the data before/after the change in coding for some disease. Concerned that this could lead to incorrect predictions of trends, we therefore restricted the analyses to the ICD-10 coded data, but broadened our data set to include data from all EU countries, which have similar high income and low mortality profile, and included GDP per capita into the model as an explanatory variable.

Deaths coded to heart failure (I50) were redistributed to the primary causes (e.g. coronary heart disease (CHD), hypertensive heart disease, COPD and chronic kidney disease)[24]. Deaths were grouped into three age groups: <35, 35-64 and 65+. For each age group, we determined country-specific mortality for each risk factor-related disease, and all other diseases, as a proportion of all-cause mortality in each country. Using methods described by Salomon and Murray[21] we specified

a multivariate normal model for the log of the ratios of each cause fraction to the cause fraction for all other diseases, using the log of all-cause mortality rate and GDP per capita[25] as explanatory variables. We then derived parameter values for the disease projections models, for each age group, using seemingly unrelated regression[26].

To project disease rates forward in time for the UK, we applied the mortality projections from our population forecasts and GDP projections from the World Bank[25] in the disease projections models, to determine the annual average change in disease rates for the UK out to 2030.

Evaluating disease burden

To determine the future changes in population if the WHO or ideal risk reduction targets are achieved we first calculated the new population mortality, using the PIFs to determine future changes in mortality from the NCDs. We then re-simulated the future population out to 2030, using the new rates of mortality, but assuming no change in forecasts of fertility and migration.

Effects on premature mortality were estimated as the change in probability of death from NCDs between the ages of 30 and 69[3]. As was done in the global modelling of the WHO NCD reduction targets[4], our estimate was unconditional, in that it excluded deaths from other causes (e.g. injuries), but due to the broader range of diseases of interest in the PROMISE study, we included all NCDs, rather than restricting the analysis to the four main NCD groups (cardiovascular, cancer, diabetes and chronic respiratory diseases).

We defined the morbidity burden associated with non-communicable diseases as the reduction in one year of life at full health. This was calculated at each age and sex, from Global Burden of Disease estimates of prevalent years lived with disability (YLDs). We included a business-as-usual trend in morbidity if there had been a significant change in Global Burden of Disease YLD estimates between 1990 and 2010. For diabetes and depression, we estimated a morbidity effect of achieving the WHO targets, which we estimated using the PIFs for these diseases in the same way that the PIFs were applied to mortality for all other NCDs.

RESULTS

With a continuation of current trends in mortality, fertility and migration, the number of 30 to 69 year olds in the UK population is expected to increase from around 32.5 million in 2010 to 33.4 million in 2025, with the proportion of the whole population aged over 70 rising from 12.5% in 2010 to 16.2% by 2025. With business-as-usual, the probability of premature mortality (30-69 years) from non-communicable diseases among men is expected to fall from 17.6% in 2010 to 13.7% in 2025 (Figure 1). This equates to a relative reduction of 22%, which is just short of the WHO 25% reduction target. Premature mortality among women, is expected to reach the WHO target, falling from 11.9% in 2010 to 8.9% in 2025 (Figure 1), which equates to a relative reduction of 25%. If we assume trends in risk factors and diseases continue to 2030, the outcomes follow the same pattern, with men (30%) falling short of the 33% reduction target and women (33%) just reaching it.

There is added benefit from achieving the WHO 2025 behavioural risk factor targets (Table 3), which ranges from an added relative reduction of 0.1% (reduced physical inactivity) to 2.3% (rise in obesity halted). The combined effect of achieving all seven risk factor targets (relative reduction of 6.1% for men and 3.0% for women) is sufficient for both men and women to reach the 25% premature mortality reduction target by 2025 (Figure 1). Achieving the WHO targets would, however, achieve only a quarter of what could potentially be achieved for men and less than a fifth of what could potentially be achieved for women.

Achieving all seven behavioural risk factor targets would avert a total of 300,000 deaths (at all ages) and 1.3 million YLDs from the reductions in related NCDs (excluding effects on depression and dementia) between 2010 and 2025 (Table 4). The majority of improvements in mortality are due to fewer deaths from CHD and stroke, while the majority of improvements in morbidity are due to reduced rates of diabetes, CHD and stroke (Figure 2). Figure 2 also shows that there is potentially a substantial additional gain in morbidity from reduced rates of depression in the 30-69 and 70+ age

groups; and substantial additional gains in both morbidity and mortality from reduced rates of dementia in 70+ year olds.

The results demonstrate that, for the UK, achieving the obesity target will result in the biggest overall impact on mortality and morbidity (Figure 3). Halting the rise in diabetes and achieving a 30% reduction in salt intake would also achieve a large impact on NCD mortality, and reducing tobacco consumption by 30% would have a large impact on morbidity.

Over time, achieving the combination of WHO risk factor targets would address an increasing proportion of the health that could potentially be gained if everyone could adjust their risk behaviour to ideal levels in 2010 (Figure 4 and Appendix 2 for deaths and YLDs averted under the ideal risk scenario). Taking both morbidity and mortality into account, by 2025, 29% of the health gain would be achieved for men and 26% for women. If we assume trends in risk factors and diseases continue beyond 2025, the proportions would reach 35% for men and 33% for women by 2030.

Table 3 Relative reduction in probability of premature mortality from non-communicable diseases by 2025.

	WHO risk factor targets		Ideal risk reduction		Proportion of ideal risk addressed by meeting WHO target	
	Men	**Women**	**Men**	**Women**	**Men**	**Women**
Business-as-usual	22%	25%				
Additional reduction if achieving risk factor targets or ideal risk scenario:						
Obesity	2.3% (1.6% to 2.9%)	1.1% (0.3% to 1.9%)	7.9% (5.9% to 9.8%)	4.8% (2.6% to 7.1%)	29%	24%
Tobacco use	0.6% (0.6% to 0.7%)	0.6% (0.6% to 0.7%)	12.1% (10.1% to 14.0%)	9.7% (8.2% to 11.1%)	5%	7%
Diabetes	1.4% (1.2% to 1.7%)	0.7% (0.6% to 0.8%)	2.7% (2.2% to 3.2%)	1.4% (1.2% to 1.7%)	53%	51%
Raised blood pressure	0.4% (0.4% to 0.4%)	0.2% (0.2% to 0.2%)	1.6% (1.6% to 1.7%)	0.7% (0.7% to 0.8%)	25%	25%
Salt intake	0.8% (0.8% to 0.9%)	0.3% (0.3% to 0.3%)	2.1% (2.0% to 2.2%)	0.7% (0.7% to 0.8%)	39%	40%
Harmful alcohol use*	0.6% (0.4% to 0.8%)	0.3% (0.22% to 0.5%)	0.9% (-4.6% to 4.0%)	3.2% (-1.08% to 6.9%)	62%	11%
Physical inactivity	0.1% (0.08% to 0.1%)	0.1% (0.0% to 0.1%)	1.1% (0.81% to 1.4%)	0.6% (0.4% to 0.7%)	10%	10%
Combined scenario	6.5% (5.4% to 7.5%)	3.2% (2.2% to 4.1%)	26.2% (21.9% to 29.7%)	18.4% (14.3% to 22.2%)	25%	17%

NB. Values are mean and 95% uncertainty intervals. * Low-level consumption of alcohol is associated with a decreased risk of some diseases (e.g. CHD, hypertensive heart disease and diabetes), which partly counter the modelled health benefits of abstaining from alcohol.

Table 4 Total non-communicable disease deaths and YLDs that are averted or delayed between 2010 and 2025, for each of the risk factor target scenarios

	30-69 years		70+ years	
	Men	Women	Men	Women
Deaths				
Obesity	13,000 (8,900 to 17,000)	4,500 (500 to 8,600)	47,000 (34,000 to 60,000)	26,000 (11,000 to 40,000)
Tobacco use	5,100 (4,800 to 5,400)	4,300 (4,100 to 4,400)	14,000 (13,000 to 15,000)	15,000 (14,000 to 15,000)
Diabetes	7,200 (5,900 to 8,600)	2,500 (2,000 to 2,900)	38,000 (30,000 to 45,000)	32,000 (26,000 to 38,000)
Raised blood pressure	5,700 (5,400 to 6,100)	2,300 (2,100 to 2,500)	25,000 (24,000 to 26,000)	23,000 (22,000 to 24,000)
Salt intake	9,000 (8,700 to 9,400)	2,500 (2,400 to 2,600)	38,000 (37,000 to 39,000)	26,000 (25,000 to 27,000)
Harmful alcohol use	4,900 (3,000 to 6,900)	2,000 (1,200 to 2,800)	11,000 (7,100 to 16,000)	6,100 (800 to 11,000)
Physical inactivity	920 (660 to 1,200)	320 (240 to 400)	4,300 (3,200 to 5,400)	3,900 (2,800 to 4,900)
Combined scenario	38,000 (32,000 to 44,000)	13,000 (8,500 to 17,000)	150,000 (130,000 to 170,000)	99,000 (79,000 to 120,000)
YLDs				
Obesity	79,000 (66,000 to 93,000)	50,000 (38,000 to 63,000)	150,000 (120,000 to 170,000)	98,000 (66,000 to 130,000)
Tobacco use	20,000 (20,000 to 21,000)	25,000 (25,000 to 26,000)	27,000 (26,000 to 28,000)	37,000 (36,000 to 38,000)
Diabetes	190,000 (190,000 to 190,000)	160,000 (160,000 to 160,000)	330,000 (320,000 to 340,000)	290,000 (290,000 to 300,000)
Raised blood pressure	18,000 (17,000 to 19,000)	12,000 (11,000 to 13,000)	40,000 (38,000 to 42,000)	31,000 (29,000 to 33,000)
Salt intake	29,000 (28,000 to 30,000)	14,000 (14,000 to 15,000)	60,000 (57,000 to 62,000)	34,000 (33,000 to 36,000)
Harmful alcohol use	6,200 (-18,000 to 30,000)	-280 (-8,700 to 8,100)	14,000 (-25,000 to 53,000)	3,100 (-12,000 to 18,000)
Physical inactivity	6,200 (5,300 to 7,000)	5,500 (4,700 to 6,200)	13,000 (11,000 to 15,000)	13,000 (11,000 to 14,000)
Combined scenario	260,000 (240,000 to 280,000)	200,000 (190,000 to 210,000)	480,000 (430,000 to 520,000)	370,000 (350,000 to 400,000)

NB. Values are mean and 95% uncertainty intervals..

DISCUSSION

There have been considerable achievements in addressing the risks for non-communicable disease in the UK over the last three decades. Although prevalence of obesity and diabetes have risen, initiatives such as increasing access to blood pressure-lowering drugs, reducing salt in processed foods, and strengthening tobacco control, have all contributed to the reduction in these risk factors over time. These changes in lifestyle behaviours, along with advances in treatment, have contributed to the reduction in non-communicable diseases that we observed. Our projections show that if these trends continue, there is likely to be a substantial further reduction in NCD burden by 2025, which will see the UK very nearly reach the current WHO target of 25% reduction in premature mortality and very likely reach the proposed 30% reduction by 2030.

It will be critical that past investments in prevention (and treatment) are sustained so that the UK does not lose the momentum built over previous decades. Preventive efforts must also be increased if the UK is to meet the 2025 target. While the targets do provide a worthwhile objective, a further two-thirds of the preventable NCD burden could potentially be reduced with an even more ambitious prevention program in the future.

Although current WHO targets focus on premature mortality, our modelling predicted substantial added benefits from reduced NCD morbidity, particularly at older ages. Around 16% of Government spending in the UK is allocated to health, which is high compared to other European countries[27]. The large reductions in NCD burden, particularly for CHD, stroke, diabetes, depression and dementia, would help reduce these costs. The social and economic burden of diseases such as depression and dementia is also high. Depression for example is associated with increased workplace absenteeism and reduced productivity[28], and dementia is associated with substantial social care costs[29]. In 2012 the cost of health and social care services for dementia patients in the UK was greater than the costs of CHD, stroke and cancer care combined[29].

Unfortunately the drivers of mental and neurological disorders, despite a high global burden, are poorly understood[30]. Further research is needed to strengthen the epidemiological evidence of the

links between lifestyle risks and prevention of diseases, such as depression and dementia, and to better understand how prevalence of these diseases may in turn increase risk of other NCDs. In the UK, funding for dementia and mental health research is low in comparison to the size of the burden[29, 31]. However, a review of costs and burden of mental and neurological disorders in the EU estimated that the return on investment in research would be highly favourable when taking the full cost to society into account[32].

Cost-effectiveness analysis can be used to identify which interventions will provide best value-for-money. Modelling of interventions for improving diet and body mass in England, suggest that fiscal measures and regulation may be more cost-effective than more individually targeted approaches such as physician counselling and worksite programs[33], which is consistent with findings from modelling studies in comparable high income countries such as Australia[34, 35] and New Zealand[36]. But further work is needed to identify the most effective and cost-effective interventions for addressing a wider range of risk factor targets in the UK, including a number of dietary risks associated with a high NCD burden that are not included in the WHO targets (e.g. fruits and vegetables, fats and cholesterol[30]). Modelling is also needed to better understand and quantify the health impacts of underlying drivers of change, such as global marketing and trade, the design of urban environments and climate change.

This modelling study contributes to the evidence about the potential impact of changes in risk factor prevalence, but to implement change evidence is needed on interventions designed to tackle behavioural risk factors. The relative magnitude of health gain associated with the WHO risk factor targets is not necessarily a good guide for setting priorities for intervention. The apparently smaller benefits of addressing physical inactivity and harmful alcohol use, for example, are in large part because the WHO targets are relatively modest. The modelling of alcohol targets also does not capture any benefits from reduced injury rates, which fall outside of the NCD focus of the WHO targets. In addition, the modelling of some risk factors was limited by the available data (e.g. self-reported physical activity) and WHO definitions (e.g. prevalence of hypertension rather than the full distribution of blood pressure).

Early population health impact studies typically modelled effects on a population cohort without forward projection of disease trends or they modelled effects on a population cohort forward in time without replacement (i.e. following the current adult population until death or end of projection). In evaluating global NCD impact of the WHO targets, Kontis et al[4] advanced this approach by modelling the population impacts between 2010 and 2025 in three five-year intervals, incorporating projections of disease trends and allowing for population growth and ageing between each modelled time interval. We have taken the modelling a step further by incorporating risk factor prevalence rates and model outputs of disease rates that are directly comparable to past trends, and integrating this with a population demographic model that stochastically forecasts trends in mortality, fertility and migration. This approach could facilitate future integration with other models, including economic models (e.g. AgMIP models, which focus on food security under climate change[1]) allowing health outcomes to be included in broader systems modelling studies. In addition, while focused on a select range of WHO risk factor targets and NCD outcomes for these analyses, the model could potentially be adapted to address a more diverse range of risks factors and disease outcomes in the future.

This modelling study illustrates the large health gains that could be achieved by addressing unhealthy risk factors for disease. For countries such as the UK that can capitalise on many decades of effort in prevention and treatment, the WHO premature mortality target is an achievable goal. But with a further two-thirds of the NCD burden still potentially preventable, it is imperative that the UK capitalises on the momentum of past decades with further effort in prevention. For low- and middle-income countries the potential benefits are likely to be even greater[4], as is the need for evidence to develop cost-effective policies for prevention in these countries. Given the growing global burden of diseases such as diabetes, depression and dementia, the WHO should consider future global targets that provide incentives for addressing these diseases, which carry a high health burden for the individual and place a substantial burden on health and social care systems in society.

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COMPETING INTERESTS

AUTHOR CONTRIBUTIONS

ETHICS APPROVAL

Not required

FUNDING

full access to all of the data (including statistical reports and tables) in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Transparency declaration: The lead author (the manuscript's guarantor) affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

DATA SHARING

No additional data available.

REFERENCES

1.   Rosenzweig C, Jones J, Hatfield J, et al. The agricultural model intercomparison and improvement project (AgMIP): protocols and pilot studies. Agricultural and Forest Meteorology. 2013;170:166-82.

2.   United Nations. Political declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases. United Nations General Assembly, Sixty-sixth session, Agenda item 117, 2011.

3.   WHO. Global action plan for the prevention and control of noncommunicable diseases 2013–2020. Geneva: World Health Organization, 2013.

4.   Kontis V, Mathers CD, Rehm J, et al. Contribution of six risk factors to achieving the 25× 25 non-communicable disease mortality reduction target: a modelling study. The Lancet. 2014;384(9941):427-37.

5.   Beaglehole R, Bonita R, Ezzati M, et al. NCD Countdown 2025: accountability for the 25× 25 NCD mortality reduction target. The Lancet. 2014;384(9938):105-7.

6.   Pearce N, Ebrahim S, McKee M, et al. The road to 25× 25: how can the five-target strategy reach its goal? The lancet global health. 2014;2(3):e126-e8.

7.   WHO. Health in 2015: from MDGs, Millennium Development Goals to SDGs, Sustainable Development Goals. Geneva: World Health Organization, 2015.

8.   The Richmond Group of Charities. [Available from: http://www.richmondgroupofcharities.org.uk/.

9.   Joint Health Surveys Unit. Health Survey for England 2013 (and previous editions). Leeds: Health and Social Care Information Centre, 2014.

10.   McPherson K, Marsh T, Brown M. Foresight. Tackling obesities – modelling future trends in obesity and the impact on health. London: Government Office for Science, 2007.

11.   WHO. Noncommunicable diseases global monitoring framework: indicator definitions and specifications. Geneva: World Health Organization, 2014.

12. He FJ, Li J, MacGregor GA. Effect of longer term modest salt reduction on blood pressure: Cochrane systematic review and meta-analysis of randomised trials. BMJ. 2013;346.

13. Baumgart M, Snyder HM, Carrillo MC, et al. Summary of the evidence on modifiable risk factors for cognitive decline and dementia: A population-based perspective. Alzheimer's & Dementia. 2015;11(6):718-26.

14. Valkanova V, Ebmeier KP. Vascular risk factors and depression in later life: a systematic review and meta-analysis. Biol Psychiatry. 2013;73(5):406-13.

15. Cheng G, Huang C, Deng H, et al. Diabetes as a risk factor for dementia and mild cognitive impairment: a meta-analysis of longitudinal studies. Intern Med J. 2012;42(5):484-91.

16. Lim S, Vos T, Flaxman A, et al. The burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions 1990-2010: a systematic analysis. The Lancet. 2013;380(9859):2224-60.

17. Fishman G. Monte Carlo: concepts, algorithms, and applications. New York: Springer-Verlag 1995.

18. University of California Berkeley (USA), Max Planck Institute for Demographic Research (Germany). Human Mortality Database [Available from: www.mortality.org.

19. Max Planck Institute for Demographic Research (Germany), Vienna Institute of Demography (Austria). Human Fertility Database [Available from: www.humanfertility.org.

20. Hyndman RJ, Booth H, Yasmeen F. Coherent mortality forecasting: the product-ratio method with functional time series models. Demography. 2013;50(1):261-83.

21. Salomon JA, Murray CJ. The epidemiologic transition revisited: compositional models for causes of death by age and sex. Population and Development Review. 2002;28(2):205-28.

22. World Health Organization. WHO Mortality Database [Available from: http://www.who.int/healthinfo/statistics/mortality_rawdata/en/.

23. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med. 2006;3(11):e442.

24.   Naghavi M, Makela S, Foreman K, et al. Research Algorithms for enhancing public health utility of national causes-of-death data. Popul Health Metr. 2010;8:9.

25.   The World Bank. World Development Indicators [Available from: http://data.worldbank.org/data-catalog/world-development-indicators.

26.   Greene WH. Econometric analysis. 5th ed. Upper Saddle River, New Jersey: Prentice Hall; 2003.

27.   WHO. National health accounts: country health information Geneva: World Health Organization; 2015 [Available from: http://apps.who.int/nha/database/Country_Profile/Index/en.

28.   Donohue JM, Pincus HA. Reducing the societal burden of depression. Pharmacoeconomics. 2007;25(1):7-24.

29.   Luengo-Fernandez R, Leal J, Gray A. UK research spend in 2008 and 2012: comparing stroke, cancer, coronary heart disease and dementia. BMJ open. 2015;5(4):e006648.

30.   Forouzanfar MH, Alexander L, Anderson HR, et al. Global, regional, and national comparative risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of risks in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013. The Lancet. 2015;386:2287-323.

31.   Kingdon D. Health research funding: Mental health research continues to be underfunded. BMJ. 2006;332(7556):1510.

32.   Gustavsson A, Svensson M, Jacobi F, et al. Cost of disorders of the brain in Europe 2010. Eur Neuropsychopharmacol. 2011;21(10):718-79.

33.   Cecchini M, Sassi F, Lauer JA, et al. Tackling of unhealthy diets, physical inactivity, and obesity: health effects and cost-effectiveness. The Lancet. 2010;376(9754):1775-84.

34.   Cobiac LJ, Vos T, Doran C, et al. Cost-effectiveness of interventions to prevent alcohol-related disease and injury in Australia. Addiction. 2009;104(10):1646-55.

35.   Cobiac LJ, Vos T, Veerman JL. Cost-effectiveness of interventions to reduce dietary salt intake. Heart. 2010;96(23):1920-5.

36.   Nghiem N, Blakely T, Cobiac LJ, et al. Health and economic impacts of eight different dietary salt reduction interventions. PLoS ONE. 2015;10(4).

37.   Prospective Studies Collaboration. Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. The Lancet. 2009;373(9669):1083-96.

38.   Norat T, Aune D, Vieira R, et al. The Associations between Food, Nutrition and Physical Activity and the Risk of Pancreatic Cancer. WCRF/AICR Systematic Literature Review Continuous Update Project Report, 2011.

39.   Luppino FS, de Wit LM, Bouvy PF, et al. Overweight, obesity, and depression: a systematic review and meta-analysis of longitudinal studies. Arch Gen Psychiatry. 2010;67(3):220-9.

40.   Beydoun M, Beydoun H, Wang Y. Obesity and central obesity as risk factors for incident dementia and its subtypes: a systematic review and meta-analysis. Obes Rev. 2008;9(3):204-18.

41.   Thun MJ, Apicella LF, Henley SJ. Smoking vs other risk factors as the cause of smoking-attributable deaths. Confounding in the courtroom. JAMA. 2000;284(6):706-12.

42.   Willi C, Bodenmann P, Ghali WA, et al. Active smoking and the risk of type 2 diabetes: A systematic review and meta-analysis. JAMA. 2007;298(22):2654-64.

43.   Gandini S, Botteri E, Iodice S, et al. Tobacco smoking and cancer: A meta-analysis. Int J Cancer. 2008;122(1):155-64.

44.   Lee Y-CA, Cohet C, Yang Y-C, et al. Meta-analysis of epidemiologic studies on cigarette smoking and liver cancer. Int J Epidemiol. 2009:dyp280.

45.   Luger TM, Suls J, Vander Weg MW. How robust is the association between smoking and depression in adults? A meta-analysis using linear mixed-effects models. Addict Behav. 2014;39(10):1418-29.

46.   Zhong G, Wang Y, Zhang Y, et al. Smoking Is Associated with an Increased Risk of Dementia: A Meta-Analysis of Prospective Cohort Studies with Investigation of Potential Effect Modifiers. PLoS ONE. 2015;10(3):e0118333.

47.   Peters SA, Huxley RR, Woodward M. Diabetes as risk factor for incident coronary heart disease in women compared with men: a systematic review and meta-analysis of 64 cohorts including 858,507 individuals and 28,203 coronary events. Diabetologia. 2014;57(8):1542-51.

48.   Peters SA, Huxley RR, Woodward M. Diabetes as a risk factor for stroke in women compared with men: a systematic review and meta-analysis of 64 cohorts, including 775 385 individuals and 12 539 strokes. The Lancet. 2014;383(9933):1973-80.

49.   Rotella F, Mannucci E. Diabetes mellitus as a risk factor for depression. A meta-analysis of longitudinal studies. Diabetes Res Clin Pract. 2013;99(2):98-104.

50.   Gudala K, Bansal D, Schifano F, et al. Diabetes mellitus and risk of dementia: a meta-analysis of prospective observational studies. Journal of diabetes investigation. 2013;4(6):640-50.

51.   Lewington S. Prospective studies collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies (vol 360, pg 1903, 2002). Lancet. 2003;361(9362):1060-.

52.   Shield KD, Parry C, Rehm J. Chronic diseases and conditions related to alcohol use. Alcohol research: current reviews. 2014;35(2):155.

53.   Patra J, Taylor B, Irving H, et al. Alcohol consumption and the risk of morbidity and mortality for different stroke types - a systematic review and meta-analysis. BMC Public Health. 2010;10.

54.   Baliunas DM, Taylor BM, Irving HM, et al. Alcohol as a risk factor for type 2 diabetes: a systematic review and meta-analysis. Diabetes Care. 2009;32(11):2123.

55.   Rehm J, Taylor B, Mohapatra S, et al. Alcohol as a risk factor for liver cirrhosis: A systematic review and meta-analysis. Drug Alcohol Rev. 2010;29(4):437-45.

56.   Corrao G, Bagnardi V, Zambon A, et al. A meta-analysis of alcohol consumption and the risk of 15 diseases. Prev Med. 2004;38(5):613-9.

57.   Physical Activity Guidelines Advisory Committee. Physical Activity Guidelines Advisory Committee Report. Washington, DC: U.S. Department of Health and Human Services, 2008.

58.   Blondell SJ, Hammersley-Mather R, Veerman JL. Does physical activity prevent cognitive decline and dementia?: A systematic review and meta-analysis of longitudinal studies. BMC Public Health. 2014;14(1):510.

FIGURES

Figure 1 Projected trends in the probability of dying prematurely from non-communicable disease for the WHO risk factor target scenarios.

Figure 2 Non-communicable disease deaths and YLDs that are averted or delayed between 2010 and 2025, for the combined risk factor target scenario.

(Note: the small increase in COPD YLDs is due to a shift in the age distribution of the population, primarily as a result of reductions in CHD and stroke mortality, and does not reflect an increase in COPD rates).

Figure 3 DALYs averted for the WHO risk factor target scenarios.

Figure 4 DALYs averted for the combined WHO risk factor target scenario and the ideal risk reduction scenario.

SUPPORTING DOCUMENTS

Appendix 1: Calculating the combined effect of meeting all risk factor targets

Appendix 2: Ideal risk scenario results

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Projected trends in the probability of dying prematurely from non-communicable disease for the WHO risk factor target scenarios.
Figure 1
928x1164mm (96 x 96 DPI)
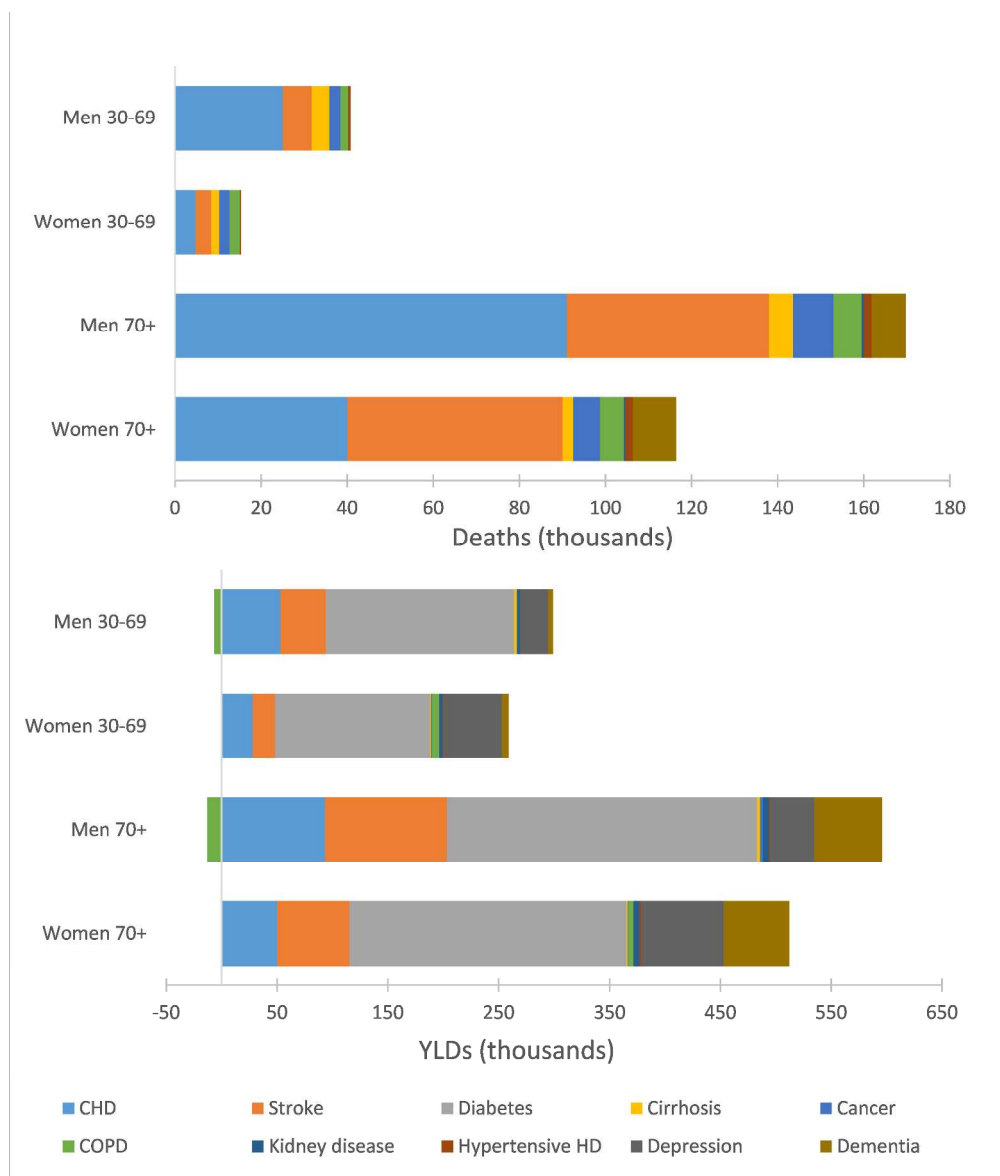
Non-communicable disease deaths and YLDs that are averted or delayed between 2010 and 2025, for the combined risk factor target scenario. (Note: the small increase in COPD YLDs is due to a shift in the age distribution of the population, primarily as a result of reductions in CHD and stroke mortality, and does not reflect an increase in COPD rates).
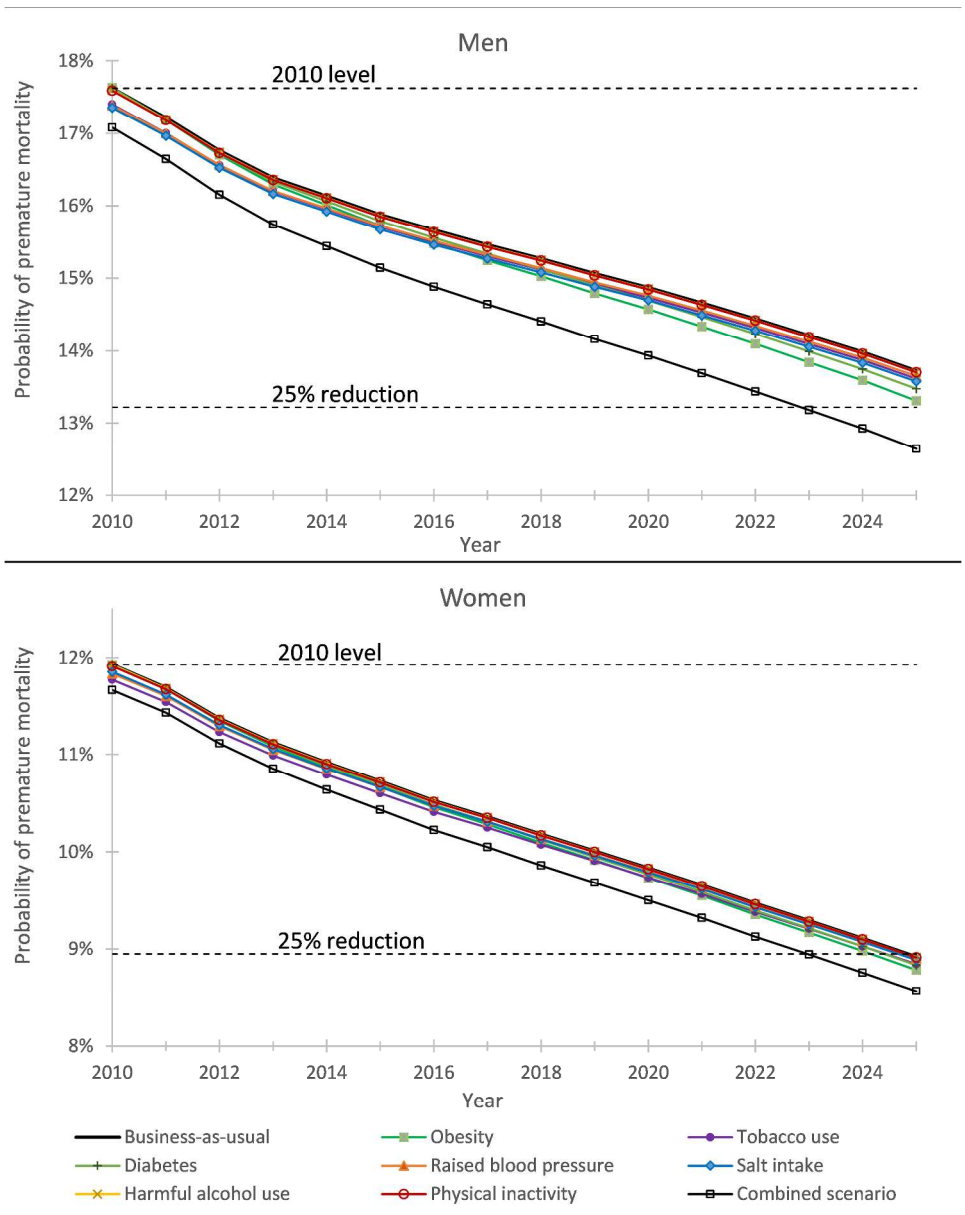Figure 2
945x1101mm (96 x 96 DPI)
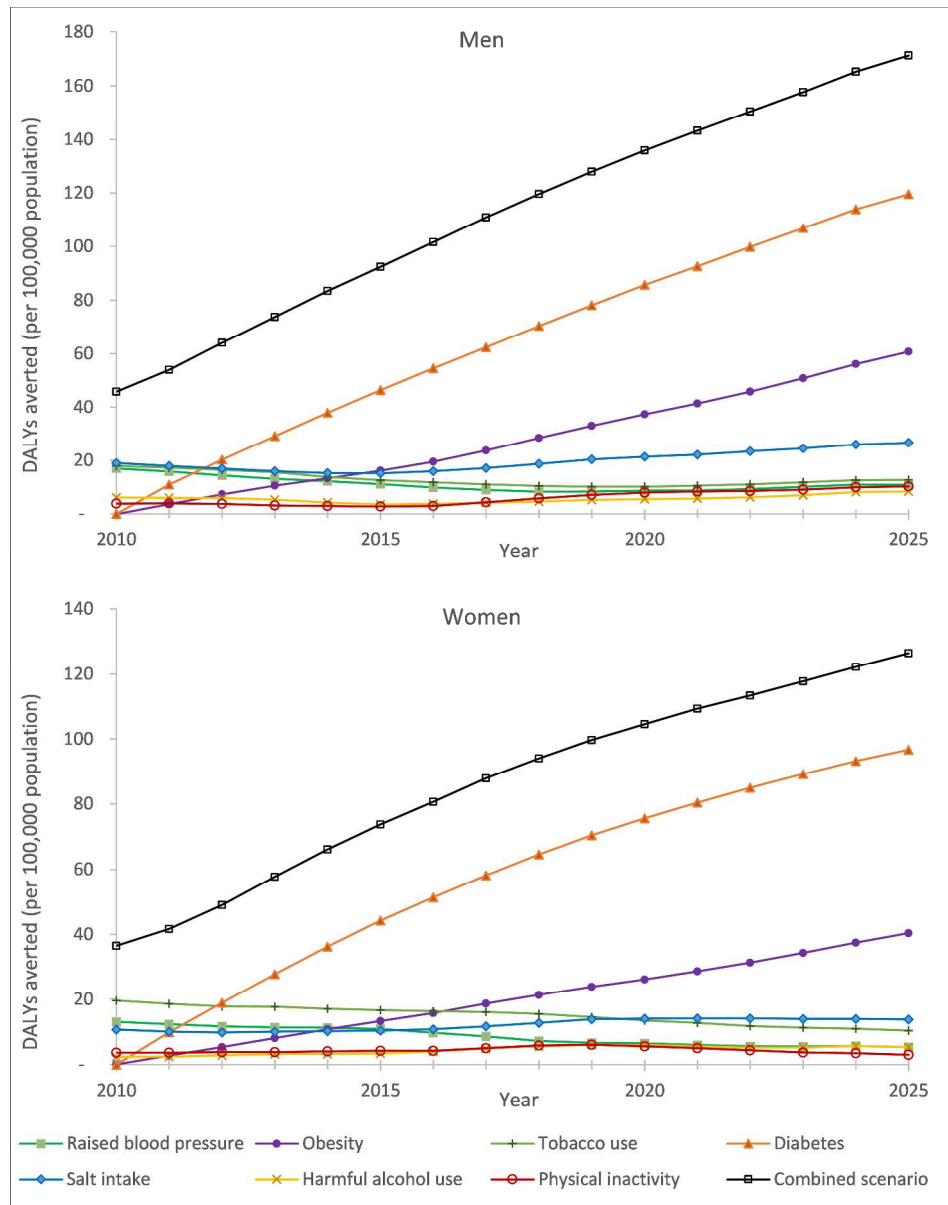
DALYs averted for the WHO risk factor target scenarios.
Figure 3
946x1204mm (96 x 96 DPI)

DALYs averted for the combined WHO risk factor target scenario and the ideal risk reduction scenario
Figure 4
943x625mm (96 x 96 DPI)

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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.

$$PIF_{Combined} = 1 - (1 - PIF_{BP}) \times (1 - PIF_{Diab}) \times (1 - PIF_{PA}) \times (1 - PIF_{BMI}) \times (1 - PIF_{Alc}) \times (1 - PIF_{Tob})$$

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 1 Methods for the calculation of population impact fractions (PIFs) for the combined risk factor scenario

PIF	Calculations	Sources
PIF_{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_{BP} = 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_{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)	Cobiac et al[6] (adjustment estimate) Peters et al[7,8]
	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_{Diab} = the biggest of the PIFs calculated in steps 4 and 5	
PIF_{PA} (excluding effects via BP and Diabetes)	PIF_{PA} = PIF calculated for the direct **PA** using RR CHD/Stroke estimates (see Note 2 below)	Wahid et al Under review Health Survey for England 2012[9] Global Burden of Disease[10]
PIF_{BMI} (excluding effects via BP and Diabetes)	PIF_{BMI} = PIF calculated for the direct **BMI** using RR CHD/Stroke estimates (see Note 2 below)	Prospective Studies Collaboration[5] Cobiac et al[6] (adjustment estimate) Health Survey for England (HSE) 2012[9] Global Burden of Disease (GBD)[10]
PIF_{Alc}	PIF_{Alc} = PIF calculated using RR CHD/Stroke estimates from meta-analyses	Shield et al[11] Patra et al[12]
PIF_{Tob}	PIF_{Tob} = PIF calculated using RR CHD/Stroke estimates from meta-analyses	Cancer Prevention Study II[13]

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].
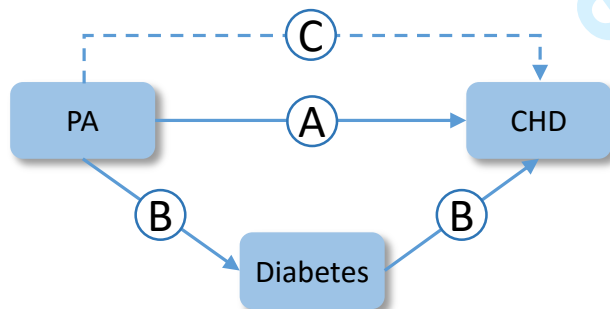

Figure 2 Conceptual diagram of the pathways between risk factor (physical activity), intermediate variable (diabetes) and disease (CHD) in the optimisation process.

References

1. Cornelissen VA, Fagard RH (2005) Effects of endurance training on blood pressure, blood pressure–regulating mechanisms, and cardiovascular risk factors. Hypertension 46: 667-675.

2. Neter JE, Stam BE, Kok FJ, Grobbee DE, Geleijnse JM (2003) Influence of weight reduction on blood pressure a meta-analysis of randomized controlled trials. Hypertension 42: 878-884.

3. He FJ, Li J, MacGregor GA (2013) Effect of longer term modest salt reduction on blood pressure: Cochrane systematic review and meta-analysis of randomised trials. BMJ: British Medical Journal 346.

4. Prospective Studies Collaboration (2002) Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. The Lancet 360: 1903-1913.

5. Prospective Studies Collaboration (2009) Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. The Lancet 373: 1083-1096.

6. Cobiac LJ, Vos T, Veerman JL (2010) Cost-effectiveness of Weight Watchers and the Lighten Up to a Healthy Lifestyle program. Australian and New Zealand Journal of Public Health 34: 240-247.

7. Peters SA, Huxley RR, Woodward M (2014) Diabetes as risk factor for incident coronary heart disease in women compared with men: a systematic review and meta-analysis of 64 cohorts including 858,507 individuals and 28,203 coronary events. Diabetologia 57: 1542-1551.

8. Peters SA, Huxley RR, Woodward M (2014) Diabetes as a risk factor for stroke in women compared with men: a systematic review and meta-analysis of 64 cohorts, including 775 385 individuals and 12 539 strokes. The Lancet 383: 1973-1980.

9. Joint Health Surveys Unit (2014) Health Survey for England 2013 (and previous editions). Leeds: Health and Social Care Information Centre.

10. Wang H, Dwyer-Lindgren L, Lofgren KT, Rajaratnam JK, Marcus JR, et al. (2013) Age-specific and sex-specific mortality in 187 countries, 1970–2010: a systematic analysis for the Global Burden of Disease Study 2010. The Lancet 380: 2071-2094.

11. Shield KD, Parry C, Rehm J (2014) Chronic diseases and conditions related to alcohol use. Alcohol research: current reviews 35: 155.

12. Patra J, Taylor B, Irving H, Roerecke M, Baliunas D, et al. (2010) Alcohol consumption and the risk of morbidity and mortality for different stroke types - a systematic review and meta-analysis. BMC Public Health 10.

13. Thun MJ, Apicella LF, Henley SJ (2000) Smoking vs other risk factors as the cause of smoking-attributable deaths: confounding in the courtroom. Jama 284: 706-712.

14. Hall KD, Sacks G, Chandramohan D, Chow CC, Wang YC, et al. (2011) Quantification of the effect of energy imbalance on bodyweight. The Lancet 378: 826-837.

15. Heitmann BL, Garby L (2002) Composition (lean and fat tissue) of weight changes in adult Danes. The American journal of clinical nutrition 75: 840-847.

16. Mifflin MD, St Jeor ST, Hill LA, Scott BJ, Daugherty SA, Koh Y (1990) A new predictive equation for resting energy expenditure in healthy individuals. The American journal of clinical nutrition 51: 241-247.

17. FAO (2001) Human Energy Requirements: Report of a Joint FAO/WHO/UNU Expert Consultation. Rome: Food and Agriculture Organization of the United Nations, World Health Organization, United Nations University.

18. Ainsworth BE, Haskell WL, Herrmann SD, Meckes N, Bassett Jr DR, et al. (2011) 2011 Compendium of Physical Activities: a second update of codes and MET values. Medicine and science in sports and exercise 43: 1575-1581.

Appendix 2: Ideal risk scenario results

Table 1 Total non-communicable disease deaths and YLDs that are averted or delayed between 2010 and 2025, for the ideal risk scenario

	30-69 years		70+ years	
	Men	Women	Men	Women
Deaths				
Obesity	63,000 (46,000 to 80,000)	26,000 (13,000 to 39,000)	230,000 (170,000 to 280,000)	170,000 (120,000 to 230,000)
Tobacco use	88,000 (72,000 to 100,000)	61,000 (51,000 to 70,000)	360,000 (290,000 to 430,000)	290,000 (230,000 to 340,000)
Diabetes	19,000 (16,000 to 23,000)	7,800 (6,300 to 9,200)	98,000 (80,000 to 120,000)	96,000 (78,000 to 110,000)
Raised blood pressure	24,000 (23,000 to 25,000)	9,300 (8,600 to 10,000)	110,000 (100,000 to 110,000)	98,000 (92,000 to 100,000)
Salt intake	24,000 (23,000 to 25,000)	6,200 (5,900 to 6,500)	95,000 (91,000 to 99,000)	62,000 (59,000 to 64,000)
Harmful alcohol use	6,800 (-31,000 to 45,000)	20,000 (-2,300 to 43,000)	-8,400 (-120,000 to 100,000)	72,000 (-170,000 to 320,000)
Physical inactivity	10,000 (7,200 to 13,000)	3,700 (2,700 to 4,700)	48,000 (34,000 to 62,000)	42,000 (31,000 to 54,000)
Combined scenario	190,000 (150,000 to 230,000)	94,000 (69,000 to 120,000)	800,000 (660,000 to 940,000)	640,000 (460,000 to 810,000)
YLDs (Thousands)				
Obesity	390,000 (320,000 to 470,000)	320,000 (250,000 to 390,000)	720,000 (570,000 to 860,000)	640,000 (490,000 to 790,000)
Tobacco use	770,000 (700,000 to 840,000)	860,000 (810,000 to 920,000)	1,300,000 (1,200,000 to 1,500,000)	1,500,000 (1,400,000 to 1,600,000)
Diabetes	620,000 (610,000 to 630,000)	510,000 (510,000 to 520,000)	1,100,000 (1,000,000 to 1,100,000)	990,000 (970,000 to 1,000,000)
Raised blood pressure	75,000 (71,000 to 79,000)	51,000 (46,000 to 55,000)	170,000 (160,000 to 180,000)	130,000 (120,000 to 140,000)
Salt intake	76,000 (72,000 to 79,000)	36,000 (34,000 to 37,000)	150,000 (150,000 to 160,000)	83,000 (80,000 to 87,000)
Harmful alcohol use	-82,000 (-260,000 to 100,000)	-120,000 (-260,000 to 23,000)	-120,000 (-410,000 to 170,000)	-180,000 (-450,000 to 80,000)
Physical inactivity	69,000 (58,000 to 80,000)	60,000 (51,000 to 70,000)	140,000 (120,000 to 170,000)	130,000 (110,000 to 160,000)
Combined scenario	1,600,000 (1,500,000 to 1,700,000)	1,500,000 (1,400,000 to 1,600,000)	2,900,000 (2,700,000 to 3,100,000)	2,800,000 (2,500,000 to 3,000,000)

NB. Values are mean and 95% uncertainty intervals.

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Translating the World Health Organization 25x25 goals into a United Kingdom context: The PROMISE modelling study

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Translating the World Health Organization 25x25 goals into a United Kingdom context: The PROMISE modelling study

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1 ## ABSTRACT

2 Objective – Model the impact of targets for obesity, diabetes, raised blood pressure, tobacco use,

3 salt intake, physical inactivity and harmful alcohol use, as outlined in the Global Non-Communicable

4 Disease Action Plan 2013-2020, on mortality and morbidity in the UK population.

5 Design – Dynamic population modelling study

6 Setting – UK population

7 Participants - NA

8 Main outcome measures – Mortality and morbidity (Years Lived with Disability) from non-

9 communicable diseases (NCDs) that are averted or delayed. Probability of achieving a 25% reduction

10 in premature mortality from NCDs by 2025 (current WHO target) and a 33% reduction by 2030

11 (proposed target).

12 Results – The largest improvements in mortality would be achieved by meeting the obesity target

13 and the largest improvements in morbidity would be achieved by meeting the diabetes target. The

14 UK could achieve the 2025 and 2030 targets for reducing premature mortality with only a little

15 additional preventive effort compared to current practice. Achieving all seven risk targets could

16 avert a total of 300,000 deaths (95% uncertainty interval: 250,000 to 350,000) and 1.3 million Years

17 Lived with Disability (1.2 million to 1.4 million) from NCDs by 2025, with the majority of health gains

18 due to reduced mortality and morbidity from heart disease and stroke, and reduced morbidity from

19 diabetes. Potential reductions in morbidity from depression and in morbidity and mortality from

20 dementia at older ages are also substantial.

21 Conclusions - The global premature mortality targets are a potentially achievable goal for countries

22 such as the UK that can capitalise on many decades of effort in prevention and treatment. High

23 morbidity diseases and diseases in later life are not addressed in the Global NCD Action Plan and

24 targets, but must also be considered a priority for prevention in the UK where the population is

25 ageing and the costs of health and social care are rising.

26

27

ARTICLE SUMMARY

Strengths and limitations of the study:

- The study combined functional demographic modelling of population forecasting, logistic regression modelling of 'business-as-usual' trends in NCD rates and NCD risk factors, and dynamic modelling of population health outcomes.

- We simulated the future changes in NCD mortality and morbidity that would occur: (1) with 'business-as-usual'; (2) if the UK could achieve the World Health Organization's risk factor reduction targets; and (3) if all NCD burden could be addressed.

- We also estimated the probability that the UK would meet the current WHO target of a 25% reduction in premature mortality by 2025 and the new target of a 30% reduction by 2030.

- The modelling does not include known NCD risk factors for which there are no WHO 2025 targets (e.g. intake of fruits and vegetables, red and processed meats, transfats, etc.) and relies on limited evidence (e.g. observational studies) to simulate the relationships between risk factors and avoid the double-counting of target impacts on NCDs.

- Integrating projections of risk factor and disease trends with a population demographic model that stochastically forecasts trends in mortality, fertility and migration, is an important advance on existing global modelling methods.

1 INTRODUCTION

2 Non-communicable diseases (NCDs) have been recognised as a major challenge for all nations in the

3 21st century, affecting people of all ages, gender, race and income level[2]. It is a burden that is in

4 large part preventable; closely linked to a range of risky behaviours, including tobacco use,

5 unhealthy diet, physical inactivity and harmful use of alcohol; risks that are themselves closely

6 related to the societies and environments in which we live. In response to the United Nations

7 declaration on addressing prevention and control of NCDs[2], the World Health Organization (WHO)

8 developed a Global NCD Action Plan 2013-2020[3], which outlines global targets for improving

9 prevalence of NCD risk factors (obesity, diabetes, raised blood pressure, tobacco use, salt intake,

10 physical inactivity and harmful use of alcohol) with an overarching goal of achieving a 25% reduction

11 in premature mortality from the four main NCDs (cardiovascular diseases, chronic respiratory

12 diseases, cancers and diabetes) by the year 2025. Global modelling of the risk factor impacts on

13 NCDs shows that premature mortality from the four main NCDs could be reduced globally by 22% in

14 men and 19% in women, between 2010 and 2025, if the targets could be achieved[4].

15 It is the responsibility of individual countries to initiate actions to achieve the targets, and regularly

16 measure and review national progress[5]. However, it is not clear to what extent the NCD and risk

17 factor targets should guide priorities for action or to what extent progress will reflect a nation's

18 improvement in health. While the four main NCDs are responsible for 87% of all NCD deaths

19 worldwide, they only contribute to 57% of the ill health burden from NCDs[6]. There are also

20 indications that targets for reducing tobacco use could be more ambitious[4]. These concerns are to

21 some extent reflected in the new set of 'Sustainable Development Goals' (SDGs) and targets for

22 2030 that were adopted by United Nations world leaders in September 2015. The new health-

23 related NCD goals aim to 'promote mental health and well-being' and to strengthen implementation

24 of the WHO Framework Convention on Tobacco Control, alongside a revision of the premature

1 mortality goal to a one-third reduction by 2030. In response to the SDGs, the WHO has signalled its

2 intent to expand work on prevention of NCDs in 2016-17[7].

3 More information is needed about the impact of achieving the WHO risk factor targets on morbidity

4 from NCDs and about the impact on a broad range of NCDs including mental health and neurological

5 disorders. In a study funded by the Richmond Group of Charities[8], PROMISE, we have examined

6 the implications of the WHO risk factor targets for priority setting in the UK. We modelled the

7 impact of meeting the risk factor targets on morbidity and mortality from a wide range of NCDs, and

8 examined whether the UK is likely to achieve a 25% reduction in premature mortality by 2025. In

9 addition, in order to estimate how much of the potentially preventable portion of NCD burden could

10 be addressed by the WHO targets, we evaluated an 'ideal risk reduction' scenario in which everyone

11 in the UK achieves a normal weight, is physically active, non-smoking, without diabetes or raised

12 blood pressure, has an ideal salt intake and does not drink alcohol at harmful levels. In this paper,

13 we report on the results of this study, and consider the implications for setting future targets for risk

14 reduction.

METHODS

16 We developed a dynamic model for simulating the effect of annual changes in risk factors on annual

17 burden of non-communicable diseases in the UK. The modelling was carried out in two parts. First,

18 we used historical data on risk factors in England to project trends in salt consumption, physical

19 activity, alcohol consumption, smoking, body mass index, diabetes and blood pressure forward to

20 2025, and then used these trends to estimate the proportional impact on NCDs of achieving the

21 25x25 targets. Second, we developed a population and mortality forecast model which estimated

22 business-as-usual projections of NCD morbidity and mortality to 2025. This was then used as the

23 baseline to apply the proportional changes in disease, which were calculated in the first model to

24 estimate the impact of achieving the WHO 25x25 targets and the ideal risk reduction on NCD

25 mortality and morbidity.

1 ## Risk factor projections model

2 Historical risk factor data were obtained from the Health Survey for England series[9]. This survey is

3 conducted annually and collects data on a representative sample of community-living adults in

4 England. Annual sample sizes are approximately 11,000 adults aged 18 and over. Data are collected

5 on health behaviour (including diet, smoking, alcohol consumption and physical activity) using a

6 standard questionnaire delivered and recorded by a trained interviewer. Anthropometric data,

7 including body mass index and blood pressure, are recorded by a trained nurse. For the PROMISE

8 project, we compiled a dataset (Stata Version 11) with data on the seven WHO targets from all

9 surveys conducted between 1995 and 2012.

10 All risk factor projections were stratified by sex and broad age group (18 to 35; 36 to 55; 56+). For

11 each stratum, following a method used for the UK Foresight 'Modelling future trends in obesity and

12 their impact on health' project[10], we modelled the relationship between prevalence of the risk

13 factor (p) and time (**t**) using the following equation (where *a* and *b* are model parameters):

$$p(\mathbf{t}) = \frac{1}{2}\left(1 + \tanh(a + b\mathbf{t})\right)$$

14 This relationship is convenient for modelling future projections, as it results in smooth changes over

15 time that are constrained between minimum and maximum values of 0 and 100%. For each risk

16 factor, we derived variables from the Health Survey for England dataset to match the risk factor

17 definitions used for the WHO targets[11], and then used logistic regression to fit the above equation,

18 with survey year providing the time variable. We then projected prevalence forward to 2025,

19 assuming the equations hold until this time. Table 1 provides further details regarding projections

20 for each of the seven risk factors.

21 Relative risks for the relationship between risk factors and diseases were taken from meta-analyses

22 of prospective studies (Table 2). In most cases, these were restricted to meta-analyses of cohort

23 studies, but in some cases meta-analyses that combined results from cohort studies and prospective

1 case control studies (i.e. nested in cohort studies) were also included. With the exception of salt, the

2 relationship between the risk factors and disease outcomes was modelled directly, and preference

3 was given to relative risks that were adjusted for the most of the other risk factors. The effect of salt

4 on blood pressure levels was modelled using a meta-analysis of salt reduction trials[12], and then

5 the subsequent impact of blood pressure on disease was modelled as described above.

6 The evidence relating a link between the risk factors and both dementia and depression is less

7 established than for the other disease outcomes. In some cases the mechanisms are unclear[13], or

8 previous results investigating the relationship have been highly heterogeneous[14]. Meta-analyses

9 of the relationship between risk factors and depression and dementia are often not based on

10 analyses adjusted for other risk factors, increasing the risk of confounding[15]. For this reason, we

11 present two sets of modelled results, for analyses that both include and do not include depression

12 and dementia as outcomes.

13 Evaluating population impact fractions (PIFs)

14 The WHO targets and the ideal risk reduction scenarios for salt consumption, physical activity,

15 alcohol consumption, smoking, body mass index, diabetes and blood pressure are described in Table

16 2. Our implementation of the WHO targets depended on whether the risk reductions were relative

17 reductions (e.g. a 30% reduction in smoking) or absolute reductions (e.g. halt the rise in obesity). For

18 relative reductions in the prevalence of a risk factor (smoking, blood pressure, alcohol, physical

19 inactivity), the reduction was applied to the projected prevalence in every year between 2010 and

20 2025. For absolute reductions in the prevalence of a risk factor (obesity, diabetes), the target

21 prevalence was assumed to be the actual prevalence in 2010. For relative reductions in a mean

22 consumption of a risk factor (salt), the reduction was applied in every year between 2010 and 2025,

23 and the standard deviation of the distribution for each age-sex stratum was assumed to remain

24 constant (i.e. the entire distribution was shifted). The ideal risk reduction scenarios were based on

25 definitions in the Global Burden of Disease study[16].

1   Table 1 Methods for the projection of risk factors.

Risk factor	WHO definition	HSE years used	Comments
Overweight and obesity	Overweight: adults with BMI between 25 and 30. Obese: adults with BMI greater than 30.	All years between 1995 and 2012.	Five BMI categories were projected: ≤20; 20-≤25; 25-≤30; 30-≤35; >35. The relationship between prevalence of each BMI category and survey year was modelled separately. Projections combined proportionately, in order to ensure the sum of all BMI categories was exactly 100% in any year.
Smoking	Prevalence of adult population currently using any tobacco product.	All years between 1995 and 2012.	The prevalence of current smoking and never smoking were projected. The prevalence of former smoking was assumed to be 100% - prevalence of never and current smokers.
Diabetes	Prevalence of raised blood glucose, or medication for raised glucose.	1998; 2003; 2006; 2009; 2010; 2011; 2012	We used prevalence of doctor-diagnosed diabetes. The WHO definition could not be used due to lack of representative data in England.
Blood pressure	Prevalence of adult population with SBP≥140mmHg or DBP≥90mmHg.	All years between 1995 and 2012.	Prevalence of raised blood pressure projected. To estimate health impact of raised blood pressure, relative risks are based on median SBP of age-sex-raised blood pressure groups in HSE2012.
Alcohol	Prevalence of heavy episodic drinking (consuming ≥60g alcohol on a single occasion at least monthly)	All years between 1998 and 2012.	Three alcohol categories were projected: abstainers (≤1g alcohol per week); non-harmful drinkers; harmful drinkers. Projections were combined proportionately, in order to ensure the sum of all alcohol categories was exactly 100% in any year. Relationships between alcohol and disease outcomes were based on difference in weekly alcohol consumption between alcohol groups, estimated using the HSE2012. A dummy variable was included in regression analyses to isolate the impact of changes in alcohol measurement in the HSE in 2006.
Physical inactivity	Prevalence of physical inactivity (less than 150 minutes of moderate-intensity activity per week, or equivalent).	1997; 1998; 2003; 2004; 2006; 2008; 2012	Three physical activity categories were projected: sedentary (≤0.2METh/d); not sedentary, but inactive; active. Logistic regression models estimated the trend in the prevalence of first two groups combined, and we separated between these two groups based on proportion of adults in HSE2012. The prevalence of activity was assumed to be 100% - prevalence of inactivity. Data between 1997 and 2012 were available on a consistent measure of inactivity, but only HSE2012 measured inactivity equivalent to the WHO definition. Regression models were based on the consistent measure of inactivity then adjusted according to the difference in the two measures recorded in HSE2012. The risk relationship between physical activity and disease outcomes based on difference in amount of physical activity (METh/d) between physical activity categories, estimated using HSE2012 data.
Salt (mediated by blood pressure)	Mean population intake of salt.	2008; 2009; 2010; 2011*	National Diet and Nutrition Survey urinary analyses data used to assess trends by age-sex groups. No trends apparent, so projections assume no change from current mean consumption levels. Mean and standard deviations used to generate normal distributions of salt consumption, which were converted into salt-related blood pressure using the prevalence of normotensives and hypertensives derived from the blood pressure projections, and parameters drawn from meta-analyses of salt reduction trials.

NB. HSE: Health Survey for England. BMI: Body Mass Index. SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure.
* Note that salt estimates are taken from urinary analyses in the National Diet and Nutrition Survey.

1 Table 2 WHO risk factor definitions, target levels and modelled disease outcomes.

Risk factor	Risk definitions and targets	Modelled NCD outcomes
Overweight and obesity	Overweight: adults with BMI between 25 and 30. Obese: adults with BMI greater than 30. WHO target: Halt the rise in obesity. Ideal target: Everyone normal weight (BMI 20-25; median 22)	CHD[17]; Stroke[17]; Diabetes[17]; Cirrhosis[17]; Colorectal cancer[17]; Kidney cancer[17]; Breast cancer[17]; Pancreas cancer[18]; Liver cancer[17]; Hypertensive heart disease[17]; Kidney disease[17]; Depression[19]; Dementia[20]
Smoking	Prevalence of adult population currently using any tobacco product. WHO target: 30% relative reduction. Ideal target: No current or past use of tobacco	COPD[21]; CHD[21]; Stroke[21]; Diabetes[22]; Lung cancer[23]; Oesophagus cancer[23]; Larynx cancer[23]; Stomach cancer[23]; Liver cancer[24]; Pancreas cancer[23]; Kidney cancer[23]; Cervix cancer[23]; Bladder cancer[23]; Depression[25]; Dementia[26]
Diabetes	Prevalence of doctor-diagnosed diabetes. WHO target: Halt the rise in diabetes. Ideal target: No prevalence of diabetes	CHD[27]; Stroke[28]; Depression[29]; Dementia[30]
Blood pressure	Prevalence of adult population with SBP≥140mmHg or DBP≥90mmHg. WHO target: 25% relative reduction in raised blood pressure. Ideal target: No prevalence of raised blood pressure	CHD[31]; Stroke[31]
Alcohol	Prevalence of heavy episodic drinking (consuming ≥60g alcohol on a single occasion at least monthly) and per capita consumption. WHO target: 10% relative reduction. Ideal target: No consumption of alcohol	CHD[32]; Stroke[33]; Hypertensive heart disease[32]; Diabetes[34]; Cirrhosis[35]; Liver cancer[36]; Mouth cancer[36]; Colorectal cancer[36]; Breast cancer[36]; Oesophagus cancer[36]
Physical inactivity	Prevalence of physical inactivity (less than 150 minutes of moderate-intensity activity per week, or equivalent). WHO target: 10% relative reduction. Ideal target: Everyone physically active	CHD*; Stroke*; Diabetes*; Breast cancer[37]; Colorectal cancer[37]; Depression[38]; Dementia[39]
Salt (mediated by blood pressure)	Mean population intake of salt. WHO target: 30% relative reduction. Ideal target: Mean intake of 1000mg/day	CHD[12, 31]; Stroke[12, 31]

NB. CHD: Coronary Heart Disease; COPD: Chronic Obstructive Pulmonary Disease. * Wahid et al. In press, Journal of American Heart Association.

2

3 Using the disease projections and the relative risk estimates, we calculated PIFs for each disease-risk

4 factor relationship, in each age-sex stratum, in every year between 2010 and 2025. PIFs estimate the

5 proportion of disease in a population that is removed under a counterfactual scenario (in this case,

6 in the scenario where the WHO targets or ideal levels are achieved). We calculated PIFs using the

7 following equation, where there are k risk factor categories, p_i is the proportion of the population in

8 risk factor category i in the estimate year based on projections, p'_i is the proportion of the

1 population in risk factor category *i* in the estimate year based on achieving the WHO or ideal risk

2 reduction target, and RR_i is the relative risk for the disease in risk factor category *i*:

$$PIF = \frac{\sum_{i=1}^{k} p_i RR_i - \sum_{i=1}^{k} p'_i RR_i}{\sum_{i=1}^{k} p_i RR_i}$$

3 We present results separately for each risk factor (i.e. when only the single risk factor target is

4 achieved) and in combination (i.e. if all risk factor targets are achieved). For the combined scenario,

5 we multiplicatively combined PIFs for blood pressure, diabetes, physical activity, BMI, alcohol and

6 tobacco:

$$PIF_{Combined} = 1 - (1 - PIF_{BP}) \times (1 - PIF_{Diab}) \times (1 - PIF_{PA}) \times (1 - PIF_{BMI}) \times (1 - PIF_{Alc}) \times (1 - PIF_{Tob})$$

7 We adjusted for potential double-counting of risk factor effects on CHD and stroke where there are

8 interdependencies in risks (e.g. physical activity affects CHD directly and via changes in BMI; BMI

9 affects CHD directly and via changes in blood pressure). Figure 1 shows a conceptual model of the

10 relationships between the risk factor targets for these diseases.

11 The effects of changes in alcohol and tobacco were assumed to be independent of each other and of

12 all other risk factors. However, where risk factors were both mediating variables and the subject of

13 WHO targets (blood pressure and diabetes), we took the larger of the effects. For example, we

14 calculated the combined effects of meeting physical activity, BMI and salt targets on BP (assuming

15 they are independent i.e. additive), we then calculated the effect of the hypertension target on BP,

16 and took only the larger of these two effects. Similarly, we calculated the combined effect of

17 meeting physical activity and BMI targets on diabetes (adjusting for the effects of physical activity on

18 BMI), then estimated the effect of the diabetes target on diabetes prevalence, and took only the

19 larger of the two effects. Further details on the methods for avoiding double counting are provided

20 in Appendix 1.We calculated 95% uncertainty intervals for all PIFs, based on lognormal distributions

21 for the relative risks and normal distributions for other variables as reported in the literature (e.g.

22 effect of salt on blood pressure), using Monte Carlo analysis[40].

1 ### Disease projections model

2 The PIFs were applied to projected disease rates in a UK population and mortality forecast model in

3 order to estimate disease outcomes of meeting WHO targets. The model was built in R (version

4 3.1.2) using packages *demography* and *systemfit*.

5 The UK population was forecast out to 2025 based on historical demographic patterns. We used

6 data from the period 1938 to 2010, obtaining population and mortality from the Human Mortality

7 Database[41], fertility from the Human Fertility Database[42], and deriving net migration for the

8 same time period, from these data. These demographic rates were smoothed using penalised

9 regression splines. We then fitted functional demographic models[43] to mortality, fertility and

10 migration rates from 1938 to 2010, and used these models to forecast future rates out to 2030.

11 Finally, we simulated the population over time to 2030, using bootstrapping to estimate uncertainty

12 in the population from the errors in the mortality, fertility and migration models.

13 For projecting disease-specific mortality, we developed regression models using methods described

14 by Salomon and Murray[44] that ensure that disease-specific mortality projections are consistent

15 with the projected all-cause mortality envelope. We obtained cause-specific mortality data from the

16 WHO database[45], focusing on deaths coded using the most recent version of the International

17 Classification of Diseases (ICD-10). ICD-10 was only adopted in the UK in 2001, which limited the

18 analyses to only 10 years of past data points. Including deaths coded using the preceding ICD-9

19 version, increased the years of available data back to 1980, but although we applied translations

20 from ICD-9 to ICD-10[46], there remained visible anomalies in the data before/after the change in

21 coding for some disease. Concerned that this could lead to incorrect predictions of trends, we

22 therefore restricted the analyses to the ICD-10 coded data, but broadened our data set to include

23 data from all EU countries, which have similar high income and low mortality profile, and included

24 GDP per capita into the model as an explanatory variable.

1. Deaths coded to heart failure (I50) were redistributed to the primary causes (e.g. coronary heart

2. disease (CHD), hypertensive heart disease, COPD and chronic kidney disease)[47]. Deaths were

3. grouped into three age groups: <35, 35-64 and 65+. For each age group, we determined country-

4. specific mortality for each risk factor-related disease, and all other diseases, as a proportion of all-

5. cause mortality in each country. Using methods described by Salomon and Murray[44] we specified

6. a multivariate normal model for the log of the ratios of each cause fraction to the cause fraction for

7. all other diseases, using the log of all-cause mortality rate and GDP per capita[48] as explanatory

8. variables. We then derived parameter values for the disease projections models, for each age group,

9. using seemingly unrelated regression[49].

10. To project disease rates forward in time for the UK, we applied the mortality projections from our

11. population forecasts and GDP projections from the World Bank[48] in the disease projections

12. models, to determine the annual average change in disease rates for the UK out to 2030.

Evaluating disease burden

14. To determine the future changes in population if the WHO or ideal risk reduction targets are

15. achieved we first calculated the new population mortality, using the PIFs to determine future

16. changes in mortality from the NCDs. We then re-simulated the future population out to 2030, using

17. the new rates of mortality, but assuming no change in forecasts of fertility and migration.

18. Effects on premature mortality were estimated as the change in probability of death from NCDs

19. between the ages of 30 and 69[3]. As was done in the global modelling of the WHO NCD reduction

20. targets[4], our estimate was unconditional, in that it excluded deaths from other causes (e.g.

21. injuries), but due to the broader range of diseases of interest in the PROMISE study, we included all

22. NCDs, rather than restricting the analysis to the four main NCD groups (cardiovascular, cancer,

23. diabetes and chronic respiratory diseases).

24. We defined the morbidity burden associated with non-communicable diseases as the reduction in

25. one year of life at full health. This was calculated at each age and sex, from Global Burden of Disease

1   estimates of prevalent years lived with disability (YLDs). We included a business-as-usual trend in

2   morbidity if there had been a significant change in Global Burden of Disease YLD estimates between

3   1990 and 2010. For diabetes and depression, we estimated a morbidity effect of achieving the WHO

4   targets, which we estimated using the PIFs for these diseases in the same way that the PIFs were

5   applied to mortality for all other NCDs.

RESULTS

7   With a continuation of current trends in mortality, fertility and migration, the number of 30 to 69

8   year olds in the UK population is expected to increase from around 32.5 million in 2010 to 33.4

9   million in 2025, with the proportion of the whole population aged over 70 rising from 12.5% in 2010

10 to 16.2% by 2025. With business-as-usual, the probability of premature mortality (30-69 years) from

11 non-communicable diseases among men is expected to fall from 17.6% in 2010 to 13.7% in 2025

12 (Figure 2). This equates to a relative reduction of 22%, which is just short of the WHO 25% reduction

13 target. Premature mortality among women, is expected to reach the WHO target, falling from 11.9%

14 in 2010 to 8.9% in 2025 (Figure 2), which equates to a relative reduction of 25%. If we assume trends

15 in risk factors and diseases continue to 2030, the outcomes follow the same pattern, with men (30%)

16 falling short of the 33% reduction target and women (33%) just reaching it.

17 There is added benefit from achieving the WHO 2025 behavioural risk factor targets (Table 3), which

18 ranges from an added relative reduction of 0.1% (reduced physical inactivity) to 2.3% (rise in obesity

19 halted). The combined effect of achieving all seven risk factor targets (relative reduction of 6.1% for

20 men and 3.0% for women) is sufficient for both men and women to reach the 25% premature

21 mortality reduction target by 2025 (Figure 2). Achieving the WHO targets would, however, achieve

22 only a quarter of what could potentially be achieved for men and less than a fifth of what could

23 potentially be achieved for women.

1   Achieving all seven behavioural risk factor targets would avert a total of 300,000 deaths (at all ages)

2   and 1.3 million YLDs from the reductions in related NCDs (excluding effects on depression and

3   dementia) between 2010 and 2025 (Table 4). The majority of improvements in mortality are due to

4   fewer deaths from CHD and stroke, while the majority of improvements in morbidity are due to

5   reduced rates of diabetes, CHD and stroke (Figure 3). Figure 3 also shows that there is potentially a

6   substantial additional gain in morbidity from reduced rates of depression in the 30-69 and 70+ age

7   groups; and substantial additional gains in both morbidity and mortality from reduced rates of

8   dementia in 70+ year olds.

9   The results demonstrate that, for the UK, achieving the obesity target will result in the biggest

10 overall impact on mortality and morbidity (Figure 4). Halting the rise in diabetes and achieving a 30%

11 reduction in salt intake would also achieve a large impact on NCD mortality, and reducing tobacco

12 consumption by 30% would have a large impact on morbidity.

13 Over time, achieving the combination of WHO risk factor targets would address an increasing

14 proportion of the health that could potentially be gained if everyone could adjust their risk

15 behaviour to ideal levels in 2010 (Figure 5 and Appendix 2 for deaths and YLDs averted under the

16 ideal risk scenario). Taking both morbidity and mortality into account, by 2025, 29% of the health

17 gain would be achieved for men and 26% for women. If we assume trends in risk factors and

18 diseases continue beyond 2025, the proportions would reach 35% for men and 33% for women by

19 2030.

Table 3 Relative reduction in probability of premature mortality from non-communicable diseases by 2025.

	WHO risk factor targets		Ideal risk reduction		Proportion of ideal risk addressed by meeting WHO target	
	Men	**Women**	**Men**	**Women**	**Men**	**Women**
Business-as-usual	22%	25%				
Additional reduction if achieving risk factor targets or ideal risk scenario:						
Obesity	2.3% (1.6% to 2.9%)	1.1% (0.3% to 1.9%)	7.9% (5.9% to 9.8%)	4.8% (2.6% to 7.1%)	29%	24%
Tobacco use	0.6% (0.6% to 0.7%)	0.6% (0.6% to 0.7%)	12.1% (10.1% to 14.0%)	9.7% (8.2% to 11.1%)	5%	7%
Diabetes	1.4% (1.2% to 1.7%)	0.7% (0.6% to 0.8%)	2.7% (2.2% to 3.2%)	1.4% (1.2% to 1.7%)	53%	51%
Raised blood pressure	0.4% (0.4% to 0.4%)	0.2% (0.2% to 0.2%)	1.6% (1.6% to 1.7%)	0.7% (0.7% to 0.8%)	25%	25%
Salt intake	0.8% (0.8% to 0.9%)	0.3% (0.3% to 0.3%)	2.1% (2.0% to 2.2%)	0.7% (0.7% to 0.8%)	39%	40%
Harmful alcohol use*	0.6% (0.4% to 0.8%)	0.3% (0.22% to 0.5%)	0.9% (-4.6% to 4.0%)	3.2% (-1.08% to 6.9%)	62%	11%
Physical inactivity	0.1% (0.08% to 0.1%)	0.1% (0.0% to 0.1%)	1.1% (0.81% to 1.4%)	0.6% (0.4% to 0.7%)	10%	10%
Combined scenario	6.5% (5.4% to 7.5%)	3.2% (2.2% to 4.1%)	26.2% (21.9% to 29.7%)	18.4% (14.3% to 22.2%)	25%	17%

NB. Values are mean and 95% uncertainty intervals. * Low-level consumption of alcohol is associated with a decreased risk of some diseases (e.g. CHD, hypertensive heart disease and diabetes), which partly counter the modelled health benefits of abstaining from alcohol.

15

Table 4 Total non-communicable disease deaths and YLDs that are averted or delayed between 2010 and 2025, for each of the risk factor target scenarios

	30-69 years		70+ years	
	Men	Women	Men	Women
Deaths				
Obesity	13,000 (8,900 to 17,000)	4,500 (500 to 8,600)	47,000 (34,000 to 60,000)	26,000 (11,000 to 40,000)
Tobacco use	5,100 (4,800 to 5,400)	4,300 (4,100 to 4,400)	14,000 (13,000 to 15,000)	15,000 (14,000 to 15,000)
Diabetes	7,200 (5,900 to 8,600)	2,500 (2,000 to 2,900)	38,000 (30,000 to 45,000)	32,000 (26,000 to 38,000)
Raised blood pressure	5,700 (5,400 to 6,100)	2,300 (2,100 to 2,500)	25,000 (24,000 to 26,000)	23,000 (22,000 to 24,000)
Salt intake	9,000 (8,700 to 9,400)	2,500 (2,400 to 2,600)	38,000 (37,000 to 39,000)	26,000 (25,000 to 27,000)
Harmful alcohol use	4,900 (3,000 to 6,900)	2,000 (1,200 to 2,800)	11,000 (7,100 to 16,000)	6,100 (800 to 11,000)
Physical inactivity	920 (660 to 1,200)	320 (240 to 400)	4,300 (3,200 to 5,400)	3,900 (2,800 to 4,900)
Combined scenario	38,000 (32,000 to 44,000)	13,000 (8,500 to 17,000)	150,000 (130,000 to 170,000)	99,000 (79,000 to 120,000)
YLDs				
Obesity	79,000 (66,000 to 93,000)	50,000 (38,000 to 63,000)	150,000 (120,000 to 170,000)	98,000 (66,000 to 130,000)
Tobacco use	20,000 (20,000 to 21,000)	25,000 (25,000 to 26,000)	27,000 (26,000 to 28,000)	37,000 (36,000 to 38,000)
Diabetes	190,000 (190,000 to 190,000)	160,000 (160,000 to 160,000)	330,000 (320,000 to 340,000)	290,000 (290,000 to 300,000)
Raised blood pressure	18,000 (17,000 to 19,000)	12,000 (11,000 to 13,000)	40,000 (38,000 to 42,000)	31,000 (29,000 to 33,000)
Salt intake	29,000 (28,000 to 30,000)	14,000 (14,000 to 15,000)	60,000 (57,000 to 62,000)	34,000 (33,000 to 36,000)
Harmful alcohol use	6,200 (-18,000 to 30,000)	-280 (-8,700 to 8,100)	14,000 (-25,000 to 53,000)	3,100 (-12,000 to 18,000)
Physical inactivity	6,200 (5,300 to 7,000)	5,500 (4,700 to 6,200)	13,000 (11,000 to 15,000)	13,000 (11,000 to 14,000)
Combined scenario	260,000 (240,000 to 280,000)	200,000 (190,000 to 210,000)	480,000 (430,000 to 520,000)	370,000 (350,000 to 400,000)

NB. Values are mean and 95% uncertainty intervals..

16

1 ## DISCUSSION

2 There have been considerable achievements in addressing the risks for non-communicable disease in

3 the UK over the last three decades. Although prevalence of obesity and diabetes have risen,

4 initiatives such as increasing access to blood pressure-lowering drugs, reducing salt in processed

5 foods, and strengthening tobacco control, have all contributed to the reduction in these risk factors

6 over time. These changes in lifestyle behaviours, along with advances in treatment, have contributed

7 to the reduction in non-communicable diseases that we observed. Our projections show that if these

8 trends continue, there is likely to be a substantial further reduction in NCD burden by 2025, which

9 will see the UK very nearly reach the current WHO target of 25% reduction in premature mortality

10 and very likely reach the proposed 30% reduction by 2030.

11 It will be critical that past investments in prevention (and treatment) are sustained so that the UK

12 does not lose the momentum built over previous decades. Preventive efforts must also be increased

13 if the UK is to meet the 2025 target. While the targets do provide a worthwhile objective, a further

14 two-thirds of the preventable NCD burden could potentially be reduced with an even more ambitious

15 prevention program in the future.

16 Although current WHO targets focus on premature mortality, our modelling predicted substantial

17 added benefits from reduced NCD morbidity, particularly at older ages. Around 16% of Government

18 spending in the UK is allocated to health, which is high compared to other European countries[50].

19 The large reductions in NCD burden, particularly for CHD, stroke, diabetes, depression and dementia,

20 would help reduce these costs. The social and economic burden of diseases such as depression and

21 dementia is also high. Depression for example is associated with increased workplace absenteeism

22 and reduced productivity[51], and dementia is associated with substantial social care costs[52]. In

23 2012 the cost of health and social care services for dementia patients in the UK was greater than the

24 costs of CHD, stroke and cancer care combined[52].

25 Unfortunately the drivers of mental and neurological disorders, despite a high global burden, are

26 poorly understood[37]. Further research is needed to strengthen the epidemiological evidence of the

1 links between lifestyle risks and prevention of diseases, such as depression and dementia, and to

2 better understand how prevalence of these diseases may in turn increase risk of other NCDs. In the

3 UK, funding for dementia and mental health research is low in comparison to the size of the

4 burden[52, 53]. However, a review of costs and burden of mental and neurological disorders in the

5 EU estimated that the return on investment in research would be highly favourable when taking the

6 full cost to society into account[54].

7 Cost-effectiveness analysis can be used to identify which interventions will provide best value-for-

8 money. Modelling of interventions for improving diet and body mass in England, suggest that fiscal

9 measures and regulation may be more cost-effective than more individually targeted approaches

10 such as physician counselling and worksite programs[55], which is consistent with findings from

11 modelling studies in comparable high income countries such as Australia[56, 57] and New

12 Zealand[58]. But further work is needed to identify the most effective and cost-effective

13 interventions for addressing a wider range of risk factor targets in the UK, including a number of

14 dietary risks associated with a high NCD burden that are not included in the WHO targets (e.g. fruits

15 and vegetables, fats and cholesterol[37]). Modelling is also needed to better understand and

16 quantify the health impacts of underlying drivers of change, such as global marketing and trade, the

17 design of urban environments and climate change.

18 The WHO's inclusion of dietary risk factors as targets in the Global NCD Action Plan was minimal,

19 given the high level of attributable NCD burden[37]. For example, while a 30% reduction target was

20 set for salt intake, no targets were defined for reducing intake of transfats, red and processed meats

21 or sugar-sweetened beverages, or increasing intake of fibre, whole grains, fruits and vegetables. The

22 omission of these risk factors does mean that our study and previous global modelling estimates[4]

23 are likely to have underestimated the potential for reduction in premature mortality from NCDs.

24 To model the impact of changing risk factors on NCDs, it is necessary to draw on a wide variety of

25 different levels of evidence to calculate the dependencies between risk factors and avoid double-

26 counting of outcomes. For example, to calculate impacts on BMI from changes in physical activity we

1   relied on models of human energy-balance derived by Hall et al[59]; to calculate impacts on blood

2   pressure levels from changes in salt intake, we used measures from meta-regression of randomised

3   controlled trials of blood pressure reduction; and to determine dose-response relationships between

4   risk factors and diseases we drew on a variety of meta-analyses of observational studies. While most

5   studies adjust for potential confounding factors (e.g. age, sex, smoking) it is impossible to rule out

6   residual confounding from missing or poorly measured explanatory variables. In addition, where

7   there are multiple pathways between a risk factor and disease (e.g. there is risk of CHD from physical

8   inactivity directly and indirectly via diabetes) we have estimated the relative risks for the two

9   pathways from studies of the risk for the pathways combined and the prevalence of the risk factors

10 (see Note 2 in Appendix 1). These approximations are necessary in the absence of large, long-term

11 studies that measure and adjust for all possible risks simultaneously. Consequently, it is likely that

12 there is greater uncertainty in our results than is reflected in the uncertainty intervals we have

13 estimated.

14 This modelling study contributes to the evidence about the potential impact of changes in risk factor

15 prevalence, but to implement change evidence is needed on interventions designed to tackle

16 behavioural risk factors. The relative magnitude of health gain associated with the WHO risk factor

17 targets is not necessarily a good guide for setting priorities for intervention. The apparently smaller

18 benefits of addressing physical inactivity and harmful alcohol use, for example, are in large part

19 because the WHO targets are relatively modest. The modelling of alcohol targets also does not

20 capture any benefits from reduced injury rates, which fall outside of the NCD focus of the WHO

21 targets. In addition, the modelling of some risk factors was limited by the available data (e.g. self-

22 reported physical activity) and WHO definitions (e.g. prevalence of hypertension rather than the full

23 distribution of blood pressure). In addition, past decades of successful intervention in the UK (e.g.

24 blood pressure lowering drugs, tobacco taxes, smoking cessation programs) has seen the prevalence

25 of high blood pressure and prevalence of smoking decline, so that the WHO targets (25% relative

26 reduction in high BP and 30% relative reduction in smoking) are relatively less beneficial than the

1 targets to halt the rise in prevalence of obesity and diabetes, both of which are rising steeply in the

2 UK.

3 Early population health impact studies typically modelled effects on a population cohort without

4 forward projection of disease trends or they modelled effects on a population cohort forward in time

5 without replacement (i.e. following the current adult population until death or end of projection). In

6 evaluating global NCD impact of the WHO targets, Kontis et al[4] advanced this approach by

7 modelling the population impacts between 2010 and 2025 in three five-year intervals, incorporating

8 projections of disease trends and allowing for population growth and ageing between each modelled

9 time interval. We have taken the modelling a step further by incorporating risk factor prevalence

10 rates and model outputs of disease rates that are directly comparable to past trends, and integrating

11 this with a population demographic model that stochastically forecasts trends in mortality, fertility

12 and migration. This approach could facilitate future integration with other models, including

13 economic models (e.g. AgMIP models, which focus on food security under climate change[1])

14 allowing health outcomes to be included in broader systems modelling studies. In addition, while

15 focused on a select range of WHO risk factor targets and NCD outcomes for these analyses, the

16 model could potentially be adapted to address a more diverse range of risks factors and disease

17 outcomes in the future.

18 This modelling study illustrates the large health gains that could be achieved by addressing unhealthy

19 risk factors for disease. For countries such as the UK that can capitalise on many decades of effort in

20 prevention and treatment, the WHO premature mortality target is an achievable goal. But with a

21 further two-thirds of the NCD burden still potentially preventable, it is imperative that the UK

22 capitalises on the momentum of past decades with further effort in prevention. For low- and middle-

23 income countries the potential benefits are likely to be even greater[4], as is the need for evidence to

24 develop cost-effective policies for prevention in these countries. Given the growing global burden of

25 diseases such as diabetes, depression and dementia, the WHO should consider future global targets

26 that provide incentives for addressing these diseases, which carry a high health burden for the

27 individual and place a substantial burden on health and social care systems in society.

1 ## ACKNOWLEDGMENTS

4 ## COMPETING INTERESTS

5 All authors have completed the Unified Competing Interest form at

6 www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare

7 that (1) LC and PS have support from the Richmond Group of Charities

8 (www.richmondgroupofcharities.org.uk) for the submitted work; (2) LC and PS have no relationships

9 with any companies that might have an interest in the submitted work in the previous 3 years; (3)

10 their spouses, partners, or children have no financial relationships that may be relevant to the

11 submitted work; and (4) LC and PS have no non-financial interests that may be relevant to the

12 submitted work."

13 ## AUTHOR CONTRIBUTIONS

14 LC and PS conceived of the study, collected and analysed the data, interpreted the results and

15 contributed to writing and editing the manuscript.

16 ## ETHICS APPROVAL

17 Not required

18 ## FUNDING

1   full access to all of the data (including statistical reports and tables) in the study and take

2   responsibility for the integrity of the data and the accuracy of the data analysis.

3   Transparency declaration: The lead author (the manuscript's guarantor) affirms that the manuscript

4   is an honest, accurate, and transparent account of the study being reported; that no important

5   aspects of the study have been omitted; and that any discrepancies from the study as planned (and,

6   if relevant, registered) have been explained.

DATA SHARING

8   No additional data available.

9

REFERENCES

1. Rosenzweig C, Jones J, Hatfield J, et al. The agricultural model intercomparison and improvement project (AgMIP): protocols and pilot studies. *Agricultural and Forest Meteorology*. 2013;170:166-82.

2. United Nations. Political declaration of the High-level Meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases. United Nations General Assembly, Sixty-sixth session, Agenda item 117, 2011.

3. WHO. Global action plan for the prevention and control of noncommunicable diseases 2013–2020. Geneva: World Health Organization, 2013.

4. Kontis V, Mathers CD, Rehm J, et al. Contribution of six risk factors to achieving the 25× 25 non-communicable disease mortality reduction target: a modelling study. *The Lancet*. 2014;384(9941):427-37.

5. Beaglehole R, Bonita R, Ezzati M, et al. NCD Countdown 2025: accountability for the 25× 25 NCD mortality reduction target. *The Lancet*. 2014;384(9938):105-7.

6. Pearce N, Ebrahim S, McKee M, et al. The road to 25× 25: how can the five-target strategy reach its goal? *The lancet global health*. 2014;2(3):e126-e8.

7. WHO. Health in 2015: from MDGs, Millennium Development Goals to SDGs, Sustainable Development Goals. Geneva: World Health Organization, 2015.

8. The Richmond Group of Charities. [15 December 2015]. Available from: http://www.richmondgroupofcharities.org.uk/.

9. Joint Health Surveys Unit. Health Survey for England 2013 (and previous editions). Leeds: Health and Social Care Information Centre, 2014.

10. McPherson K, Marsh T, Brown M. Foresight. Tackling obesities – modelling future trends in obesity and the impact on health. London: Government Office for Science, 2007.

11. WHO. Noncommunicable diseases global monitoring framework: indicator definitions and specifications. Geneva: World Health Organization, 2014.

12. He FJ, Li J, MacGregor GA. Effect of longer term modest salt reduction on blood pressure: Cochrane systematic review and meta-analysis of randomised trials. *BMJ*. 2013;346.

13. Baumgart M, Snyder HM, Carrillo MC, et al. Summary of the evidence on modifiable risk factors for cognitive decline and dementia: A population-based perspective. *Alzheimer's & Dementia*. 2015;11(6):718-26.

14. Valkanova V, Ebmeier KP. Vascular risk factors and depression in later life: a systematic review and meta-analysis. *Biol Psychiatry*. 2013;73(5):406-13.

15. Cheng G, Huang C, Deng H, et al. Diabetes as a risk factor for dementia and mild cognitive impairment: a meta-analysis of longitudinal studies. *Intern Med J*. 2012;42(5):484-91.

16. Lim S, Vos T, Flaxman A, et al. The burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions 1990-2010: a systematic analysis. *The Lancet*. 2013;380(9859):2224-60.

17. Prospective Studies Collaboration. Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. *The Lancet*. 2009;373(9669):1083-96.

18. Norat T, Aune D, Vieira R, et al. The Associations between Food, Nutrition and Physical Activity and the Risk of Pancreatic Cancer. WCRF/AICR Systematic Literature Review Continuous Update Project Report, 2011.

19. Luppino FS, de Wit LM, Bouvy PF, et al. Overweight, obesity, and depression: a systematic review and meta-analysis of longitudinal studies. *Arch Gen Psychiatry*. 2010;67(3):220-9.

20. Beydoun M, Beydoun H, Wang Y. Obesity and central obesity as risk factors for incident dementia and its subtypes: a systematic review and meta-analysis. *Obes Rev*. 2008;9(3):204-18.

21. Thun MJ, Apicella LF, Henley SJ. Smoking vs other risk factors as the cause of smoking-attributable deaths. Confounding in the courtroom. *JAMA*. 2000;284(6):706-12.

22. Willi C, Bodenmann P, Ghali WA, et al. Active smoking and the risk of type 2 diabetes: A systematic review and meta-analysis. *JAMA*. 2007;298(22):2654-64.

23. Gandini S, Botteri E, Iodice S, et al. Tobacco smoking and cancer: A meta-analysis. *Int J Cancer*. 2008;122(1):155-64.

1 24. Lee Y-CA, Cohet C, Yang Y-C, et al. Meta-analysis of epidemiologic studies on cigarette

2 smoking and liver cancer. *Int J Epidemiol*. 2009:dyp280.

3 25. Luger TM, Suls J, Vander Weg MW. How robust is the association between smoking and

4 depression in adults? A meta-analysis using linear mixed-effects models. *Addict Behav*.

5 2014;39(10):1418-29.

6 26. Zhong G, Wang Y, Zhang Y, et al. Smoking Is Associated with an Increased Risk of Dementia: A

7 Meta-Analysis of Prospective Cohort Studies with Investigation of Potential Effect Modifiers. *PLoS

8 ONE*. 2015;10(3):e0118333.

9 27. Peters SA, Huxley RR, Woodward M. Diabetes as risk factor for incident coronary heart

10 disease in women compared with men: a systematic review and meta-analysis of 64 cohorts

11 including 858,507 individuals and 28,203 coronary events. *Diabetologia*. 2014;57(8):1542-51.

12 28. Peters SA, Huxley RR, Woodward M. Diabetes as a risk factor for stroke in women compared

13 with men: a systematic review and meta-analysis of 64 cohorts, including 775 385 individuals and 12

14 539 strokes. *The Lancet*. 2014;383(9933):1973-80.

15 29. Rotella F, Mannucci E. Diabetes mellitus as a risk factor for depression. A meta-analysis of

16 longitudinal studies. *Diabetes Res Clin Pract*. 2013;99(2):98-104.

17 30. Gudala K, Bansal D, Schifano F, et al. Diabetes mellitus and risk of dementia: a meta-analysis

18 of prospective observational studies. *Journal of diabetes investigation*. 2013;4(6):640-50.

19 31. Lewington S. Prospective studies collaboration. Age-specific relevance of usual blood

20 pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61

21 prospective studies (vol 360, pg 1903, 2002). *Lancet*. 2003;361(9362):1060-.

22 32. Shield KD, Parry C, Rehm J. Chronic diseases and conditions related to alcohol use. *Alcohol

23 research: current reviews*. 2014;35(2):155.

24 33. Patra J, Taylor B, Irving H, et al. Alcohol consumption and the risk of morbidity and mortality

25 for different stroke types - a systematic review and meta-analysis. *BMC Public Health*. 2010;10.

26 34. Baliunas DM, Taylor BM, Irving HM, et al. Alcohol as a risk factor for type 2 diabetes: a

27 systematic review and meta-analysis. *Diabetes Care*. 2009;32(11):2123.

1   35.   Rehm J, Taylor B, Mohapatra S, et al. Alcohol as a risk factor for liver cirrhosis: A systematic

2   review and meta-analysis. *Drug Alcohol Rev*. 2010;29(4):437-45.

3   36.   Corrao G, Bagnardi V, Zambon A, et al. A meta-analysis of alcohol consumption and the risk

4   of 15 diseases. *Prev Med*. 2004;38(5):613-9.

5   37.   Forouzanfar MH, Alexander L, Anderson HR, et al. Global, regional, and national comparative

6   risk assessment of 79 behavioural, environmental and occupational, and metabolic risks or clusters of

7   risks in 188 countries, 1990–2013: a systematic analysis for the Global Burden of Disease Study 2013.

8   *The Lancet*. 2015;386:2287-323.

9   38.   Physical Activity Guidelines Advisory Committee. Physical Activity Guidelines Advisory

10   Committee Report. Washington, DC: U.S. Department of Health and Human Services, 2008.

11   39.   Blondell SJ, Hammersley-Mather R, Veerman JL. Does physical activity prevent cognitive

12   decline and dementia?: A systematic review and meta-analysis of longitudinal studies. *BMC Public

13   Health*. 2014;14(1):510.

14   40.   Fishman G. Monte Carlo: concepts, algorithms, and applications. New York: Springer-Verlag

15   1995.

16   41.   University of California Berkeley (USA), Max Planck Institute for Demographic Research

17   (Germany). Human Mortality Database [2 April 2015]. Available from: www.mortality.org.

18   42.   Max Planck Institute for Demographic Research (Germany), Vienna Institute of Demography

19   (Austria). Human Fertility Database [29 April 2015]. Available from: www.humanfertility.org.

20   43.   Hyndman RJ, Booth H, Yasmeen F. Coherent mortality forecasting: the product-ratio method

21   with functional time series models. *Demography*. 2013;50(1):261-83.

22   44.   Salomon JA, Murray CJ. The epidemiologic transition revisited: compositional models for

23   causes of death by age and sex. *Population and Development Review*. 2002;28(2):205-28.

24   45.   World Health Organization. WHO Mortality Database [4 November 2014]. Available from:

25   http://www.who.int/healthinfo/statistics/mortality_rawdata/en/.

26   46.   Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to

27   2030. *PLoS Med*. 2006;3(11):e442.

47. Naghavi M, Makela S, Foreman K, et al. Research Algorithms for enhancing public health utility of national causes-of-death data. *Popul Health Metr*. 2010;8:9.

48. The World Bank. World Development Indicators [1 May 2015]. Available from: http://data.worldbank.org/data-catalog/world-development-indicators.

49. Greene WH. Econometric analysis. 5th ed. Upper Saddle River, New Jersey: Prentice Hall; 2003.

50. WHO. National health accounts: country health information Geneva: World Health Organization; 2015 [15 December 2015]. Available from: http://apps.who.int/nha/database/Country_Profile/Index/en.

51. Donohue JM, Pincus HA. Reducing the societal burden of depression. *Pharmacoeconomics*. 2007;25(1):7-24.

52. Luengo-Fernandez R, Leal J, Gray A. UK research spend in 2008 and 2012: comparing stroke, cancer, coronary heart disease and dementia. *BMJ open*. 2015;5(4):e006648.

53. Kingdon D. Health research funding: Mental health research continues to be underfunded. *BMJ*. 2006;332(7556):1510.

54. Gustavsson A, Svensson M, Jacobi F, et al. Cost of disorders of the brain in Europe 2010. *Eur Neuropsychopharmacol*. 2011;21(10):718-79.

55. Cecchini M, Sassi F, Lauer JA, et al. Tackling of unhealthy diets, physical inactivity, and obesity: health effects and cost-effectiveness. *The Lancet*. 2010;376(9754):1775-84.

56. Cobiac LJ, Vos T, Doran C, et al. Cost-effectiveness of interventions to prevent alcohol-related disease and injury in Australia. *Addiction*. 2009;104(10):1646-55.

57. Cobiac LJ, Vos T, Veerman JL. Cost-effectiveness of interventions to reduce dietary salt intake. *Heart*. 2010;96(23):1920-5.

58. Nghiem N, Blakely T, Cobiac LJ, et al. Health and economic impacts of eight different dietary salt reduction interventions. *PLoS ONE*. 2015;10(4).

59. Hall KD, Sacks G, Chandramohan D, et al. Quantification of the effect of energy imbalance on bodyweight. *The Lancet*. 2011;378(9793):826-37.

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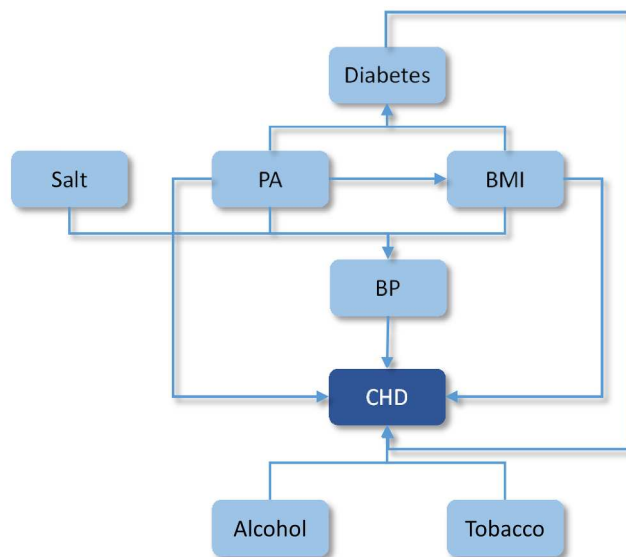48
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FIGURES

Figure 1 The modelled relationships between the WHO risk factor targets and CHD or stroke (Note: PA – physical activity; BMI – body mass index; BP – blood pressure; CHD – coronary heart disease).

Figure 2 Projected trends in the probability of dying prematurely from non-communicable disease for the WHO risk factor target scenarios.

Figure 3 Non-communicable disease deaths and YLDs that are averted or delayed between 2010 and 2025, for the combined risk factor target scenario. (Note: the small increase in COPD YLDs is due to a shift in the age distribution of the population, primarily as a result of reductions in CHD and stroke mortality, and does not reflect an increase in COPD rates).

Figure 4 DALYs averted for the WHO risk factor target scenarios.

Figure 5 DALYs averted for the combined WHO risk factor target scenario and the ideal risk reduction scenario.

SUPPORTING DOCUMENTS

Appendix 1: Calculating the combined effect of meeting all risk factor targets

Appendix 2: Ideal risk scenario results

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Figure 1 The modelled relationships between the WHO risk factor targets and CHD or stroke (Note: PA – physical activity; BMI – body mass index; BP – blood pressure; CHD – coronary heart disease).
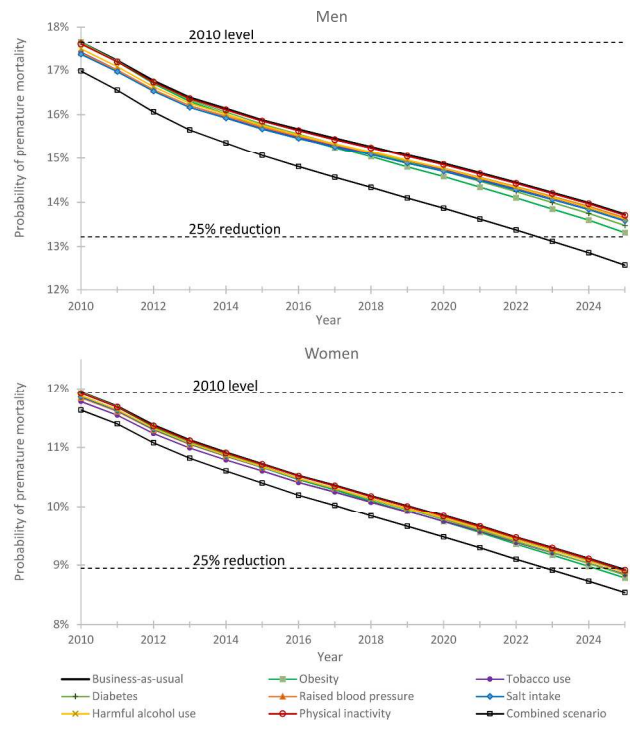
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Figure 2 Projected trends in the probability of dying prematurely from non-communicable disease for the WHO risk factor target scenarios.

297x420mm (300 x 300 DPI)

Deaths

Years Lived with Disability

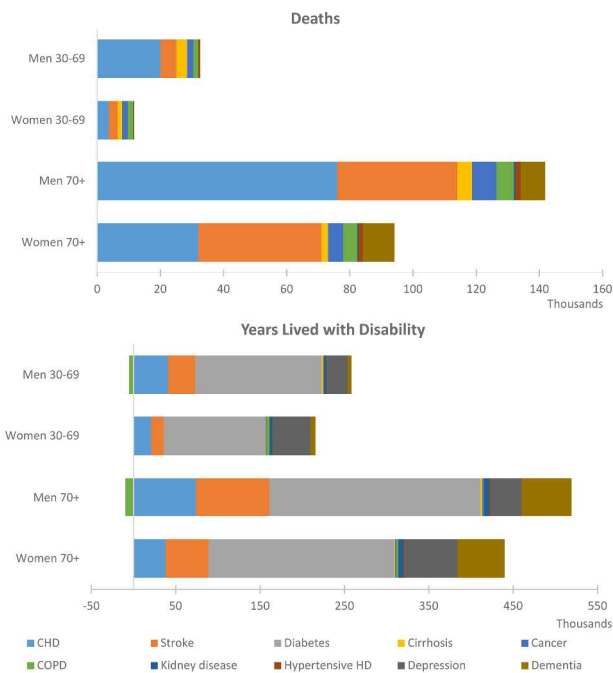Legend: CHD, Stroke, Diabetes, Cirrhosis, Cancer, COPD, Kidney disease, Hypertensive HD, Depression, Dementia

Figure 3 Non-communicable disease deaths and YLDs that are averted or delayed between 2010 and 2025, for the combined risk factor target scenario. (Note: the small increase in COPD YLDs is due to a shift in the age distribution of the population, primarily as a result of reductions in CHD and stroke mortality, and does not reflect an increase in COPD rates).
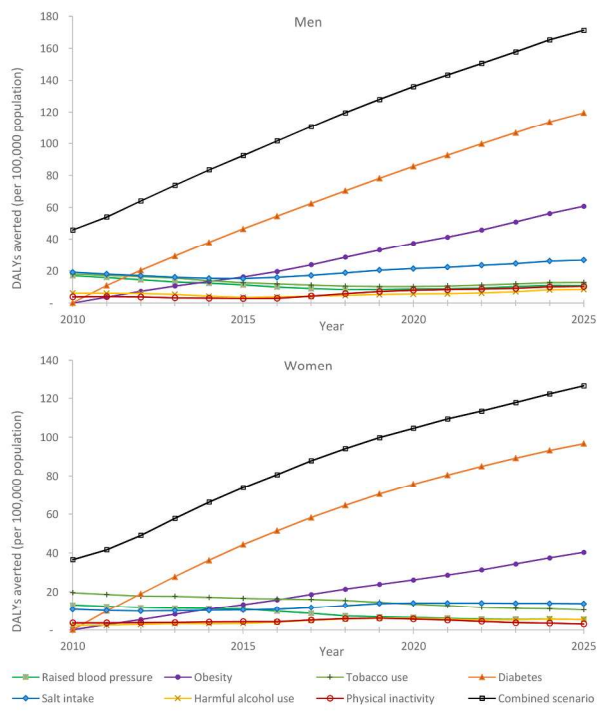
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Figure 4 DALYs averted for the WHO risk factor target scenarios.
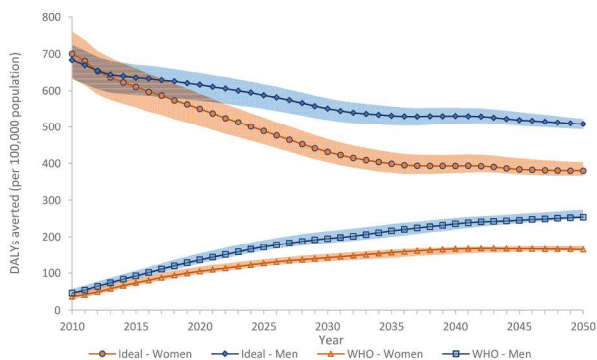
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Figure 5 DALYs averted for the combined WHO risk factor target scenario and the ideal risk reduction scenario.

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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.

$$PIF_{Combined} = 1 - (1 - PIF_{BP}) \times (1 - PIF_{Diab}) \times (1 - PIF_{PA}) \times (1 - PIF_{BMI}) \times (1 - PIF_{Alc}) \times (1 - PIF_{Tob})$$

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.)
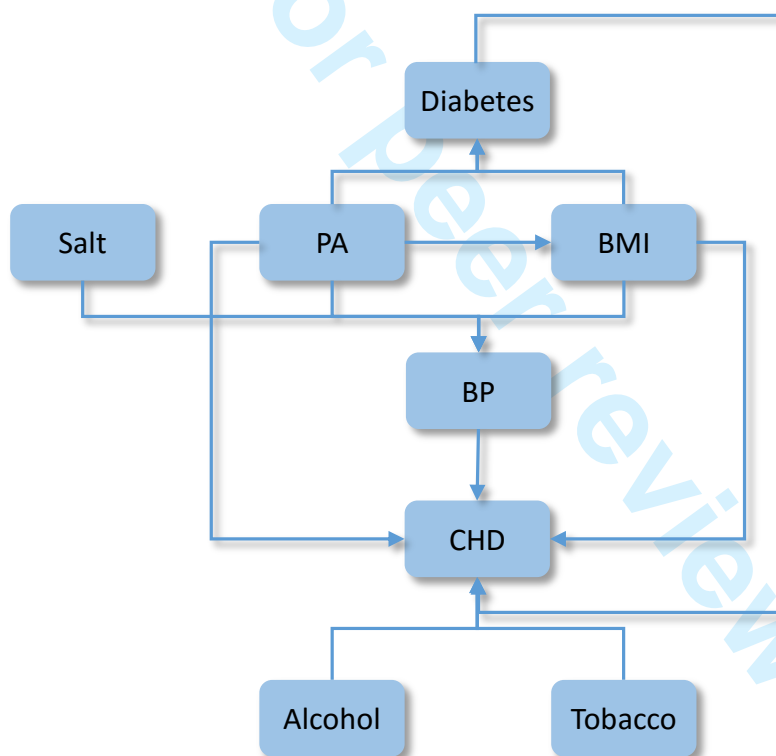

Table 1 Methods for the calculation of population impact fractions (PIFs) for the combined risk factor scenario

PIF	Calculations	Sources
PIF_{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_{BP} = 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_{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]

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	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)	Cobiac et al[6] (adjustment estimate) Peters et al[7,8]
	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_{Diab} = the biggest of the PIFs calculated in steps 4 and 5	
PIF_{PA} (excluding effects via BP and Diabetes)	PIF_{PA} = PIF calculated for the direct **PA** using RR CHD/Stroke estimates (see Note 2 below)	Wahid et al Under review Health Survey for England 2012[9] Global Burden of Disease[10]
PIF_{BMI} (excluding effects via BP and Diabetes)	PIF_{BMI} = PIF calculated for the direct **BMI** using RR CHD/Stroke estimates (see Note 2 below)	Prospective Studies Collaboration[5] Cobiac et al[6] (adjustment estimate) Health Survey for England (HSE) 2012[9] Global Burden of Disease (GBD)[10]
PIF_{Alc}	PIF_{Alc} = PIF calculated using RR CHD/Stroke estimates from meta-analyses	Shield et al[11] Patra et al[12]
PIF_{Tob}	PIF_{Tob} = PIF calculated using RR CHD/Stroke estimates from meta-analyses	Cancer Prevention Study II[13]

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].
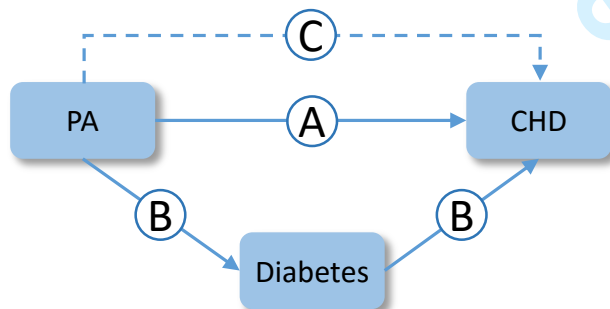

Figure 2 Conceptual diagram of the pathways between risk factor (physical activity), intermediate variable (diabetes) and disease (CHD) in the optimisation process.

References

1. Cornelissen VA, Fagard RH (2005) Effects of endurance training on blood pressure, blood pressure–regulating mechanisms, and cardiovascular risk factors. Hypertension 46: 667-675.

2. Neter JE, Stam BE, Kok FJ, Grobbee DE, Geleijnse JM (2003) Influence of weight reduction on blood pressure a meta-analysis of randomized controlled trials. Hypertension 42: 878-884.

3. He FJ, Li J, MacGregor GA (2013) Effect of longer term modest salt reduction on blood pressure: Cochrane systematic review and meta-analysis of randomised trials. BMJ: British Medical Journal 346.

4. Prospective Studies Collaboration (2002) Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. The Lancet 360: 1903-1913.

5. Prospective Studies Collaboration (2009) Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. The Lancet 373: 1083-1096.

6. Cobiac LJ, Vos T, Veerman JL (2010) Cost-effectiveness of Weight Watchers and the Lighten Up to a Healthy Lifestyle program. Australian and New Zealand Journal of Public Health 34: 240-247.

7. Peters SA, Huxley RR, Woodward M (2014) Diabetes as risk factor for incident coronary heart disease in women compared with men: a systematic review and meta-analysis of 64 cohorts including 858,507 individuals and 28,203 coronary events. Diabetologia 57: 1542-1551.

8. Peters SA, Huxley RR, Woodward M (2014) Diabetes as a risk factor for stroke in women compared with men: a systematic review and meta-analysis of 64 cohorts, including 775 385 individuals and 12 539 strokes. The Lancet 383: 1973-1980.

9. Joint Health Surveys Unit (2014) Health Survey for England 2013 (and previous editions). Leeds: Health and Social Care Information Centre.

10. Wang H, Dwyer-Lindgren L, Lofgren KT, Rajaratnam JK, Marcus JR, et al. (2013) Age-specific and sex-specific mortality in 187 countries, 1970–2010: a systematic analysis for the Global Burden of Disease Study 2010. The Lancet 380: 2071-2094.

11. Shield KD, Parry C, Rehm J (2014) Chronic diseases and conditions related to alcohol use. Alcohol research: current reviews 35: 155.

12. Patra J, Taylor B, Irving H, Roerecke M, Baliunas D, et al. (2010) Alcohol consumption and the risk of morbidity and mortality for different stroke types - a systematic review and meta-analysis. BMC Public Health 10.

13. Thun MJ, Apicella LF, Henley SJ (2000) Smoking vs other risk factors as the cause of smoking-attributable deaths: confounding in the courtroom. Jama 284: 706-712.

14. Hall KD, Sacks G, Chandramohan D, Chow CC, Wang YC, et al. (2011) Quantification of the effect of energy imbalance on bodyweight. The Lancet 378: 826-837.

15. Heitmann BL, Garby L (2002) Composition (lean and fat tissue) of weight changes in adult Danes. The American journal of clinical nutrition 75: 840-847.

16. Mifflin MD, St Jeor ST, Hill LA, Scott BJ, Daugherty SA, Koh Y (1990) A new predictive equation for resting energy expenditure in healthy individuals. The American journal of clinical nutrition 51: 241-247.

17. FAO (2001) Human Energy Requirements: Report of a Joint FAO/WHO/UNU Expert Consultation. Rome: Food and Agriculture Organization of the United Nations, World Health Organization, United Nations University.

18. Ainsworth BE, Haskell WL, Herrmann SD, Meckes N, Bassett Jr DR, et al. (2011) 2011 Compendium of Physical Activities: a second update of codes and MET values. Medicine and science in sports and exercise 43: 1575-1581.

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Appendix 2: Ideal risk scenario results

Table 1 Total non-communicable disease deaths and YLDs that are averted or delayed between 2010 and 2025, for the ideal risk scenario

	30-69 years		70+ years	
	Men	Women	Men	Women
Deaths				
Obesity	63,000 (46,000 to 80,000)	26,000 (13,000 to 39,000)	230,000 (170,000 to 280,000)	170,000 (120,000 to 230,000)
Tobacco use	88,000 (72,000 to 100,000)	61,000 (51,000 to 70,000)	360,000 (290,000 to 430,000)	290,000 (230,000 to 340,000)
Diabetes	19,000 (16,000 to 23,000)	7,800 (6,300 to 9,200)	98,000 (80,000 to 120,000)	96,000 (78,000 to 110,000)
Raised blood pressure	24,000 (23,000 to 25,000)	9,300 (8,600 to 10,000)	110,000 (100,000 to 110,000)	98,000 (92,000 to 100,000)
Salt intake	24,000 (23,000 to 25,000)	6,200 (5,900 to 6,500)	95,000 (91,000 to 99,000)	62,000 (59,000 to 64,000)
Harmful alcohol use	6,800 (-31,000 to 45,000)	20,000 (-2,300 to 43,000)	-8,400 (-120,000 to 100,000)	72,000 (-170,000 to 320,000)
Physical inactivity	10,000 (7,200 to 13,000)	3,700 (2,700 to 4,700)	48,000 (34,000 to 62,000)	42,000 (31,000 to 54,000)
Combined scenario	190,000 (150,000 to 230,000)	94,000 (69,000 to 120,000)	800,000 (660,000 to 940,000)	640,000 (460,000 to 810,000)
YLDs (Thousands)				
Obesity	390,000 (320,000 to 470,000)	320,000 (250,000 to 390,000)	720,000 (570,000 to 860,000)	640,000 (490,000 to 790,000)
Tobacco use	770,000 (700,000 to 840,000)	860,000 (810,000 to 920,000)	1,300,000 (1,200,000 to 1,500,000)	1,500,000 (1,400,000 to 1,600,000)
Diabetes	620,000 (610,000 to 630,000)	510,000 (510,000 to 520,000)	1,100,000 (1,000,000 to 1,100,000)	990,000 (970,000 to 1,000,000)
Raised blood pressure	75,000 (71,000 to 79,000)	51,000 (46,000 to 55,000)	170,000 (160,000 to 180,000)	130,000 (120,000 to 140,000)
Salt intake	76,000 (72,000 to 79,000)	36,000 (34,000 to 37,000)	150,000 (150,000 to 160,000)	83,000 (80,000 to 87,000)
Harmful alcohol use	-82,000 (-260,000 to 100,000)	-120,000 (-260,000 to 23,000)	-120,000 (-410,000 to 170,000)	-180,000 (-450,000 to 80,000)
Physical inactivity	69,000 (58,000 to 80,000)	60,000 (51,000 to 70,000)	140,000 (120,000 to 170,000)	130,000 (110,000 to 160,000)
Combined scenario	1,600,000 (1,500,000 to 1,700,000)	1,500,000 (1,400,000 to 1,600,000)	2,900,000 (2,700,000 to 3,100,000)	2,800,000 (2,500,000 to 3,000,000)

NB. Values are mean and 95% uncertainty intervals.