

The contributions of risk factor trends to cardiometabolic mortality decline in 26 industrialized countries

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Background Cardiovascular disease mortality has declined and diabetes mortality has increased in high-income countries. We estimated the potential role of trends in population body mass index, systolic blood pressure, serum total cholesterol and smoking in cardiometabolic mortality decline in 26 industrialized countries.

Methods Mortality data were from national vital statistics. Body mass index, systolic blood pressure and serum total cholesterol were from a systematic analysis of population-based data. We estimated the associations between change in cardiometabolic mortality and changes in risk factors, adjusted for change in per-capita gross domestic product. We calculated the potential contribution of risk factor trends to mortality decline.

Results Between 1980 and 2009, age-standardized cardiometabolic mortality declined in all 26 countries, with the annual decline between <1% in Mexico to ~5% in Australia. Across the 26 countries together, risk factor trends may have accounted for ~48% (men) and ~40% (women) of cardiometabolic mortality decline. Risk factor trends may have accounted for >60% of decline among men and women in Finland and Switzerland, men in New Zealand and France, and women in Italy; their benefits were smallest in Mexican, Portuguese, and Japanese men and Mexican women. Risk factor trends may have slowed down mortality decline in Chilean men and women and had virtually no effect in Argentinean women. The contributions of risk factors to mortality decline seemed substantially larger among men than among women in the USA, Canada and The Netherlands.

Conclusions Industrialized countries have varied widely in the extent of risk factor prevention, and its likely benefits for cardiometabolic mortality.

Keywords Cardiovascular disease, diabetes, blood pressure, cholesterol, obesity, smoking

Introduction

Cardiovascular disease (CVD) mortality has declined for decades in high-income countries.^{1–6} The effects of smoking, high blood pressure and cholesterol, and excess weight on the CVD risk of individuals have been established in randomized trials and/or prospective cohorts. This knowledge has led to clinical interventions and public health actions to reduce risk factors in individual patients as well as populations. The question however remains whether, and how much, changes in risk factors have contributed to the observed CVD decline at the population level in different countries.

The contributions of risk factor trends to long-term mortality decline have been assessed using repeated surveys in Finland.⁷ Some studies, including by the authors of the current work, have used modelling to quantify the mortality and disease burden attributable to risk factors⁸ or to assign a portion of the CVD mortality decline to risk factor trends in selected populations;^{9–12} these studies have assumed that the causal effects from individual-level epidemiological studies apply to whole populations. In the 1980s, the MONICA (Multinational MONItoring of trends and determinants in CARDiovascular disease) Project was established to empirically examine the relationship between risk factor changes in the population and CVD trends over a 10-year period using data from 38 centres in 21 countries.¹³ In the MONICA Project, changes in smoking, blood pressure, serum cholesterol and body mass index (BMI) partially explained the cross-population variation in CHD decline but there was substantial unexplained variation.¹⁴

During the 15+ years since the MONICA Project, CVD mortality has further declined but diabetes prevalence and mortality has increased in high-income countries, with substantial differences in trends across countries and between men and women.^{4,15,16} Risk factor trends also had similarities as well as noticeable differences by sex and country.^{17–19} For example, BMI increased more among men and women in Australia and USA than in Western Europe,¹⁷ but American men and Australian women had the fourth and eighth largest decline in systolic blood pressure (SBP) among industrialized countries; in contrast, American women had the third smallest SBP decline.¹⁹ Serum total cholesterol (TC) declined more in Nordic countries and New Zealand than in Southern Europe, with Sweden and Finland now having lower TC than Italy.¹⁸

There are no empirical cross-country assessments of the associations between trends in multiple risk factors and CVD mortality since the MONICA Project, especially at the national level; only modelling studies have been done in specific countries. Further, the role of risk factors in the rise in diabetes mortality has not been assessed. We used advances in data on mortality and risk factors to examine the effect of trends in risk factors on cardiometabolic (CVD and diabetes)

mortality trends empirically in national populations of industrialized countries. Our aim was to answer the important question of how much changes in risk factors may have contributed to the observed mortality decline at the population level.

Methods

We analysed the association between changes in cardiometabolic mortality with changes in BMI, SBP, TC and smoking between 1980 and 2009. We analysed CVD and diabetes together for two reasons. First, at least three of the risk factors analysed (BMI, smoking and SBP) increase the risk of diabetes disease and/or mortality (for SBP, the increased risk is primarily through effects on chronic kidney disease and its complications).^{20–25} Second, most persons with diabetes die of heart disease and stroke. Although the International Classification of Disease (ICD) system considers CVD the underlying cause of death in these instances, a proportion of these deaths may be certified to diabetes,²⁶ making the division between the two at least incomparable across countries, if not somewhat ambiguous. Results based on CVD alone are presented in [Supplementary Figure 6](#) and [Supplementary Table 2](#) (available as [Supplementary Data](#) at *IJE* online).

We used mean BMI, SBP and TC because associations with cardiometabolic mortality are linear in commonly observed ranges. Following previous analyses,^{27–29} we measured cumulative population exposure to smoking using lung cancer mortality because in industrialized countries data on lung cancer mortality trends are more widely available and more reliable than on smoking prevalence and intensity.

The analysis was done for 26 industrialized countries with reliable mortality data. We analysed associations for ages 25–79 years because there are few cardiometabolic deaths in younger ages. There may be differences across countries in the age composition of those older than 80 years and there may also be more error or incomparability in the assignment of underlying cause of death due to co-morbidities. Further, risk factor estimates in the oldest age groups were more uncertain due to fewer data sources.^{17–19} Between the ages of 25 and 79 years, death rates and risk factors were age-standardized to total population of the analysis countries over the analysis period.

Data sources

CVD, diabetes and lung cancer mortality were from vital registration data through the World Health Organization (WHO).^{30,31} High-income countries and some middle-income countries in Latin America now have complete or near-complete registration of deaths with medical certification of causes of death.³² WHO uses demographic methods to test and, if needed,

adjust for completeness of death registration, and re-distributes ill-defined and improbable causes of death based on patterns in countries with high-quality cause of death assignment.³³

Mean BMI, SBP and TC were from a systematic analysis of population-based data described in detail elsewhere.^{17–19} In brief, we reviewed and accessed published and unpublished population-based health examination surveys and epidemiological studies to collate comprehensive data on these four risk factors. For each risk factor, we developed and applied a Bayesian hierarchical model, which uses all available data to make estimates of risk factor levels, and their uncertainties, by age group, country and year separately for each sex. In the hierarchical model, estimates for each country-year were informed by data from that country-year itself, if available, and by data from other years in the same country and in other countries, especially those in the same region with data in similar time periods. The hierarchical model shares information to a greater degree where data are nonexistent or weakly informative (i.e. have large uncertainty), and to a lesser degree in data-rich countries and regions. The estimates were also informed by covariates that help predict risk factor levels, e.g. level of urbanization. The model incorporated non-linear time trends and non-linear age patterns for risk factors and allowed the age patterns to vary across populations.^{34–36} Finally, the model accounted for the fact that subnational and community data, although informative, might systematically differ from nationally representative ones, because they might be undertaken in areas with high or low risk factor levels; they also tend to have larger variability than national studies. The uncertainties are larger for risk factors, countries and years without data or with data that were not from a nationally representative survey (see Discussion for the implication of using risk factor exposure from a Bayesian model). Data on per-capita gross domestic product (GDP) were from a recent pooled global analysis which accounted for differences in purchasing power across countries and for inflation.³⁷

Statistical methods

All analyses were done separately for men and women. In primary analysis, we analysed the association between change in (natural-log-transformed, Ln) mortality and change in risk factors, similar to the MONICA Project;¹⁴ the regression model is provided below:

$$\begin{aligned} (\ln(\text{cardiometabolic mortality}))_{\text{change}} &= \beta_0 \\ &+ \beta_1 \text{BMI}_{\text{change}} + \beta_2 \text{SBP}_{\text{change}} \\ &+ \beta_3 \text{TC}_{\text{change}} + \beta_3 (\ln(\text{lung cancer mortality}))_{\text{change}} \\ &+ \beta_4 (\ln(\text{GDP}))_{\text{change}} \end{aligned}$$

where subscript ‘change’ refers to the slope of their linear trend over the 29 analysis years. Data from all

29 years were used in estimating change to have more stable estimates. The risk factors in the model were BMI, SBP and TC, Ln(lung cancer mortality), with adjustment for Ln(per-capita GDP). GDP is commonly used as a measure of economic status of a country in cross-country analyses of health outcomes.³⁸

Modelling the association of change in mortality with change in risk factors, by design, removes the effects of time-invariant country characteristics that affect mortality. In addition to the above model, we estimated the association of change in Ln(mortality) with BMI with adjustment for smoking and GDP but not for SBP and TC, which are mediators of its effects on CVD; the regression model is provided below.

$$\begin{aligned} (\ln(\text{cardiometabolic mortality}))_{\text{change}} &= \beta_0 \\ &+ \beta_1 \text{BMI}_{\text{change}} + \beta_3 (\ln(\text{lung cancer mortality}))_{\text{change}} \\ &+ \beta_4 (\ln(\text{GDP}))_{\text{change}} \end{aligned}$$

The latter analysis estimates the total effects of BMI increase whereas the earlier model only measures effects that are not mediated through the impacts of BMI rise on population SBP and TC.

We estimated how much of the change in cardiometabolic mortality in each country would occur if only its risk factors had changed as they did. We first calculated change in mortality under two scenarios (i) GDP, smoking and metabolic risk factors had their actual change in each country and (ii) risk factors had their actual change but GDP remained unchanged and there was no additional ‘secular’ change. We did these calculations by applying the estimated coefficients of the above models to (a) actual changes in GDP, smoking and metabolic risk factors, and (b) changes in smoking and metabolic risk factors while setting change in GDP to zero and removing the effect of the regression constant (which measures secular change). We note that in a model that uses Ln(mortality) as the dependent variable, the contributions of risk factors, GDP and secular change are not additive. For example, lower risk factor levels have reduced the need for treatment; and better treatment would have saved some of the deaths that may have also been prevented through reducing risk factor levels. This specification, also used in the MONICA Project, reflects multi-causality of cardiometabolic diseases and the fact that many deaths are preventable by multiple interventions; it is also consistent with multi-causality in proportional risk models used in individual-level studies.

Sensitivity to analytical specification

To examine sensitivity of results to the analytical approach, we used two other specifications for the risk factor-mortality association, with results provided in [Supplementary Data](#), available as [Supplementary Data](#) at *IJE* online. In Sensitivity analysis 1, we estimated the association between cardiometabolic mortality level and risk factor levels (vs the association between

changes in the main analysis), with one observation in each country-year. We adjusted for Ln(GDP), for country (to account for country-specific characteristics) and for calendar year (to account for secular trends and residual serial correlation). Sensitivity analysis 2 was similar to Sensitivity analysis 1 but used deviations of mortality and GDP and risk factors in each country from the average of all countries in each year. Compared with Sensitivity analysis 1, Sensitivity analysis 2 allows time trends to differ across variables. Sensitivity analysis 2 also adjusted for country.

All analyses were done in open-access software R, version 2.14.0.

Results

Mortality and risk factor trends

In 2009, age-standardized cardiometabolic death rate was highest in Argentina and Mexico for both men and women. It was lowest in Australia, Switzerland, France and Japan. Age-standardized death rate in Argentinean men was about three times that of men in Australia, where adult male cardiometabolic mortality was lowest; the death rate of women in Mexico was five times that of Japanese women. Between 1980 and 2009, age-standardized cardiometabolic mortality declined in all 26 countries with the relative decline ranging from <1% per year in Mexico to ~5% in Australia for both men and women.

Age-standardized mean BMI increased in most countries, with trends for women in a few Western European countries statistically indistinguishable from no change. BMI increased the most in Mexico and Chile for women (by 0.16 kg/m² per year) and in Mexico and the USA for men (0.11 kg/m² per year). Except for Chilean men, SBP declined in all countries, by as much as 0.28 mmHg per year in Finland, Luxembourg and the USA for men and 0.43 mmHg per year in Finland and France for women. TC declined by 0.03–0.04 mmol/l per year or more in men and women in Finland, Sweden, New Zealand and the UK. The decline was smaller in countries in Southern Europe, Germany and Argentina; it was nearly zero in Mexico and Chile and increased by over 0.01 mmol/l per year in Japan. SBP and TC declined by a smaller amount where BMI rose more (Figure 1). In contrast, there was an inverse association between change in BMI and change in lung cancer, the proxy for smoking, in both sexes. Country mortality and risk factor trends are presented in Supplementary Figures 1–5, available as Supplementary Data at IJE online.

Associations of risk factor changes with change in cardiometabolic mortality

Before adjustment, changes in mean population BMI, SBP, TC and (for men only) lung cancer were positively associated with change in cardiometabolic mortality (Figure 2). The associations were steeper for

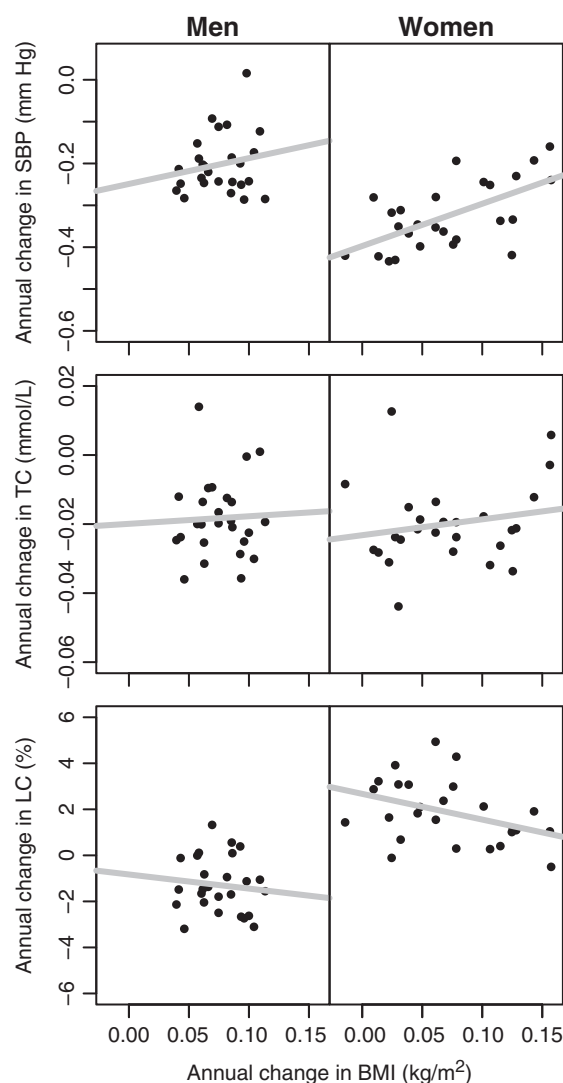


Figure 1 The cross-country associations between change in BMI and changes in SBP, TC and lung cancer mortality. Each point shows one country. The lines show the fitted linear association

men than for women except that of BMI. After adjustment for other risk factors and GDP, each 10-mmHg reduction in mean population SBP was associated with 46% (95% CI 4 to 70) decline in cardiometabolic mortality for men and 41% (95% CI -7 to 67) for women. One mmol/l reduction in mean TC was associated with 21% (95% CI -11 to 43) decline in cardiometabolic mortality in men and 18% (95% CI -13 to 40) in women. When adjusted for SBP and TC in addition to smoking and GDP, 1 kg/m² rise in mean BMI was associated with 5% (95% CI -10 to 18) increase in cardiometabolic mortality in men and 6% (95% CI -3 to 14) in women; the association was larger without adjustment for SBP and TC (9% in men and 10% in women). Each doubling of LC mortality was associated with a 5% increase in cardiometabolic mortality among men and 16% among women.

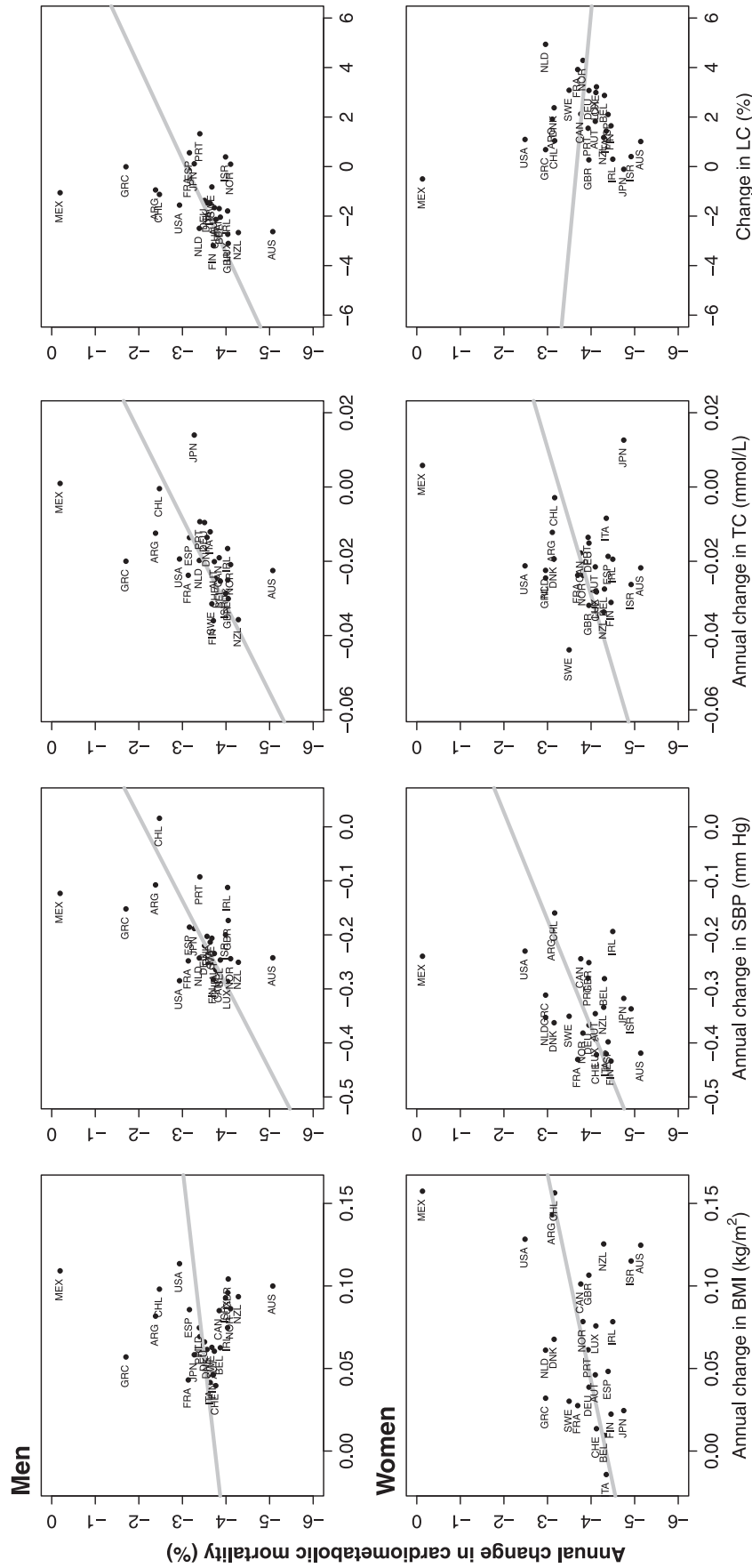


Figure 2 The cross-country associations between change in risk factors and change in cardiometabolic (CVD and diabetes) death rates. All variables were age-standardized as described in Methods. Each point shows one country. The lines show the fitted linear associations. See [Supplementary Figure 6](#) for results for CVD alone (available as [Supplementary Data](#) at *IJE* online)

Our conclusions about the role of risk factors in cardiometabolic mortality at the population level were similar in Sensitivity analyses 1 and 2 (see [Supplementary Table 1](#), available as [Supplementary data](#) at IJE online). The magnitudes of the associations were smaller for SBP and for BMI among men without adjustment for GDP; the confidence intervals of adjusted and unadjusted effect sizes overlapped in all instances.

Contributions of risk factor trends to mortality decline

Risk factor trends may have adversely affected cardiometabolic mortality trajectory in Chilean men and women (i.e. slowed down the mortality decline), and had virtually no effect among Argentinean women. The populations of the other countries are likely to have benefited from lower risk factor levels in 2009 compared with 1980 ([Figure 3](#)). If the above associations reflect the causal effects of risk factor change on mortality decline, trends in these four risk factors alone might have led to over 60% of cardiometabolic

mortality decline among men and women in Finland and Switzerland, men in New Zealand and France and women in Italy. Most of these countries had above average improvements in SBP and TC, and for men in smoking; Switzerland, Finland, France and Italy also had below-average rise in BMI. At the low end, the risk factors accounted for ~11–26% of mortality decline in Mexican, Portuguese, and Japanese men and for ~18% in Mexican women. These countries performed poorly in terms of risk factor trends compared with most other countries, with either smaller declines (e.g. in SBP) or larger increase (e.g. BMI in Mexican women and TC in Japanese men). Portugal was also one of the three countries where cumulative smoking increased among men and Japan one of the few without a decline. In the USA, risk factor trends accounted for an estimated 56% of the reduction in mortality among men and 28% among women. The male-female difference was due to smaller SBP decline and later decline of smoking among American women compared with American men. The male-female differential in the role of risk factors also

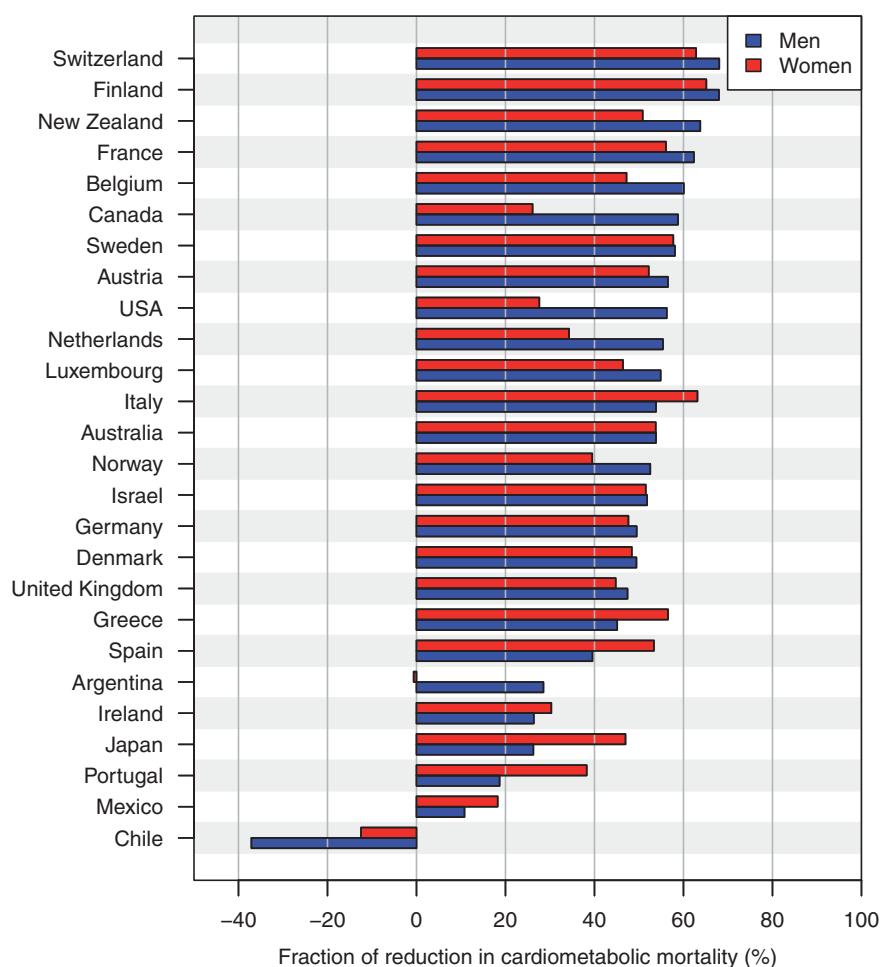


Figure 3 Proportion of decline in cardiometabolic mortality due to changes in BMI, SBP, TC and smoking. A negative fraction should be interpreted as a situation in which risk factor trends slowed down mortality decline

seemed relatively large in Canada and The Netherlands. In Southern European countries, especially Portugal, and in Japan, risk factor trends may have accounted for noticeably more of the mortality decline among women compared to men.

Not only did countries differ in the proportional contributions of risk factors to cardiometabolic mortality decline, but they also differed in their absolute contributions (Figure 4). The estimated absolute benefits were largest among men in Finland and New Zealand, with about 381 and 346 fewer deaths per 100 000, respectively, in 2009 due to risk factor trends. In contrast, the estimated absolute mortality benefits were close to zero in Mexico, and between 70 and 90 deaths per 100 000 in Japanese, Portuguese and Greek men. Chilean men had about 109 more deaths per 100 000 in 2009 than they would have experienced if their risk factor profiles had not changed. The absolute benefits were smaller in women, who experienced smaller overall reduction in cardiometabolic mortality than men in most countries. The largest estimated benefits among women were in Finland, Israel, Italy and New Zealand about 150–180 fewer deaths per 100 000 in 2009 due to risk factor trends. Women in Chile had about 29 more deaths per 100 000 in 2009 than they would have had if their risk factor profiles had not changed.

In 2009, there were about 810 000 deaths from CVD and diabetes among men and about 490 000 among women aged 25–79 years in these 26 countries. This is approximately 1 210 000 fewer (for men) and 710 000 fewer (for women) than would have occurred had death rates remained at their 1980 levels. The observed risk factor trends alone would have achieved an estimated 48% (men) and 40% (women) of these avoided deaths. If all countries had experienced the risk factor changes of the best performing countries, the number of cardiometabolic deaths in these countries in 2009 would be lower by an impressive 27% for men and 42% for women, larger than the proposed global goal for reducing noncommunicable disease (NCD) mortality.

Discussion

Our results indicate that trends in major cardiovascular risk factors are likely to have beneficially contributed to the observed cardiometabolic mortality decline in most industrialized countries. Risk factor trends alone may have been able to bring about a substantial proportion of the observed decline even if other factors had remained unchanged. The benefits would have been even larger had BMI remained at its 1980 levels and, for women, had smoking not increased in most industrialized countries. However, countries differed substantially in the role of risk factors in mortality decline, with those countries that had experienced larger risk factor reductions realizing

more of their potential. In contrast, lagging behind in reducing tobacco, blood pressure or cholesterol and experiencing larger rises in BMI led to smaller benefits.

Our findings are broadly consistent with the MONICA Project,¹⁴ but the associations between changes in risk factors and mortality had less heterogeneity in our study. Our estimates of the contributions of risk factors to mortality decline are similar to the estimated role of primary prevention in model-based analysis of CHD in specific countries.^{7,10–12} Differences with modelled estimates may be due to the separation of primary and secondary prevention in most modelling studies, differences in outcome (CHD and heart failure vs all cardiometabolic causes) and because all but one⁷ model-based analyses forced the contributions of individual preventive and therapeutic interventions to sum to 100%, thus not allowing multi-causality and overlap among various risk factors and treatment. Even the seemingly paradoxical finding that cardiometabolic mortality declined in places like Chile, where the population's risk factor profile did not improve, is consistent with the early stages of CVD mortality decline in currently industrialized countries, which began before the favourable trends in risk factors.³⁹ This early start may be due to better foetal and early life nutrition,⁴⁰ less infections and inflammation, and improvements in post-event treatment. Importantly, the associations in our population-level analysis were broadly consistent with those in randomized trials and prospective studies of individual subjects, strengthening the conclusion that population-based risk factor reduction is likely to translate to lower mortality. For example, a 10-mmHg reduction in SBP was associated with a 22% reduction in CHD and 41% reduction in stroke in randomized trials,⁴¹ compared with a 41–46% reduction in cardiometabolic mortality in our study. Similarly, a 5-kg/m² higher baseline BMI was associated with about 40% higher risk of IHD and stroke and 120% higher risk of diabetes in the Prospective Studies Collaboration,²⁰ compared with ~32–65% with and without adjustment for SBP and TC in our analysis for cardiometabolic mortality.

The strengths of our study include being a direct empirical analysis of the association between risk factors and mortality in multiple countries, using consistent and comparable mortality and risk factor data at the national level, allowing for multi-causality and overlap among risk factor effects and using multiple statistical approaches to assess the robustness of our results to analytical specification. The main limitation of our analysis is its observational design to estimate the contribution of risk factors to mortality decline, necessitated by the fact that an experimental or even quasi-experimental design would be very difficult in whole populations.⁴² Our risk factor exposures were from a Bayesian analysis of worldwide population-based data. This provided consistent and

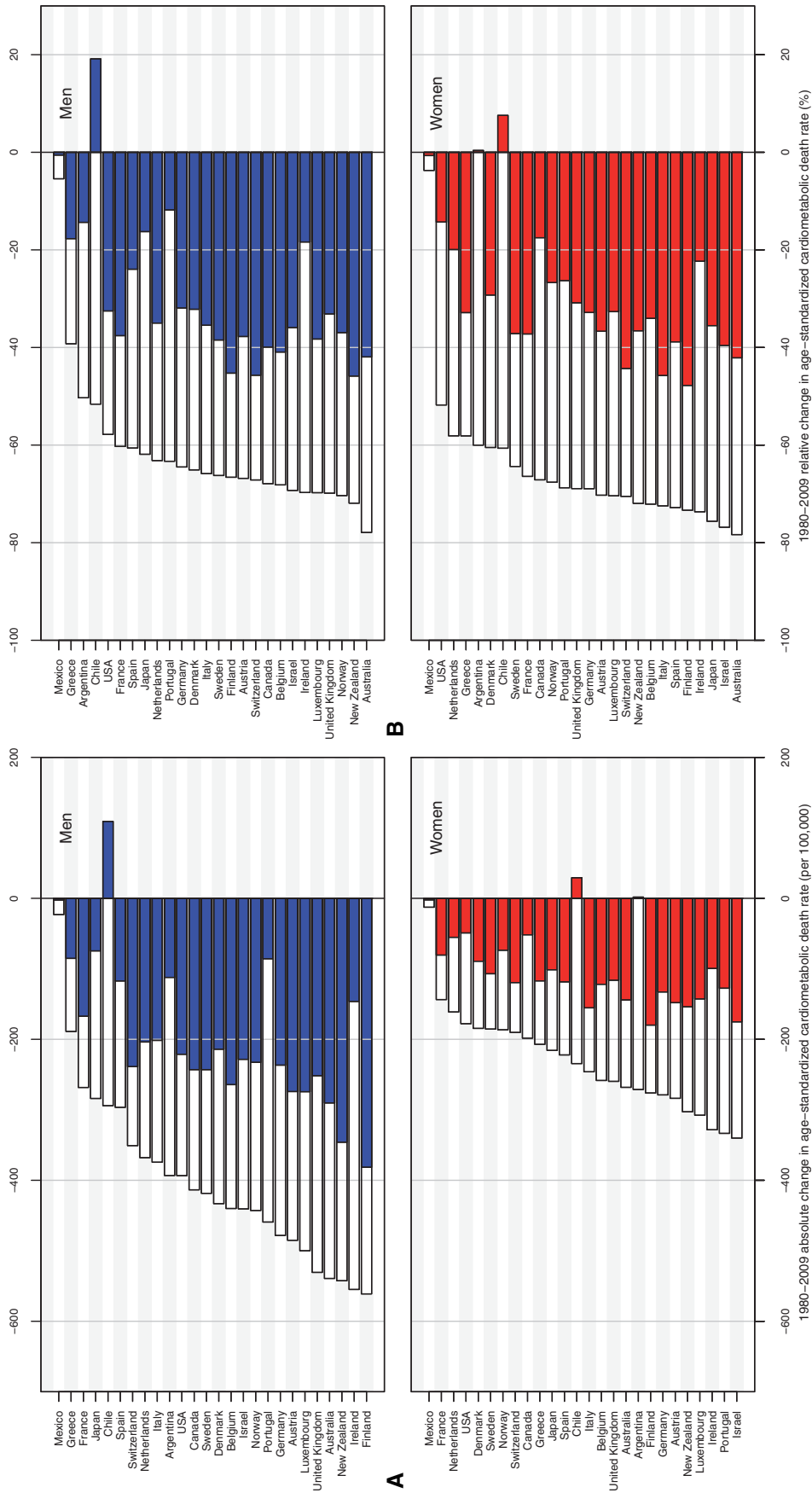


Figure 4 Change in age-standardized cardiometabolic death rates between 1980 and 2009 (total length of each bar) and change that would have been expected solely due to risk factor trends in age-standardized section (the coloured section) (A) absolute and (B) relative

comparable risk factor estimates for all countries, but the estimated country trends have varying degrees of uncertainty ranging from extremely certain in countries like Japan, the USA and Italy with multiple national sources to somewhat uncertain in Chile, Argentina and Luxembourg. It has been shown that using risk factor exposure from a Bayesian model is statistically equivalent to measuring exposure with error, which tends to overestimate standard errors and/or attenuate the associations between risk factors and mortality.^{43–46} Therefore, our results may be conservative estimates of the population-level benefits of risk factor trends. Our analysis covered only 26 industrialized countries with high quality and reliable mortality and risk factor data; the roles of these four main risks as well as other risk factors should be assessed in other countries, especially those in Asia and Africa. We also restricted the analyses to ages 25–79 years because there may be differences across countries in the age composition of those older than 80 years; there may also be more error or incomparability in the assignment of underlying cause of death due to co-morbidities. Because consistent and comparable data on trends in smoking are available in very few countries, we used lung cancer to measure cumulative exposure to smoking, as used in other population-based analyses.^{27–29} Using lung cancer, which has longer latency and slower reversibility than CVD, may underestimate the role of change in smoking where there have been recent changes in population smoking, e.g. the benefits of recent smoking decline among women in some countries. Studies that have compared methods in populations with good historical smoking data show that this effect is relatively modest.⁴⁷ Similarly, we used per-capita GDP as a measure of other factors that may affect mortality including improvements in healthcare. Healthcare spending by country was not used because approximately one-third of country-years in our analysis were missing from the Organization for Economic Co-operation and Development (OECD) databases (<http://stats.oecd.org>). For country-years with data, the correlation coefficient between per-capita GDP and per-capita expenditure on health was 0.77. Our primary analysis was based on cardiometabolic (CVD and diabetes) causes together because at least three of the analysed risk factors affect the risk of diabetes disease and/or mortality and because there is potential for inconsistent or incomparable assignment of underlying cause of death at the time of certification.²⁶ More reliable and comparable data on underlying causes of death might have allowed analyses for more specific causes. We used TC and BMI because there were little population-based data on other measures of lipids and adiposity, e.g. LDL cholesterol, total-to-HDL-cholesterol ratio and waist circumference. Finally, whereas the scope of the study was on the effects of risk factor decline regardless of whether it was due to primary or secondary prevention, it would be

interesting to also estimate the specific role of secondary prevention and treatment (which, as described in Methods, are not additive with that of primary prevention).

Randomized trials and observational studies have established the effects of smoking, elevated blood pressure and lipids, and excess weight on cardiometabolic mortality risk for individuals. Our study indicates that addressing risk factors at the population level is likely to translate to lower mortality, as envisioned by Geoffrey Rose.⁴⁸ However, industrialized countries have varied substantially in how much they have benefited from the potential for reducing mortality through risk factor management. The experience of countries like Finland and New Zealand, where we found large benefits from risk factor trends and where the drivers of risk factor reduction have been documented,^{49,50} show the need to strengthen tobacco control, reduce metabolic risks through dietary interventions (reducing salt intake and replacing saturated fats with unsaturated fats) and primary care, and find strategies that can slow down the rise in obesity which can dampen the benefits of other risk factor interventions.⁶ Whereas this analysis focused on industrialized countries, the results also indicate that global targets for major risk factors are an important step in achieving reductions in mortality from cardiometabolic causes, which are the largest contributor to NCD mortality.

Supplementary Data

Supplementary Data are available at *IJE* online.

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Conflict of interest: None declared.

KEY MESSAGES

- Since 1980, age-standardized cardiometabolic (cardiovascular plus diabetes) mortality has declined in high-income industrialised countries, with Mexico having the lowest rate of decline and Australia the highest.
- Trends in body mass index (BMI), blood pressure, serum cholesterol, and smoking together may have alone accounted for nearly one half of the decline in men and about 40% in women.
- Men and women in Finland and Switzerland, men in New Zealand and France, and women in Italy have had the most favourable overall risk factor trends. Least favourable or even harmful risk factor trends were in men and women in Chile and Mexico, men in Portugal and Japan, and women in Argentina.
- The contributions of risk factors to mortality decline seemed substantially larger among men than among women in the USA, Canada and The Netherlands. The opposite was seen in countries in Southern Europe, especially in Portugal, and in Japan.
- If all countries had experienced the risk factor changes of the best performing countries, the number of cardiometabolic deaths in these countries in 2009 would be lower by an impressive 27% for men and 42% for women, larger than the proposed global goal for reducing noncommunicable disease (NCD) mortality.

References

- Uemura K, Pisa Z. Trends in cardiovascular disease mortality in industrialized countries since 1950. *World Health Stat Q* 1988;**41**:155–78.
- Uemura K, Pisa Z. Recent trends in cardiovascular disease mortality in 27 industrialized countries. *World Health Stat Q* 1985;**38**:142–62.
- Dobson AJ, Evans A, Ferrario M *et al*. Changes in estimated coronary risk in the 1980s: data from 38 populations in the WHO MONICA Project. *Ann Med* 1998;**30**:199–205.
- Levi F, Lucchini F, Negri E, La Vecchia C. Trends in mortality from cardiovascular and cerebrovascular diseases in Europe and other areas of the world. *Heart* 2002;**88**:119–24.
- Preston SH. *Mortality Patterns in National Populations : With Special Reference to Recorded Causes of Death*. New York, London: Academic Press, 1976.
- Ezzati M, Riboli E. Can noncommunicable diseases be prevented? Lessons from studies of populations and individuals. *Science* 2012;**337**:1482–87.
- Vartiainen E, Laatikainen T, Peltonen M *et al*. Thirty-five-year trends in cardiovascular risk factors in Finland. *Int J Epidemiol* 2010;**39**:504–18.
- Ezzati M, Lopez AD, Rodgers A, Vander Hoorn S, Murray CJ. Selected major risk factors and global and regional burden of disease. *Lancet* 2002;**360**:1347–60.
- Huinink MGM, Goldman L, Tosteson ANA *et al*. The recent decline in mortality from coronary heart disease, 1980–1990. The effect of secular trends in risk factors and treatment. *JAMA* 1997;**277**:535–42.
- Unal B, Critchley JA, Capewell S. Explaining the decline in coronary heart disease mortality in England and Wales between 1981 and 2000. *Circulation* 2004;**109**:1101–07.
- Wijeyesundera HC, Machado M, Farahati F *et al*. Association of temporal trends in risk factors and treatment uptake with coronary heart disease mortality, 1994–2005. *JAMA* 2010;**303**:1841–47.
- Ford ES, Ajani UA, Croft JB *et al*. Explaining the decrease in US deaths from coronary disease, 1980–2000. *N Engl J Med* 2007;**356**:2388–98.
- WHO MONICA Project Principal Investigators. The World Health Organization MONICA Project (monitoring trends and determinants in cardiovascular disease): a major international collaboration. *J Clin Epidemiol* 1988;**41**(2):105–14.
- Kuulasmaa K, Tunstall-Pedoe H, Dobson A *et al*. Estimation of contribution of changes in classic risk factors to trends in coronary-event rates across the WHO MONICA Project populations. *Lancet* 2000;**355**:675–87.
- Danaei G, Finucane MM, Lu Y *et al*. National, regional, and global trends in fasting plasma glucose and diabetes prevalence since 1980: systematic analysis of health examination surveys and epidemiological studies with 370 country-years and 2.7 million participants. *Lancet* 2011;**378**:31–40.
- Lozano R, Naghavi M, Foreman K *et al*. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet* 2013;**380**:2095–128.
- Finucane MM, Stevens GA, Cowan MJ *et al*. National, regional, and global trends in body-mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9.1 million participants. *Lancet* 2011;**377**:557–67.
- Farzadfar F, Finucane MM, Danaei G *et al*. National, regional, and global trends in serum total cholesterol since 1980: systematic analysis of health examination surveys and epidemiological studies with 321 country-years and 3.0 million participants. *Lancet* 2011;**377**:578–86.
- Danaei G, Finucane MM, Lin JK *et al*. National, regional, and global trends in systolic blood pressure since 1980: systematic analysis of health examination surveys and epidemiological studies with 786 country-years and 5.4 million participants. *Lancet* 2011;**377**:568–77.

- ²⁰ Prospective Studies Collaboration. Body-mass index and cause-specific mortality in 900 000 adults: collaborative analyses of 57 prospective studies. *Lancet* 2009;**373**: 1083–96.
- ²¹ Willi C, Bodenmann P, Ghali WA, Faris PD, Cornuz J. Active smoking and the risk of type 2 diabetes: a systematic review and meta-analysis. *JAMA* 2007;**298**: 2654–64.
- ²² de Galan BE, Perkovic V, Ninomiya T *et al.* Lowering blood pressure reduces renal events in type 2 diabetes. *J Am Soc Nephrol* 2009;**20**: 883–92.
- ²³ Parving HH, Lehnert H, Brochner-Mortensen J, Gomis R, Andersen S, Arner P. The effect of irbesartan on the development of diabetic nephropathy in patients with type 2 diabetes. *N Engl J Med* 2001;**345**:870–78.
- ²⁴ Brenner BM, Cooper ME, de Zeeuw D *et al.* Effects of losartan on renal and cardiovascular outcomes in patients with type 2 diabetes and nephropathy. *N Engl J Med* 2001;**345**:861–69.
- ²⁵ Ni Mhurchu C, Parag V, Nakamura M, Patel A, Rodgers A, Lam TH. Body mass index and risk of diabetes mellitus in the Asia-Pacific region. *Asia Pac J Clin Nutr* 2006;**15**:127–33.
- ²⁶ Murray CJ, Dias RH, Kulkarni SC, Lozano R, Stevens GA, Ezzati M. Improving the comparability of diabetes mortality statistics in the U.S. and Mexico. *Diabetes Care* 2008;**31**:451–58.
- ²⁷ Preston SH, Gleit DA, Wilmoth JR. A new method for estimating smoking-attributable mortality in high-income countries. *Int J Epidemiol* 2010;**39**:430–38.
- ²⁸ Pope CA 3rd, Ezzati M, Dockery DW. Fine-particulate air pollution and life expectancy in the United States. *N Engl J Med* 2009;**360**:376–86.
- ²⁹ Peto R, Lopez AD, Boreham J, Thun M, Heath C Jr. Mortality from tobacco in developed countries: indirect estimation from national vital statistics. *Lancet* 1992;**339**:1268–78.
- ³⁰ World Health Organization. *The Global Burden of Disease: 2004 Update*. Geneva, Switzerland: World Health Organization, 2008.
- ³¹ World Health Organization. *Global Status Report on Noncommunicable Diseases 2010*. Geneva, Switzerland: World Health Organization, 2011.
- ³² Mathers CD, Fat DM, Inoue M, Rao C, Lopez AD. Counting the dead and what they died from: an assessment of the global status of cause of death data. *Bull World Health Organ* 2005;**83**:171–77.
- ³³ Mathers CD, Lopez AD, Murray CJ. The burden of disease and mortality by condition: data, methods, and results for 2001. In Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJL (eds). *Global Burden of Disease and Risk Factors*. New York: Oxford University Press, 2006.
- ³⁴ Rodriguez BL, Labarthe DR, Huang B, Lopez-Gomez J. Rise of blood pressure with age. New evidence of population differences. *Hypertension* 1994;**24**:779–85.
- ³⁵ Elliott P, Stamler J, Nichols R *et al.* Intersalt revisited: further analyses of 24 hour sodium excretion and blood pressure within and across populations. Intersalt Cooperative Research Group. *BMJ* 1996;**312**:1249–53.
- ³⁶ Singh GM, Danaei G, Pelizzari PM *et al.* The age associations of blood pressure, cholesterol, and glucose: analysis of health examination surveys from international populations. *Circulation* 2012;**125**:2204–11.
- ³⁷ James SL, Gubbins P, Murray CJ, Gakidou E. Developing a comprehensive time series of GDP per capita for 210 countries from 1950 to 2015. *Popul Health Metrics* 2012;**10**:12.
- ³⁸ Danaei G, Singh GM, Paciorek CJ *et al.* on behalf of the Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group. The global cardiovascular risk transition: associations of four metabolic risk factors with national income, urbanization, and Western diet in 1980 and 2008. *Circulation* 2013;**127**(14):1493–1502.
- ³⁹ Nicolosi A, Casati S, Taioli E, Polli E. Death from cardiovascular disease in Italy, 1972–1981: decline in mortality rates and possible causes. *Int J Epidemiol* 1988;**17**: 766–72.
- ⁴⁰ Stevens GA, Finucane MM, Paciorek CJ, Flaxman SR *et al.* Trends in mild, moderate, and severe stunting and underweight, and progress towards MDG 1 in 141 developing countries: a systematic analysis of population representative data. *Lancet* 2012;**380**:824–34.
- ⁴¹ Law MR, Morris JK, Wald NJ. Use of blood pressure lowering drugs in the prevention of cardiovascular disease: meta-analysis of 147 randomised trials in the context of expectations from prospective epidemiological studies. *BMJ* 2009;**338**:b1665.
- ⁴² Puska P, Nissinen A, Tuomilehto J *et al.* The community-based strategy to prevent coronary heart disease: conclusions from the ten years of the North Karelia project. *Ann Rev Public Health* 1985;**6**:147–93.
- ⁴³ Szpiro AA, Paciorek CJ, Sheppard L. Does more accurate exposure prediction necessarily improve health effect estimates? *Epidemiology* 2011;**22**:680–85.
- ⁴⁴ Szpiro AA, Sheppard L, Lumley T. Efficient measurement error correction with spatially misaligned data. *Biostatistics* 2011;**12**:610–23.
- ⁴⁵ Gryparis A, Paciorek CJ, Zeka A, Schwartz J, Coull BA. Measurement error caused by spatial misalignment in environmental epidemiology. *Biostatistics* 2009;**10**:258–74.
- ⁴⁶ Carroll RJ, Ruppert D, Stefanski LA, Ciprian C. *Measurement Error in Nonlinear Models: a Modern Perspective*. 2nd edn. Boca Raton, FL: Chapman & Hall/CRC, 2006.
- ⁴⁷ Oza S, Thun MJ, Henley SJ, Lopez AD, Ezzati M. How many deaths are attributable to smoking in the United States? Comparison of methods for estimating smoking-attributable mortality when smoking prevalence changes. *Prev Med* 2011;**52**:428–33.
- ⁴⁸ Rose G. Sick individuals and sick populations. *Int J Epidemiol* 2001;**30**:427–32.
- ⁴⁹ Puska P, Vartiainen E, Tuomilehto J, Salomaa V, Nissinen A. Changes in premature deaths in Finland: successful long-term prevention of cardiovascular diseases. *Bull World Health Organ* 1998;**76**:419–25.
- ⁵⁰ Jackson R, Beaglehole R. Trends in dietary fat and cigarette smoking and the decline in coronary heart disease in New Zealand. *Int J Epidemiol* 1987;**16**:377–82.