

# Regional contributions of six preventable risk factors to achieving the 25 × 25 non-communicable disease mortality reduction target: a modelling study

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## Summary

**Background** Countries have agreed to reduce premature mortality from the four main non-communicable diseases (NCDs) by 25% from 2010 levels by 2025 (referred to as the 25 × 25 target). Countries also agreed on a set of global voluntary targets for selected NCD risk factors. Previous analyses have shown that achieving the risk factor targets can contribute substantially towards meeting the 25 × 25 mortality target at the global level. We estimated the contribution of achieving six of the globally agreed risk factor targets towards meeting the 25 × 25 mortality target by region.

**Methods** We estimated the effect of achieving the targets for six risk factors (tobacco and alcohol use, salt intake, obesity, and raised blood pressure and glucose) on NCD mortality between 2010 and 2025. Our methods accounted for multicausality of NCDs and for the fact that, when risk factor exposure increases or decreases, the harmful or beneficial effects on NCDs accumulate gradually. We used data for risk factor and mortality trends from systematic analyses of available country data. Relative risks for the effects of individual and multiple risks, and for change in risk after decreases or increases in exposure, were from reanalyses and meta-analyses of epidemiological studies.

**Findings** The probability of dying between the ages 30 years and 70 years from the four main NCDs in 2010 ranged from 19% in the region of the Americas to 29% in southeast Asia for men, and from 13% in Europe to 21% in southeast Asia for women. If current trends continue, the probability of dying prematurely from the four main NCDs is projected to increase in the African region but decrease in the other five regions. If the risk factor targets are achieved, the 25 × 25 target will be surpassed in Europe in both men and women, and will be achieved in women (and almost achieved in men) in the western Pacific; the regions of the Americas, the eastern Mediterranean, and southeast Asia will approach the target; and the rising trend in Africa will be reversed. In most regions, a more ambitious approach to tobacco control (50% reduction relative to 2010 instead of the agreed 30%) will contribute the most to reducing premature NCD mortality among men, followed by addressing raised blood pressure and the agreed tobacco target. For women, the highest contributing risk factor towards the premature NCD mortality target will be raised blood pressure in every region except Europe and the Americas, where the ambitious (but not agreed) tobacco reduction would have the largest benefit.

**Interpretation** No WHO region will meet the 25 × 25 premature mortality target if current mortality trends continue. Achieving the agreed targets for the six risk factors will allow some regions to meet the 25 × 25 target and others to approach it. Meeting the 25 × 25 target in Africa needs other interventions, including those addressing infection-related cancers and cardiovascular disease.

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## Introduction

In response to the commitments made at the 2011 UN high-level meeting on non-communicable diseases (NCDs), countries have agreed to reduce premature mortality (defined as the probability of dying between the ages of 30 years and 70 years) from the four main NCDs—cardiovascular diseases, cancers, chronic respiratory diseases, and diabetes—by 25% relative to 2010 levels by 2025 (referred to as the 25 × 25 target). Voluntary global targets for seven NCD risk factors and for two health system interventions were also agreed in 2013.<sup>1</sup>

We have previously estimated the effect of achieving the targets for six of the seven risk factors with global targets (tobacco and alcohol use, salt intake, obesity, and raised blood pressure and glucose) on global NCD mortality between 2010 and 2025.<sup>2</sup> We found that, if the agreed risk factor targets are met, global premature mortality from the four main NCDs would decrease to levels that are close to the 25 × 25 target for men and there will also be substantial benefits for women. There are striking regional variations in NCD mortality and in risk factor levels,<sup>3–10</sup> which means that information at the regional level is needed for advocacy, planning, and

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## Research in context

### Evidence before this study

We used a PubMed search done for a recent global analysis of NCD mortality and risk factor targets. The only modelling analysis of the role of risk factor targets in achieving the 25 × 25 mortality target was done at the global level, with no regional information.

### Added value of this study

This study analyses and presents the potential contributions of achieving the risk factor targets towards meeting the 25 × 25 mortality target by region. The regions were those used by WHO, and a set of regions based on geography and economic development.

### Implications of all the available evidence

No region is on-track to achieve the 25 × 25 mortality target under current trends. However, there are substantial differences across regions, with marked reductions happening in the European region and Americas region contrasted with rising premature NCD mortality in Africa, where infection-related NCDs remain leading causes of premature death. Achieving the six risk factor targets will help all regions, but with noticeable differences by region and sex in terms of which risks are most important, and how large the additional benefits are.

accountability. This study presents a regional-level analysis of the effect of achieving the targets for six risk factors on premature mortality from NCDs between 2010 and 2025.

## Methods

### Data sources

The methods and data sources have been described in detail in the earlier global publication.<sup>2</sup> In brief, we used data for risk factor and mortality trends from systematic analyses of available country data, as detailed in the appendix. Relative risks for the effects of individual and multiple risks, and for change in risk after decreases or increases in exposure, were from reanalyses and meta-analyses of epidemiological studies, as detailed in the appendix.

### Analytical approach

Our analytical approach was based on two epidemiological characteristics of NCDs. First, NCDs have many causes, the combined effects of which lead to a particular disease rate in the population. Some of these causes are non-modifiable (eg, genetic determinants), unmeasured or poorly measured (eg, health-care quality or stress), or even unknown. Therefore, trends for a specific NCD can be different from that of any single risk factor or small number of risk factors, depending on how the other determinants and medical treatment are changing. For example, cardiovascular disease mortality in high-income countries has decreased for decades, during which time some of its risk factors (eg, blood pressure, cholesterol, and, in some countries, smoking) have decreased and others (eg, obesity and smoking in other countries) have increased.<sup>11–13</sup> To account for this characteristic, and consistent with the vast empirical evidence on proportional effects, we analysed the effects of risk factors on future NCD mortality as a proportion of projected death rates.

The second characteristic of NCDs is that, when exposure to one of its risk factors increases or decreases, the harmful or beneficial effects on disease risk

accumulate gradually.<sup>14–17</sup> We accounted for this characteristic using relative risks (RRs) that were a function of time since exposure change. These two components of our approach can be incorporated in a time-based, population impact fraction (PIF) formula,<sup>18</sup> which estimates the proportion of disease-specific deaths for years between 2010 and 2025 that would be avoided if risk factor exposures were reduced according to their targets. For each disease outcome causally associated with a risk factor, we calculated the time-based PIF for a given year (20XX) between 2010 and 2025 using the following formula:

$$PIF^{20XX} = \frac{\sum_j P_j^{20XX} RR_j^{20XX} - \sum_j \hat{P}_j^{20XX} RR_j^{20XX}}{\sum_j P_j^{20XX} RR_j^{20XX}}$$

where  $P^{20XX}$  and  $\hat{P}^{20XX}$  are population distributions (which could be categorical or continuous) of risk factor exposure in year 20XX in the so-called business-as-usual scenario (BAU; ie, projections based on current trends with no additional action) and target scenario, respectively, and  $RR^{20XX}$  is the RR in 20XX (see appendix of Kontis and colleagues<sup>2</sup>). The first term in the numerator is the weighted (by prevalence) disease risk if risk factors continue their current trend and the second term is the weighted disease risk if risk factor trends are changed according to their target. The risk factor exposure categories, denoted by  $j$ , account for both the level of exposure and for time since change in exposure. The RR for each exposure category in this equation depends on time since exposure change. This relation is an extension of the commonly used population attributable or impact fraction in which RRs are a function of exposure level but not of time.

We estimated the proportional reduction in mortality from each NCD if all six risk factor targets are achieved using the formula for the joint effects of multiple risk factors, which accounts for multicausality and overlap of risk factors.<sup>19</sup> When estimating the combined effects of all six risk factors, we also accounted for the fact that raised blood pressure and glucose are mediators of the effects of

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body-mass index (BMI) on cardiovascular diseases. We obtained the direct and mediated effects from a pooled analysis of 97 prospective cohorts.<sup>20</sup> Similarly, the effects of salt intake on cardiovascular diseases were analysed as mediated through blood pressure, to be able to use effect sizes from randomised trials of salt reduction, most of which had blood pressure as an endpoint.<sup>21,22</sup>

We did all analyses separately by country, sex, 5-year age groups for people aged 30 years or older, and for each NCD causally associated with these six risk factors. We calculated regional results by aggregating age-specific and sex-specific number of deaths and population from each region's constituent countries. Results are presented for WHO regions in the main paper, and for a set of alternative regions used in previous global analyses<sup>3,4</sup> in the appendix. One of these alternative regions consisted of high-income countries in Asia Pacific (Japan, Brunei Darussalam, Singapore, and South Korea), Australia, New Zealand, North America, and western Europe. The other countries were divided based on their geography into central Asia and central and eastern Europe, Latin America and the Caribbean, Middle East and north Africa, east and southeast Asia and the Pacific, south Asia, and sub-Saharan Africa. We used age-specific death rates to calculate the probability of dying from the four main NCDs between ages 30 years and 70 years in the absence of competing causes.

### Risk factor scenarios

Our risk factor scenarios were based on the agreed global targets, with the addition of a more ambitious tobacco use target (50% relative reduction in prevalence instead of the agreed 30%; table 1). We calculated the contribution of risk factor targets based on how close achieving them would bring premature mortality to the 25×25 target compared with a baseline scenario. We used two types of baseline scenarios. First, when a risk factor had a rising trend in a country (eg, obesity and diabetes in most countries), we compared its target to the baseline of the rising trend. Second, when a risk factor already had a decreasing trend (eg, blood pressure and smoking in many high-income countries), we compared its target to a baseline of having kept the risk factor at its 2010 level. We used the second type of baseline because a decreasing risk factor trend means that progress is already being made towards the target in the BAU trend, and hence should be counted towards the estimated benefit of the risk factor target. The contribution of a risk factor towards achieving the mortality target can be greater than 100% when reducing the risk factor leads to a greater than 25% reduction in premature mortality.

### Uncertainty estimation

Projections of mortality under the BAU trends did not include measures of uncertainty,<sup>24</sup> although there is an active research agenda on projection methods.<sup>25,26</sup> To quantify the uncertainty in epidemiological associations, we used a simulation approach, in which we used

1000 draws from the uncertainty distributions of two of the inputs to the analysis—the RRs for the associations between risk factors and the proportion of excess relative risk (RR minus 1) remaining over time since exposure to a risk factor has stopped or been reduced—and repeated the calculations with these draws. The resulting uncertainty intervals are shown in the appendix and report the median of these draws as the central estimates and their 2·5th and 97·5th percentiles. Draws for different age groups were treated as correlated (ie, a higher RR in one age group implies a higher RR in other age groups); those for different disease outcomes were treated as uncorrelated. The uncertainty intervals should be treated as a lower bound to true uncertainty because they do not include the uncertainty of BAU trends.

### Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. VK, CDM, GAS, and KDS collectively had full access to all the data in the study and the corresponding author had final responsibility for the decision to submit for publication.

### Results

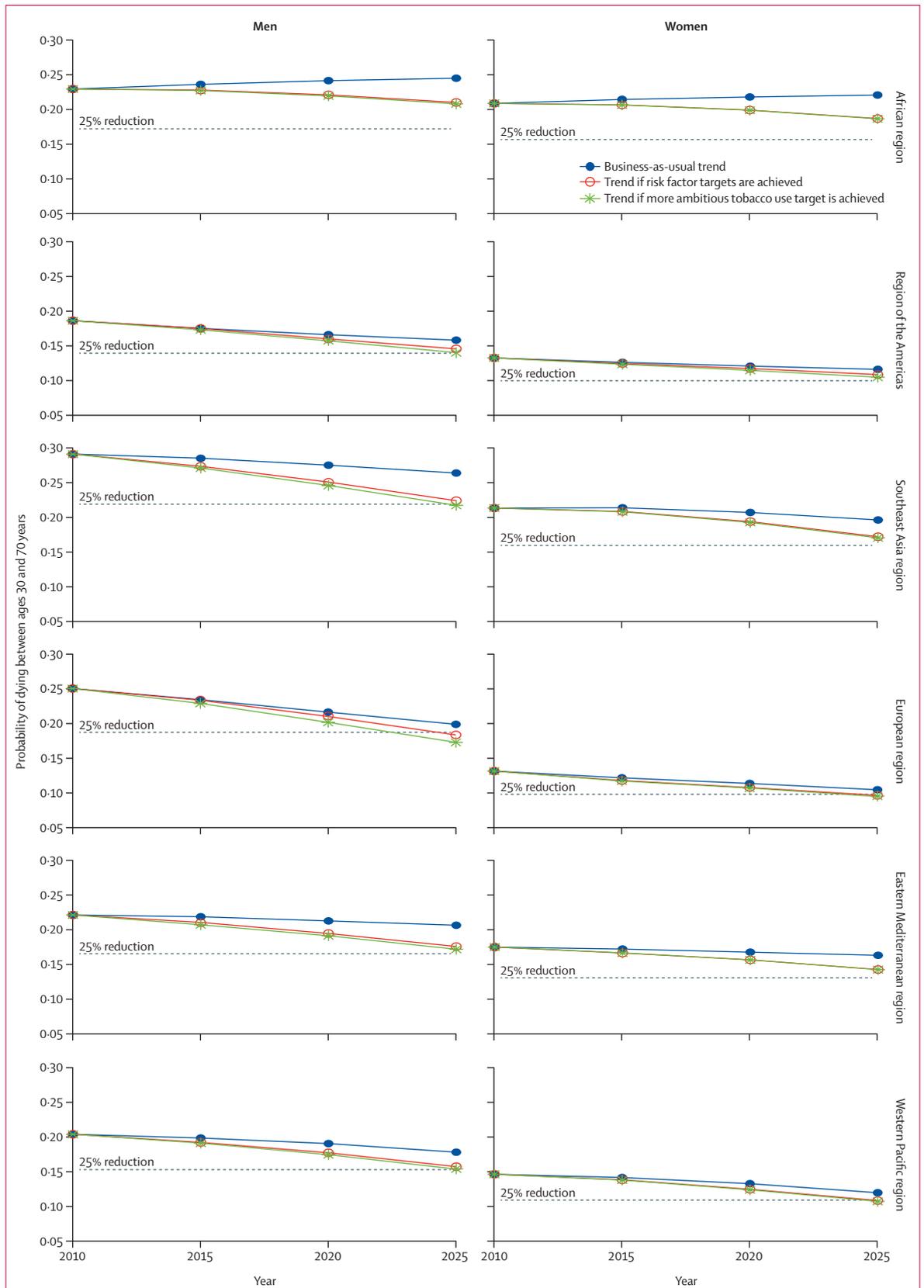
The probability of dying between ages 30 years and 70 years from the four main NCDs in 2010 varied substantially by region and was higher in men than women in every region (figure 1). In men this probability ranged from 19% in the region of the Americas to 29% in southeast Asia; in women it ranged from 13% in Europe to 21% in southeast Asia. The number of deaths from the four main NCDs in people aged 30–69 years ranged between 0·7 million in the eastern Mediterranean and 3·3 million in southeast Asia (figure 2). In people aged 70 years and older, the number of

For a list of countries in each region see <http://www.who.int/about/regions/en/>

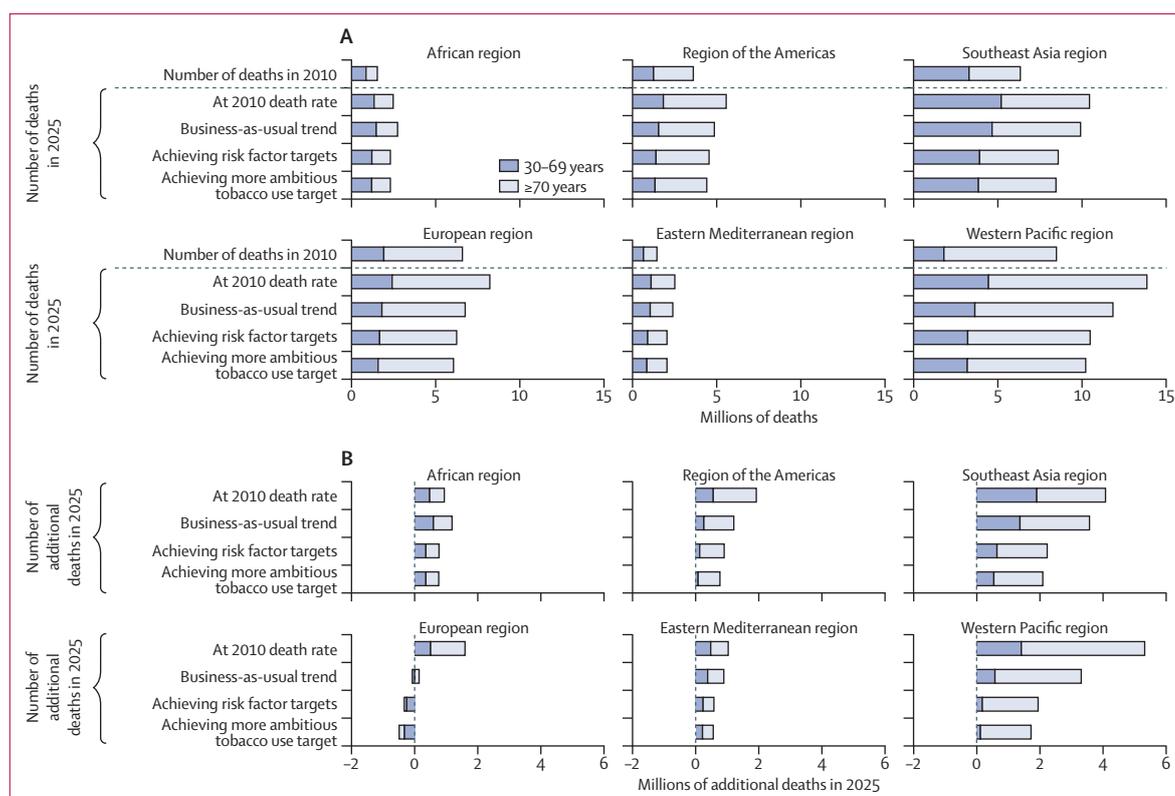
	Scenario
Tobacco use	Agreed target: 30% relative reduction in prevalence; more ambitious target: 50% relative reduction in prevalence*
Harmful alcohol use	10% reduction in per capita alcohol consumption
Salt intake	30% reduction in mean population intake of salt and sodium
Obesity	Halting the rise in the prevalence of obesity
Raised blood glucose and diabetes	Halting the rise in the prevalence of diabetes
Raised blood pressure	25% relative reduction in the prevalence of raised blood pressure

Calculations were done in three 5-year intervals for computational efficiency. Risk factor exposure reductions were applied at the midpoint of each 5-year interval, which is about equivalent to five equal annual reductions. \*For tobacco use, we estimated the effects of meeting the global target as well as a more ambitious scenario, because effective policies for reducing tobacco use have already been successfully implemented in a number of countries, making a 50% reduction a feasible target.<sup>9,23</sup>

Table 1: Risk factor scenarios



**Figure 1: Business-as-usual trends in the probability of dying from the four main non-communicable diseases (NCDs) between ages 30 years and 70 years and trends if risk factors are reduced according to their targets for WHO regions**  
 The results for the combination of all risk factors account for multicausality and for mediation as described in Methods. See the appendix for results by regions based on income and geography.



**Figure 2: Number of deaths from the main non-communicable diseases (NCDs) among those aged 30–69 years and 70 years or older**

(A) Number of deaths from the main NCDs among those aged 30–69 years and 70 years or older in 2010 and in 2025 at 2010 death rate under the business-as-usual scenario if the six risk factors are reduced according to their targets and if a more ambitious target on tobacco use is achieved for WHO regions. (B) Same information as (A) after subtracting the number of deaths in 2010. See the appendix for results by regions based on income and geography.

deaths from the four main NCDs ranged from 0·7 million in Africa to 5·5 million in the western Pacific. The variation in the number of deaths is partly due to differences in population size and age structure and partly due to differences in death rates in each age group. The share of deaths from the four main NCDs that occurred in the younger age group (30–69 years) ranged between 30% in Europe and 56% in Africa.

Under the BAU scenario, there is a projected reduction in the probability of premature death from the four main NCDs between 2010 and 2025 in five of the six WHO regions, with the reduction ranging from 6·8% (eastern Mediterranean) to 20·3% (Europe) of the 2010 levels (figure 1). The notable exception is Africa, where the probability of dying prematurely is projected to increase by 6·2% relative to 2010 if current trends continue with no additional action. Despite the decrease in the probabilities of death, population increase and ageing will lead to a projected rise in the number of deaths from the four NCDs between 2010 and 2025 in all six regions (figure 2). The smallest projected increase in the number of NCD deaths in people aged 30 years and older is predicted to occur in Europe (about 200 000 additional deaths) and the greatest in southeast Asia (3·6 million additional deaths). When focusing only on those aged

30–69 years, the BAU projected change in the number of deaths will range between a 100 000 reduction in Europe to a 1·4 million increase in southeast Asia.

Achieving the six risk factor targets will accelerate the decline in premature mortality in the five regions with projected BAU decline and will reverse the rising trend in Africa. As a result of the accelerated decline, the 25×25 target will be surpassed in Europe in both men and women (26% reduction in premature NCD mortality relative to 2010) and achieved in women, and almost in men, in the western Pacific (25% and 23% reduction relative to 2010, respectively). The regions of the Americas, the eastern Mediterranean, and southeast Asia will approach the target (19–22% reduction in premature mortality relative to 2010). In Africa, achieving the six risk factor targets will lead to an 11% reduction in the probability of dying prematurely from the four main NCDs relative to 2010 in women and 9% in men. Achieving a more ambitious tobacco use reduction of 50% relative to 2010 will lead to a further reduction in the probability of dying prematurely in all regions, and help the western Pacific surpass the 25×25 target. The additional benefit will be largest in Europe and the Americas, where the probability of dying prematurely will be reduced by a further 3% relative to 2010, above

		Men						
Tobacco use (more ambitious)		1	2	1	1	1	1	1
Raised blood pressure		2	1	2	3	2	2	2
Tobacco use (agreed)		3	3	3	2	4	3	3
Salt intake		4	4	6	4	3	4	4
Obesity		5	5	4	6	5	5	5
Raised blood glucose		6	7	5	5	7	6	7
Alcohol use		7	6	7	7	6	7	6
		Women						
Raised blood pressure		1	1	3	1	2	1	1
Tobacco use (more ambitious)		2	3	1	2	1	5	3
Tobacco use (agreed)		3	5	4	3	3	6	4
Salt intake		4	6	6	4	4	3	2
Obesity		5	2	2	6	5	2	5
Raised blood glucose		6	4	5	5	7	4	7
Alcohol use		7	7	7	7	6	7	6
		World	African region	Region of the Americas	Southeast Asia region	Eastern Mediterranean region	European region	Western Pacific region

**Figure 3: Ranking of the risk factor targets by region and by their contribution towards achieving the 25 × 25 mortality reduction target for WHO regions**

A rank of 1 corresponds to the largest contribution. See appendix for results by regions based on income and geography.

and beyond the reduction under the agreed risk factor targets.

At the regional level, achieving the six risk factor targets will help delay or prevent between 2·2 million deaths in the eastern Mediterranean (7·2% of all deaths from the four main NCDs in people 30 years and older in this region over the analysis period) and 10·6 million deaths in the western Pacific (6·5%) from the four main NCDs between 2010 and 2025 (figure 2). In people aged 30–69 years, southeast Asia alone will account for nearly a third of the worldwide deaths delayed or prevented (5·1 million deaths), followed by 3·4 million (21% of worldwide deaths delayed or prevented in this age group) in the western Pacific. The largest number of deaths delayed in those aged 70 years or older will be in the western Pacific (7·2 million deaths; 34% of worldwide deaths delayed or prevented in this age group), followed by Europe (5·1 million deaths; 24%).

The ranking of individual risk factor targets in terms of their effects on premature mortality was relatively similar across regions for men (figure 3). Among the agreed targets, in most regions those for raised blood pressure (through both changes in diet and scaling up blood pressure treatment in primary care) and tobacco use will have the largest effect in terms of reducing premature mortality among men; a more ambitious tobacco target

of 50% reduction will have an even larger effect than that of the raised blood pressure target and be the most efficacious approach in all regions except Africa. In Africa, where tobacco use is less prevalent and smokers consume fewer cigarettes than in other regions, raised blood pressure is the most important risk among men. Achieving the targets on alcohol use, raised blood glucose, and obesity had the smallest effects on premature mortality from the four main NCDs among men. Alcohol use, however, is a risk factor for a range of other NCDs, injuries, and infectious diseases, and in some former Soviet countries is the single leading risk factor for premature deaths from all causes combined among men.<sup>9,27</sup> For women, raised blood pressure is the leading risk factor in every region except Europe and the Americas, where tobacco smoking among women is more common and where the ambitious (but not agreed) tobacco reduction would have the largest benefit. In three regions (Africa, Americas, and eastern Mediterranean) achieving the obesity target would have the second largest benefit for women.

Of the four main NCD groups, cardiovascular diseases were responsible for about half of NCD deaths in four regions, and about 40% of deaths in the Americas and the western Pacific, where more deaths were caused by cancers than cardiovascular diseases. Ischaemic heart disease was the leading NCD cause of dying prematurely in every region in 2010, except the western Pacific and Africa where ischaemic heart disease followed stroke (table 2). Ischaemic heart disease was followed by stroke in all regions except in the Americas where diabetes was the second largest NCD cause of premature death. Although premature cardiovascular disease mortality is projected to decline in all regions except in Africa, only Europe and the Americas will achieve a 25% reduction in premature cardiovascular disease mortality by 2025, relative to 2010, without further action. If the risk factor targets are achieved, however, all regions, including Africa, will meet or exceed a 25% reduction in premature cardiovascular disease mortality. Further, achieving the risk factor targets will lead to a reversal of the rise in diabetes mortality in four of five regions where premature mortality from diabetes is projected to rise.

Among cancers, the largest share of premature deaths was due to lung cancer, which was one of the ten most common NCDs in every region except Africa. Liver cancer ranked second in cancer deaths globally, and was in the top ten NCDs in Africa and the western Pacific. Liver cancer was followed by stomach cancer, breast cancer, and colorectal cancer, which were each in the leading ten NCDs in three to five regions. Under a BAU scenario, premature cancer mortality is projected to rise between 2010 and 2025 in three out of the six regions (Africa, eastern Mediterranean, and southeast Asia), a trend which will be reversed in the eastern Mediterranean and southeast Asia, but not in Africa, if the risk factor targets are met. The reversal in the eastern Mediterranean

	Percentage of deaths from the main NCDs in people aged 30–69 years		BAU reduction*	Reduction if risk factor targets are achieved*	Risk factor contribution towards the 25 × 25 mortality target†	Number of deaths delayed or prevented between 2010 and 2025†	
	2010	2025				30–69 years	70 years or older
<b>African region—four main NCDs account for 29% of premature deaths in 2010 and 37% in 2025</b>							
Stroke	21.7%	19.8%	–1%	–30%	>100%	610 000	480 000
Ischaemic heart disease	16.4%	15.3%	+1%	–24%	95%	380 000	310 000
Diabetes	9.7%	9.5%	+4%	–10%	51%	130 000	60 000
Cervix uteri cancer	4.5%	4.2%	0%	0%	3%	3000	<1000
Liver cancer	4.0%	4.7%	+26%	+20%	12%	30 000	1 000
Hypertensive heart disease	3.9%	3.7%	+3%	–39%	>100%	150 000	170 000
Chronic obstructive pulmonary disease	3.8%	3.4%	–4%	–17%	66%	60 000	20 000
Breast cancer	3.8%	4.8%	+35%	+34%	1%	2000	<1000
Cardiomyopathy, myocarditis, and endocarditis	2.9%	2.8%	+5%	–11%	57%	50 000	30 000
Asthma	2.5%	2.5%	+7%	+5%	9%	8000	1000
<b>Main four NCDs</b>							
Cardiovascular diseases	49.9%	46.7%	+1%	–25%	100%	1 300 000	1 000 000
Cancers	32.0%	35.8%	+19%	+14%	12%	160 000	30 000
Diabetes	9.7%	9.5%	+4%	–10%	51%	130 000	60 000
Chronic respiratory diseases	8.4%	8.0%	+3%	–6%	31%	70 000	20 000
Total	100%	100%	+6%	–10%	52%	1 600 000	1 100 000
<b>Region of the Americas—four main NCDs account for 59% of premature deaths in 2010 and 62% in 2025</b>							
Ischaemic heart disease	20.4%	17.9%	–25%	–36%	NA	630 000	830 000
Diabetes	9.5%	15.1%	+32%	–6%	68%	440 000	410 000
Stroke	9.2%	8.1%	–25%	–38%	NA	340 000	440 000
Trachea, bronchus, and lung cancers	8.6%	7.7%	–26%	–16%	NA	140 000	170 000
Chronic obstructive pulmonary disease	4.7%	4.2%	–27%	–20%	NA	80 000	280 000
Breast cancer	4.1%	4.3%	–7%	–7%	2%	2000	<1000
Hypertensive heart disease	4.1%	3.4%	–28%	–42%	NA	190 000	370 000
Colon and rectum cancers	3.6%	3.7%	–13%	–12%	12%	8000	10 000
Stomach cancer	2.5%	2.7%	–7%	–13%	43%	20 000	30 000
Pancreatic cancer	2.2%	2.4%	–10%	–7%	18%	10 000	20 000
<b>Main four NCDs</b>							
Cancers	41.8%	42.4%	–13%	–10%	24%	240 000	290 000
Cardiovascular diseases	41.4%	36.2%	–25%	–35%	NA	1 300 000	2 000 000
Diabetes	9.5%	15.1%	+32%	–6%	68%	440 000	410 000
Chronic respiratory diseases	7.3%	6.4%	–28%	–23%	NA	90 000	320 000
Total	100%	100%	–14%	–20%	77%	2 100 000	3 000 000
<b>Eastern Mediterranean region—four main NCDs account for 54% of premature deaths in 2010 and 59% in 2025</b>							
Ischaemic heart disease	26.1%	24.0%	–15%	–33%	>100%	400 000	420 000
Stroke	14.2%	13.2%	–15%	–36%	>100%	260 000	320 000
Chronic obstructive pulmonary disease	7.3%	7.1%	–12%	–23%	82%	70 000	60 000
Diabetes	5.2%	6.5%	+12%	–9%	62%	90 000	90 000
Breast cancer	4.4%	5.0%	+11%	+10%	0%	<1000	<1000
Hypertensive heart disease	3.7%	3.5%	–13%	–40%	>100%	90 000	130 000

(Table 2 continues on next page)

	Percentage of deaths from the main NCDs in people aged 30–69 years		BAU reduction*	Reduction if risk factor targets are achieved*	Risk factor contribution towards the 25 × 25 mortality target†	Number of deaths delayed or prevented between 2010 and 2025†	
	2010	2025				30–69 years	70 years or older
(Continued from previous page)							
Trachea, bronchus, and lung cancers	2.7%	3.4%	+19%	-7%	60%	50 000	20 000
Rheumatic heart disease	2.2%	2.1%	-12%	-20%	66%	20 000	10 000
Cardiomyopathy, myocarditis, and endocarditis	2.2%	2.0%	-13%	-25%	97%	20 000	20 000
Stomach cancer	2.0%	2.2%	-1%	-11%	41%	10 000	7 000
<b>Main four NCDs</b>							
Cardiovascular diseases	51.8%	48.0%	-14%	-32%	>100%	810 000	950 000
Cancers	31.8%	34.7%	+4%	-1%	17%	110 000	40 000
Chronic respiratory diseases	11.1%	10.8%	-12%	-20%	61%	80 000	70 000
Diabetes	5.2%	6.5%	+12%	-9%	62%	90 000	90 000
Total	100%	100%	-7%	-19%	72%	1 100 000	1 100 000
<b>European region—four main NCDs account for 69% of premature deaths in 2010 and 69% in 2025</b>							
Ischaemic heart disease	30.0%	26.4%	-30%	-42%	NA	1 300 000	1 900 000
Stroke	13.2%	12.1%	-29%	-43%	NA	650 000	1 200 000
Trachea, bronchus, and lung cancers	10.1%	11.4%	-13%	-13%	55%	250 000	260 000
Colon and rectum cancers	4.3%	4.8%	-14%	-14%	18%	20 000	30 000
Breast cancer	3.9%	4.3%	-11%	-10%	3%	3 000	1 000
Stomach cancer	3.1%	3.5%	-11%	-19%	66%	50 000	60 000
Cardiomyopathy, myocarditis, and endocarditis	2.8%	2.1%	-36%	-42%	NA	70 000	60 000
Chronic obstructive pulmonary disease	2.7%	2.5%	-30%	-32%	NA	60 000	270 000
Pancreatic cancer	2.3%	2.7%	-12%	-12%	29%	20 000	30 000
Diabetes	2.0%	2.9%	+9%	-5%	47%	50 000	110 000
<b>Main four NCDs</b>							
Cardiovascular diseases	52.2%	46.3%	-30%	-41%	NA	2 300 000	4 200 000
Cancers	42.0%	47.3%	-12%	-12%	33%	450 000	470 000
Chronic respiratory diseases	3.9%	3.6%	-30%	-31%	NA	70 000	310 000
Diabetes	2.0%	2.9%	+9%	-5%	47%	50 000	110 000
Total	100%	100%	-20%	-27%	>100%	2 800 000	5 100 000
<b>Southeast Asia region—four main NCDs account for 56% of premature deaths in 2010 and 63% in 2025</b>							
Ischaemic heart disease	24.0%	22.5%	-15%	-32%	>100%	1 500 000	1 100 000
Stroke	17.6%	16.8%	-15%	-36%	>100%	1 400 000	1 200 000
Chronic obstructive pulmonary disease	14.7%	14.0%	-15%	-28%	>100%	660 000	550 000
Diabetes	6.1%	6.5%	-6%	-14%	55%	280 000	150 000
Hypertensive heart disease	3.1%	2.9%	-16%	-43%	>100%	300 000	340 000
Asthma	3.1%	2.9%	-16%	-19%	38%	40 000	30 000
Mouth and oropharynx cancers	3.0%	3.3%	+5%	-10%	50%	150 000	30 000
Trachea, bronchus, and lung cancers	2.8%	4.0%	+26%	-7%	65%	320 000	130 000
Cervix uteri cancer	2.5%	2.5%	-6%	-7%	7%	10 000	1 000

(Table 2 continues on next page)

	Percentage of deaths from the main NCDs in people aged 30–69 years		BAU reduction*	Reduction if risk factor targets are achieved*	Risk factor contribution towards the 25×25 mortality target†	Number of deaths delayed or prevented between 2010 and 2025†	
	2010	2025				30–69 years	70 years or older
(Continued from previous page)							
Breast cancer	2.4%	2.7%	+9%	+8%	0%	<1000	<1000
<b>Main four NCDs</b>							
Cardiovascular diseases	50.9%	47.9%	-14%	-32%	>100%	3 400 000	2 800 000
Cancers	24.3%	27.9%	+7%	-1%	26%	680 000	220 000
Chronic respiratory diseases	18.7%	17.7%	-15%	-26%	>100%	720 000	590 000
Diabetes	6.1%	6.5%	-6%	-14%	55%	280 000	150 000
Total	100%	100%	-9%	-22%	80%	5 100 000	3 800 000
<b>Western Pacific region—four main NCDs account for 74% of premature deaths in 2010 and 77% in 2025</b>							
Stroke	22.4%	19.3%	-29%	-45%	NA	1300 000	2 300 000
Ischaemic heart disease	13.2%	14.2%	-11%	-26%	>100%	760 000	1 700 000
Trachea, bronchus, and lung cancers	10.0%	12.7%	+7%	-5%	42%	420 000	560 000
Liver cancer	9.8%	10.3%	-6%	-9%	15%	80 000	60 000
Stomach cancer	6.7%	6.9%	-14%	-23%	85%	180 000	230 000
Chronic obstructive pulmonary disease	5.8%	4.4%	-40%	-45%	NA	120 000	1 100 000
Oesophagus cancer	3.8%	4.0%	-13%	-18%	44%	70 000	110 000
Diabetes	3.7%	4.8%	+8%	+2%	29%	100 000	110 000
Colon and rectum cancers	2.9%	3.0%	-11%	-12%	7%	8 000	20 000
Hypertensive heart disease	2.2%	1.8%	-34%	-55%	NA	170 000	520 000
<b>Main four NCDs</b>							
Cancers	46.3%	50.6%	-5%	-10%	29%	810 000	1 000 000
Cardiovascular diseases	42.7%	38.9%	-24%	-39%	>100%	2 400 000	4 900 000
Chronic respiratory diseases	7.3%	5.6%	-38%	-42%	NA	130 000	1 200 000
Diabetes	3.7%	4.8%	+8%	+2%	29%	100 000	110 000
Total	100%	100%	-15%	-24%	91%	3 400 000	7 200 000
See appendix for results by regions based on income and geography. *A negative number shows a decline and a positive number a rise in mortality. †Contributions of risk factors and number of deaths delayed or prevented are calculated compared with a situation of rising or stagnating risk factor trends as described in Methods; a contribution of 100% implies that achieving the risk factor targets will lead to exactly a 25% reduction in the probability of death from that disease; a contribution of more than 100% implies that if risk factor targets are achieved probability of death declines by more than 25%; NA refers to diseases and regions for which premature mortality is projected to decline by 25% or more under a business-as-usual (BAU) scenario; achieving the risk factor targets will further increase the decline in mortality but is not needed to achieve a 25% reduction in mortality.							
<b>Table 2: Effect of achieving risk factor targets on premature mortality from the ten leading causes of death among the four main non-communicable diseases (NCDs), by WHO region</b>							

and southeast Asia will be due to the substantial benefits of achieving risk factor targets on mortality from lung and stomach cancers. By contrast, there will be a limited effect from achieving the risk factor targets on cervical cancer, which is among the most common NCDs in Africa and southeast Asia, and on cancer of the mouth and oropharynx, which is important in southeast Asia. This diversity of cancers, and of their risk factors and interventions, shows the need for a comprehensive cancer control strategy, including vaccination and treatment of infections that cause cancers, screening and treatment of precancerous lesions, reducing carcinogenic exposures in food and the occupational and community environments, and cancer treatment.<sup>28</sup>

## Discussion

No WHO region will meet the 25×25 target if current mortality trends continue. However, if the targets for the six risk factors analysed here are achieved, both sexes in Europe and women in the western Pacific region will achieve the agreed target; with the exception of Africa, other regions will also approach this target. Meeting the mortality target in Africa needs a more diverse range of interventions than those related to the risk factor targets, including interventions for infection-related cancers and cardiovascular diseases. Tobacco use and raised blood pressure, both of which have effective interventions and have been successfully reduced in many countries,<sup>5,23,29</sup> are important risk factors in most regions in terms of

contributions towards achieving the 25×25 mortality target. A more ambitious, but feasible, target on tobacco use will further accelerate progress towards the 25×25 target. Achieving the targets of halting the rise of obesity and raised blood glucose will be important among women, who tend to smoke less than men, in some regions.

The strengths of our study include providing an integrated analysis of how the globally agreed targets related to preventable risk factors will contribute towards achieving the 25×25 NCD mortality target at the regional level. This analysis will help identify regional risk factor and disease priorities and measure how much risk factor targets contribute towards NCD mortality reduction by region, and hence what additional actions and interventions might be needed to meet the 25×25 NCD target. This information, together with other region-specific factors such as the regulatory and health-care infrastructure that are needed for delivering interventions, will support planning and advocacy. Our analysis used data for risk factor exposure and mortality trends from systematic analyses that included up-to-date, comprehensive country-level data. Similarly, the effects of risk factors on each NCD were from large epidemiological studies and meta-analyses. We accounted for multicausality and for the fact that benefits of reducing risk factors for NCDs accumulate gradually.

Analyses of future trends and scenarios of population health like ours are also affected by limitations. First, as with all estimations of future trends, there can be entirely unexpected changes in trends, which could worsen or improve population health. At the same time, analyses such as ours are needed to plan public health interventions and clinical programmes, but should be accompanied by preparedness for unexpected situations. Second, despite improvements in epidemiological surveillance, risk factor exposures and deaths in some countries and regions are affected by data shortage or poor quality of data. For example, estimates of obesity and hypertension prevalence were based on 960 and 786 country-years of data, respectively, but those of diabetes prevalence relied on 370 country-years of data. The increased global focus on NCD prevention and control should be accompanied by better country-level data on NCDs, especially on cause-specific mortality, and their risk factors. Third, we used RRs from observational studies, which could have been affected by residual confounding. To avoid overestimating the effects of risk factors, we included only diseases with strong and probable evidence and used RRs from well-adjusted studies only. Fourth, there is an active research agenda aiming to improve the methods used for projecting mortality and risk factors into the future,<sup>24–26</sup> which forms one of the essential inputs into our analysis. Fifth, we did not analyse physical inactivity because how much of its effects are mediated through obesity and raised blood pressure and glucose has not been quantified, and

because there are no consistent data for time trends. Although physical inactivity is an important NCD risk factor, mediation and multicausality mean that its exclusion is unlikely to have greatly changed the combined effect of all risk factors together. Similarly, we did not analyse other forms of tobacco use because of the relative scarcity of data for exposure, which could have led to underestimation of the benefits for some cancers in south Asia, where oral tobacco use is common. Finally, the base year in our analysis was 2010 as indicated in the global monitoring framework endorsed by the World Health Assembly in May, 2013. Conceivably, changes in risk factor trends might have occurred since 2010 and should be taken into account in planning, including reversing unfavourable risk factor trends between 2010 and 2015 to accelerate progress in the remaining 10 years.

Of the two leading risk factors contributing towards the 25×25 NCD target, there have been successes in tobacco control in a number of countries although many others are lagging behind in terms of implementing effective tobacco control measures.<sup>9,23</sup> Our results re-emphasise the important role of tobacco control as one of the most effective ways of reducing the NCD burden in every region.<sup>30</sup> Lower dietary salt and better diagnosis and treatment have contributed to reducing blood pressure in some high-income countries, which has in turn been one of the most important determinants of the decline in cardiovascular disease mortality.<sup>3,5,11–13</sup> Locally applicable salt reduction or substitution strategies are urgently needed in low-income and middle-income countries, in which salt intake remains high.<sup>30</sup> Higher coverage of blood pressure treatment requires strengthening of the primary care system and development and implementation of guidelines for use by primary care personnel.<sup>3,31</sup>

The two health system targets (treatment and counselling individuals with a cardiovascular disease risk of 30% or more including those with a previous cardiovascular event, and availability and affordability of quality, safe, and efficacious essential NCD drugs),<sup>1</sup> also agreed in 2013, will contribute towards meeting the 25×25 target in Africa and for additional health benefits in other regions. These health systems targets will require expansion of universal health coverage and strengthening of primary care to facilitate risk-based prevention of cardiovascular diseases and enhance access to essential medicines.<sup>32</sup> Drug therapy for cardiovascular risk factors also needs up-to-date risk prediction charts and simplified guidelines for use at the primary-care level.<sup>33,34</sup> In addition to current targets, the important role of NCDs that are related to infections (cervical and liver cancers, and infection-related cardiovascular diseases such as cardiomyopathy, myocarditis, and endocarditis) show the continued need for prevention and early detection and treatment of infections as an important component of addressing the rising NCD burden, especially in Africa.<sup>11,35</sup>

Debate and priority setting for action on NCDs is moving from global to regional and national levels. The July 2014 UN high-level meeting on the comprehensive review and assessment of the progress achieved in the prevention and control of NCDs reviewed progress since September, 2011. The meeting concluded that, although substantial progress has been made, the pace of progress has been insufficient and highly uneven, and that continued and increased efforts are essential for achieving a world free of the avoidable burden of NCDs. The meeting emphasised the need to move from commitments to action, in particular developing a set of national targets to complement the globally agreed voluntary targets and taking actions to meet these targets.<sup>36–38</sup> The country focus is particularly important because, even within regions, there are differences in risk factor levels and contributions to NCD mortality and in strategies to reduce risk factors. For example, within the western Pacific region, tobacco followed by obesity are the most important risk factors in Australia, whereas in China, the largest contribution towards achieving the mortality target will come from achieving the targets for raised blood pressure. In the Americas, the ambitious tobacco target, followed by obesity, are the most important targets in the USA, whereas in Mexico the targets for raised glucose and obesity will lead to the largest reductions in premature mortality. Therefore, our analysis should be followed by extending to country-level analysis to inform and facilitate national target setting and monitoring.

#### Contributors

RBe, RBo, and ME designed the study with input from other authors. VK and ME developed the analytical strategy, with input from CDM, JR, GAS, and RBe. CDM and GAS analysed mortality data. JR and KDS analysed alcohol data, with input from VK, GAS, LMR, VP, and ME. VK, RBo, and ME designed the figure graphics. VK analysed the effects of risk factors on mortality and prepared results. VK, RBo, RBe, and ME wrote the first draft of the paper. Other authors contributed to subsequent drafts. ME oversaw the research.

#### Declaration of interests

We declare that we have no competing interests. CDM, GAS, LMR, VP, RMG, and HMF are staff members of WHO. The authors alone are responsible for the views expressed in this publication and they do not necessarily represent the decisions, policy, or views of WHO.

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