



Three Public Health Interventions Could Save 94 Million Lives in 25 Years

Global Impact Assessment Analysis

Editorial, see p 726

BACKGROUND: Preventable noncommunicable diseases, mostly cardiovascular diseases, are responsible for 38 million deaths annually. A few well-documented interventions have the potential to prevent many of these deaths, but a large proportion of the population in need does not have access to these interventions. We quantified the global mortality impact of 3 high-impact and feasible interventions: scaling up treatment of high blood pressure to 70%, reducing sodium intake by 30%, and eliminating the intake of artificial trans fatty acids.

METHODS: We used global data on mean blood pressure levels and sodium and trans fat intake by country, age, and sex from a pooled analysis of population health surveys, and regional estimates of current coverage of antihypertensive medications, and cause-specific mortality rates in each country, as well, with projections from 2015 to 2040. We used the most recent meta-analyses of epidemiological studies to derive relative risk reductions for each intervention. We estimated the proportional effect of each intervention on reducing mortality from related causes by using a generalized version of the population-attributable fraction. The effect of antihypertensive medications and lowering sodium intake were modeled through their impact on blood pressure and as immediate increase/reduction to the proposed targets.

RESULTS: The combined effect of the 3 interventions delayed 94.3 million (95% uncertainty interval, 85.7–102.7) deaths during 25 years. Increasing coverage of antihypertensive medications to 70% alone would delay 39.4 million deaths (35.9–43.0), whereas reducing sodium intake by 30% would delay another 40.0 million deaths (35.1–44.6) and eliminating trans fat would delay an additional 14.8 million (14.7–15.0). The estimated impact of trans fat elimination was largest in South Asia. Sub-Saharan Africa had the largest proportion of premature delayed deaths out of all delayed deaths.

CONCLUSIONS: Three effective interventions can save almost 100 million lives globally within 25 years. National and international efforts to scale up these interventions should be a focus of cardiovascular disease prevention programs.

Vasilis Kontis, PhD
Laura K. Cobb, DrPH
Colin D. Mathers, PhD
Thomas R. Frieden, MD
Majid Ezzati, PhD
Goodarz Danaei, ScD

Key Words: cardiovascular diseases
■ global health ■ hypertension
■ mortality ■ population health ■ trans fatty acids

Sources of Funding, see page 723

© 2019 The Authors. *Circulation* is published on behalf of the American Heart Association, Inc., by Wolters Kluwer Health, Inc. This is an open access article under the terms of the [Creative Commons Attribution Non-Commercial-NoDerivs](#) License, which permits use, distribution, and reproduction in any medium, provided that the original work is properly cited, the use is noncommercial, and no modifications or adaptations are made.

<https://www.ahajournals.org/journal/circ>

Clinical Perspective

What Is New?

- Three well-known interventions, scaling up access to treatment of high blood pressure to 70%, reducing sodium intake by 30%, and eliminating the intake of artificial trans fatty acids, can delay 94 million deaths worldwide within 25 years.
- The projected impact of reducing sodium intake is as large as the impact of scaling up hypertension treatment to 70%.
- The 3 interventions combined may reduce disparities in global NCD mortality.

What Are the Clinical Implications?

- Implementing hypertension diagnosis and control guidelines is key to reducing mortality from cardiovascular diseases globally.
- Even a lower coverage of treatment at 50% of patients with diagnosed hypertension would substantially reduce cardiovascular mortality.
- Interventions that result in reductions of salt intake can further and substantially reduce the burden of cardiovascular disease.

Globally, noncommunicable diseases (NCDs) are the leading cause of death, responsible for 38 million deaths annually. Of these deaths, 40% occur among people <70 years of age and 80% of these premature NCD deaths occur in low- and middle-income countries (LMICs).¹ Historically, however, there has been insufficient global investment in NCD prevention in LMICs. Only ≤1% of all global health funding is currently invested on NCD prevention,² and most LMICs provide limited training, medications, or care for even the most preventable and treatable NCDs.

Three specific interventions have a potential to save lives on a large scale: treating high blood pressure, reducing dietary sodium intake, and eliminating artificial trans fat intake.² However, there has been limited progress addressing them, despite the fact that there are cost-effective and feasible interventions with substantial impact on preventing NCDs worldwide. These 3 interventions complement existing efforts on tobacco control, are part of the World Health Organization (WHO) 13th General Program of Work,³ and are aligned with the Sustainable Development Goal of reducing the risk of premature NCD death by one-third. High blood pressure was the leading risk factor globally, responsible for 10 million deaths worldwide in 2016.⁴ In LMICs, 31.5% of adults have high blood pressure, but only 29% of those received treatment and 7.7% were controlled.⁵ Kaiser Permanente in the United States has shown that it is possible to achieve 90% blood pressure control.⁶ Similar approaches have allowed Canada to achieve 70%

control.⁷ These models have been adapted and tested in several LMICs, leading to considerable improvements in hypertension treatment and control.^{8,9} WHO recommends consuming no more than 2 g of sodium per day (5 g/d salt), but average salt intake globally is between 9 and 12 g/d.¹⁰ High sodium intake is responsible for 2.3 million deaths per year.⁴ Reducing sodium intake reduces blood pressure which in turn lowers cardiovascular disease (CVD) risk.^{11–13} The UK Salt Initiative reduced sodium intake by 15% from 2003 to 2011, thereby reducing average systolic blood pressure (SBP) by ≈3 mm Hg.¹⁴ WHO has set a target to reduce sodium intake by 30% by 2025 under its SHAKE initiative.¹⁵ Finally, WHO recommends limiting trans fat intake to <1% of dietary energy and recently released the REPLACE action package, calling for the global elimination of artificial trans fat by 2023.¹⁶ Intake levels range widely across countries from 0.6% to 6.5% of total energy intake,¹⁷ and nonoptimal trans fat intake causes ≈500 000 deaths per year.¹⁸ Artificial trans fat is fully replaceable in the food supply and has been eliminated from a few countries, starting with Denmark¹⁹; however, progress so far has largely been limited to high-income countries.²⁰

Building on previous studies that have examined the impact of interventions on delaying deaths,²¹ we quantified the potential impact of scaling up these 3 interventions on NCD deaths worldwide.

METHODS

The data that support the findings of this study are either available online (WHO mortality data per URL mentioned below), from the corresponding author on reasonable request (global blood pressure data), or on request from a third party (global sodium and trans fat intake can be sent to the corresponding authors of the cited publications).

We estimated the impacts of 3 interventions, increasing the coverage of hypertension treatment, reducing sodium intake, and reducing trans fat intake, on NCD mortality for the years between 2015 and 2040, using global data on exposure to these risks, meta-analyses of randomized trials, observational studies for effect size, and WHO's projected mortality rates by cause for each country. Below, we explain the data sources and the analytic approach.

Data Sources

We estimated population exposure to risk factors using metrics with the most comprehensive global data. Data on mean SBP by country were derived from a recent analysis of global population health surveys (Table 1).²² For baseline coverage of antihypertensive treatment, we used regional estimates from a recent meta-analysis of observational studies (Table 1 in the online-only Data Supplement).⁵ Baseline data on sodium intake were from a global analysis of dietary and urinary sodium surveys,²³ and, finally, data on trans fat intake were available from a global pooling of dietary surveys.¹⁷

The disease outcomes affected by each intervention were chosen based on evidence from reanalyses and meta-analyses

Table 1. Selected Interventions and Data Sources for Parameters

Risk Factor	Exposure Metric	Data Sources for Exposure	Disease Outcomes	Data Sources for Relative Risks	Intervention Strategies
Raised blood pressure/hypertension	Systolic blood pressure	Systematic analysis of population-based studies for the proportion of hypertension treatment by region ⁵ ; pooled analysis of population-based surveys on blood pressure in a Bayesian hierarchical model ²²	Hypertensive heart disease; ischemic heart disease; ischemic stroke; hemorrhagic and other nonischemic stroke; other cardiovascular diseases; chronic kidney disease	Meta-analysis of relative risks from cohort studies ²⁶ ; randomized trial and systematic review for the effect of hypertension treatment on systolic blood pressure ²⁷	Increase treatment coverage from 2015 levels to 70%
Sodium intake	Urinary sodium excretion	Pooled analysis of population-based surveys in a Bayesian hierarchical model ²³	Stomach cancer; hypertensive heart disease; ischemic heart disease; ischemic stroke; hemorrhagic and other nonischemic stroke; other cardiovascular diseases; chronic kidney disease	Meta-analysis of 30 randomized trials of sodium reduction for absolute effect on blood pressure ²⁸ ; World Cancer Research Fund's systematic review and meta-analysis for stomach cancer relative risk ²⁴	Reduce mean population intake of sodium by 30% relative to 2015 levels
Trans fat intake	Mean dietary trans fat consumption	Pooled analysis of population-based surveys in a Bayesian hierarchical model ¹⁷	Ischemic heart disease	Pooled meta-analyses of prospective cohort studies ¹⁸	Reduce mean population intake of trans fatty acids from 2015 levels to 0.5% of total energy intake

of randomized trials and observational studies and included major groups of CVDs, chronic kidney disease, and stomach cancer, the latter being the only type of cancer with strong links to salt intake (Table 1).²⁴ We did not include congestive heart failure directly as one of the outcomes, because it is not considered the underlying cause of death by the WHO but rather the immediate cause of death, which is itself caused by other diseases, most often coronary heart disease.²⁵ The etiological effect sizes (as relative risks [RRs]) were derived from the same meta-analyses (Table II in the online-only Data Supplement). When exposure to a risk factor decreases, RRs decline gradually, with most of the benefits evident within 5 to 10 years after reducing exposure. The rate of change of RRs was obtained from a reanalysis of American Cancer Society Cancer Prevention Study II data.²¹

Trends in death rates from NCDs to 2040 under the business-as-usual scenario were from a comprehensive update of the WHO Global Health Estimates,²⁹ with methods described in detail elsewhere.^{29,30} In summary, a series of regression equations related age- and sex-specific mortality from clusters of diseases to a set of covariates, including national income (adjusted for differences in purchasing power), education, and smoking. The regressions also included a secular time trend above and beyond the trend associated with the covariates. The coefficients of these equations were estimated by using historical mortality data, after correction for completeness of death registration and redistribution of ill-defined and improbable causes of death. These regression equations were then used to estimate mortality by disease cluster, age group, and sex for years 2015 to 2040.

Statistical Analyses

Our analytic approach was based on 2 epidemiological features of NCDs. First, NCDs have multiple causes, the combined

effects of which lead to a particular disease rate in the population. Some of these causes may be nonmodifiable (eg, genetic determinants), unmeasured or poorly measured (eg, healthcare quality or stress), or even unknown. Therefore, it is possible for trends in a specific NCD to be different from the trend of any single risk factor or small number of risk factors, depending on how other determinants and medical treatment are changing. For example, CVD mortality in high-income countries has declined for decades, whereas some of its risk factors (eg, blood pressure, cholesterol, and, in some countries, smoking) have declined and others (eg, obesity and smoking in other countries) have increased.³¹ To account for this feature, and consistent with the vast empirical evidence on proportional effects, we analyzed the impacts of risk factors on future NCD mortality as a proportion of projected death rates. The second feature of NCDs is that when exposure to risk factors changes, the harmful/beneficial impacts accumulate gradually.²⁸ We accounted for this feature using RRs that were a function of time since exposure change.

These 2 components of our approach can be incorporated in a time-based population impact fraction relationship,³² which estimates the proportion of disease-specific deaths for years between 2015 and 2040 that would be avoided if risk factor exposures were reduced because of intervention scale-up (eg, blood pressure reduction attributable to increased access to antihypertensive medications). For each disease outcome causally associated with a risk factor, the time-based population impact fraction for year 20XX, between 2015 and 2040, is calculated using the following formula:

$$PIF^{20XX} = \frac{\sum_j P_j^{20XX} RR_j^{20XX} - \sum_j \hat{P}_j^{20XX} RR_j^{20XX}}{\sum_j P_j^{20XX} RR_j^{20XX}} \quad (1)$$

Where RR^{20XX} is the RR in 20XX, P^{20XX} is the population distribution of risk factor exposure in year 20XX in the business-as-usual scenario, and \hat{P}^{20XX} is the population distribution of risk factor under intervention scenarios. The first term in the numerator is the weighted (by prevalence) disease risk if risk factors continue their observed trend (projected linearly to 2040 using historical trends between 2000 and 2015), and the second term is the weighted disease risk under intervention scenarios. 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 Equation 1 depends on time since intervention scale-up. This relationship is an extension of the commonly used population attributable/impact fraction in which RRs are a function of exposure level but not of time.

We modeled the impact of hypertension treatment, because global data on the proportion of hypertensive patients controlled are less reliable. We quantified the effect of an immediate increase in coverage of treatment to 50% and 70% of hypertensive patients, separately. The effects of treating hypertension and reducing sodium intake on CVD were analyzed as mediated through blood pressure, which allowed us to use effect sizes from randomized trials that had blood pressure as an end point.^{24,27,28} To estimate the effect of hypertension treatment on CVD, we first estimated the proportion of patients with untreated hypertension in the business-as-usual scenario, who would receive treatment in the intervention scenario. We then estimated the population mean SBP in the intervention scenario by applying the effect of hypertension treatment to this proportion of population. We used 2 different assumptions for the effect of hypertension treatment on SBP: a 10 mmHg reduction based on the effect of a full dose of one antihypertensive medication and a more ambitious 15 mmHg reduction based on the combined effect of several antihypertensive medications.²⁷ Although a previous pooled analysis of antihypertensive trials had suggested a larger reduction in blood pressure in patients with higher baseline blood pressure,³³ a more recent pooled analysis of trials found no significant differences.³⁴ Therefore, we applied the same reduction in blood pressure to the mean SBP for each subgroup in the population. For sodium intake, we used different effects on SBP for normotensive versus hypertensive participants based on a meta-analysis of salt reduction trials.²⁸ For normotensive participants, we used 2.42 reduction versus 5.39 mmHg for hypertensive participants (for each 75 mmol/d reduction in sodium). We used the WHO recommendation of 2g/d intake as the optimal mean population intake level.¹⁰ For trans fat, we used 0.5% of total energy intake as the optimal intake level based on lowest observed consumption levels globally.¹⁸

We estimated the proportional reduction in mortality from each NCD if all 3 interventions were scaled up using the relationship for the joint effects of multiple risk factors, which accounts for multicausality and overlap among the targeted risk factors.³⁵ When analyzing combined effects of hypertension treatment and sodium intake reduction, we accounted for the fact that both their effects are mediated via blood pressure. We did so by first adding their estimated effect on blood pressure, and subsequently estimating the effect of the resulting reduction in blood pressure on disease outcomes. This approach is supported by the evidence from trials of joint

interventions with sodium reduction and antihypertensive medications.³⁶

All analyses were done separately by country, sex, 5-year age group (starting at age 20), and for each NCD causally associated with the 3 targeted risk factors. Regional and global results were calculated by aggregating age-sex-specific number of deaths and population from each region's constituent countries. The regions, used in previous analyses,³⁷ were chosen based on income and geography (see [Table III in the online-only Data Supplement](#) for a list of countries in each region).

We calculated the number of deaths delayed in a future year if interventions were scaled up by multiplying the estimated population impact fraction for that year by the projected population for that year. We calculated the deaths delayed starting from the year 2016 up to and including 2040 by adding up the estimates for each year and reported the delayed deaths for 10, 20, and 25 years of the intervention. We quantified uncertainty by randomly drawing 1000 estimates of RR from its log-normal distribution.

This research was deemed as nonhuman subject research per Harvard University's human subject research policy and therefore did not require an institutional review board approval.

RESULTS

The combined effect of the 3 selected interventions was estimated to delay 34.2 (95% uncertainty interval, 31.2–37.1) million deaths by 2025, 73.1 (66.5–79.5) million deaths by 2035, and 94.3 (85.7–102.7) million deaths by 2040, the latter corresponding to 7.7% (7.0%–8.4%) of all NCD deaths globally. Increasing the coverage of treatment for high blood pressure to 70% alone could delay 39.4 (35.9–43.0) million deaths during 25 years; adding a 30% reduction in sodium intake could add another 40.0 (35.1–44.6) million deaths (Figure 1; sodium reduction alone could save 43.4 [36.9–49.5] million lives). Both these interventions could delay slightly more deaths in men (55.9% [55.0%–56.8%] of total delayed deaths) than women. The sex difference in the projected impact was larger when considering only deaths under age 70, of which 66.6% (66.1%–67.0%) were among men (Figure 1). Eliminating trans fat intake could delay an additional 14.8 (14.7–15.0) million deaths globally. Even a more modest and feasible increase in the coverage of treatment to 50% and a lower target for sodium reduction of 10% could delay 34.5 (31.1–38.0) million deaths by 2040 (Table 2). More than 90.7% (86.3%–96.3%) of projected delayed deaths were from CVDs, mostly from ischemic heart disease and stroke, 13.2% (0.6%–21.8%) of projected delayed deaths attributable to reducing sodium were from stomach cancer, and 3.9% (2.6%–5.1%) of projected delayed deaths attributable to increasing coverage of treatment for high blood pressure were from chronic kidney disease (Figure 2).

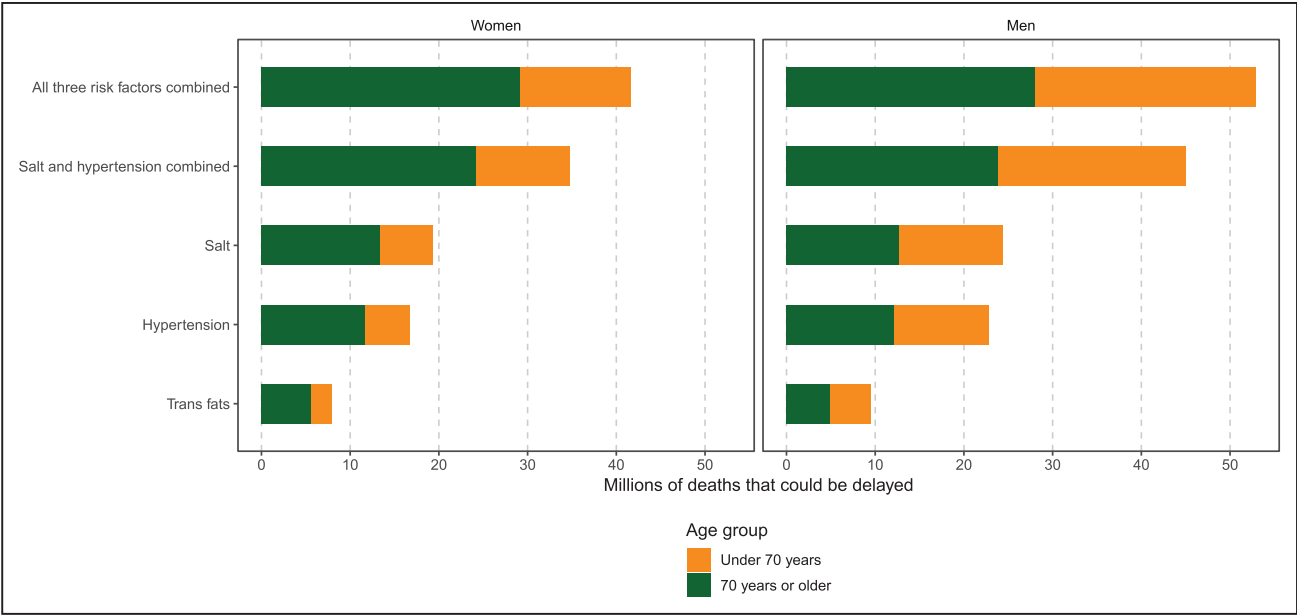


Figure 1. Deaths (million) that could be delayed by sex and age group: under and over 70 years of age.

East Asia and Pacific had the largest number of projected delayed deaths; 31.5% (29.6%–33.1%) of all projected delayed deaths occurred in this region, followed by South Asia at 24.0% (23.0%–25.2%) and Central and Eastern Europe and Central Asia at 11.9% (11.4%–12.5%). North Africa and the Middle East, Latin America and the Caribbean, and sub-Saharan Africa together contributed an additional 22.3% (21.5%–23.2%) of estimated delayed deaths. However, even in high-income countries, 9.7 (8.5–10.8) million deaths between 2015 and 2040 could be delayed by the 3 selected interventions (Figure 3 and Table IV in the online-only Data Supplement). The proportion of all NCD deaths that could be delayed varied 5 times across countries with Egypt, Uzbekistan, Tajikistan, and Kyrgyzstan having ≥14% proportion of all NCD deaths

that could be delayed versus Denmark, France, Belgium, Israel, and Vanuatu having 3% or lower (Table V in the online-only Data Supplement).

East Asia, the Pacific, and South Asia jointly accounted for 58.3% (57.2%–59.2%) of estimated delayed deaths for a combined effect of hypertension treatment and reducing sodium take, whereas Central and Eastern Europe and Central Asia ranked third at 12.5% (11.8%–13.1%) of global estimated delayed deaths. For the treatment of hypertension alone, sub-Saharan Africa ranked fourth with 4.5 (4.2–4.9) million deaths that could be delayed at 11.5% (11.1%–11.9%) of global projected delayed deaths, whereas, for reducing sodium, the fourth high-ranking region was high-income countries at 5.2 (4.2–6.1) million (11.5% [11.1%–11.9%] of global projected delayed

Table 2. Deaths That Could Be Delayed by Different Intensities of Treating High Blood Pressure and Reducing Sodium Intake

Effect of Hypertension Treatment on Systolic Blood Pressure	Percent of Patients With Hypertension Treated, %*	Sodium Intake Reduction, %†	Number (Millions) of Deaths That Could Be Delayed (95% Uncertainty Interval)		
			Women	Men	Total
10 mm Hg	50	10	11.3 (10.1–12.5)	17.0 (15.1–18.8)	28.2 (25.2–31.3)
10 mm Hg	50	30	23.5 (20.7–26.2)	32.1 (27.8–36.0)	55.6 (48.5–62.2)
10 mm Hg	70	10	17.8 (16.0–19.5)	23.5 (21.3–25.7)	41.2 (37.3–45.2)
10 mm Hg	70	30	29.6 (26.4–32.8)	38.2 (33.5–42.4)	67.8 (59.9–75.2)
15 mm Hg	50	10	13.5 (12.1–14.9)	21.0 (19.0–23.1)	34.5 (31.1–38.0)
15 mm Hg	50	30	25.6 (22.6–28.4)	35.9 (31.4–40.1)	61.5 (54.0–68.5)
15 mm Hg	70	10	23.0 (20.8–25.2)	30.5 (27.8–33.3)	53.5 (48.6–58.5)
15 mm Hg	70	30	34.6 (31.1–38.2)	44.8 (39.9–49.5)	79.5 (71.0–87.7)

*Increasing hypertension coverage alone to 50% could delay 13.4 million (12.2–14.6) deaths if assuming a 10-mmHg decline and 19.8 million (18.1–21.7) deaths if assuming a 15-mmHg decline. With 70% coverage, the deaths delayed could be 26.7 million (24.3–29.2) with a 10-mmHg decline and 39.4 million (35.9–43.0) with a 15-mmHg decline.

†Reducing salt intake by 10% could delay 15.3 million (12.9–17.7) deaths, and reducing salt intake by 30% could delay 43.4 million (36.9–49.5) deaths globally.

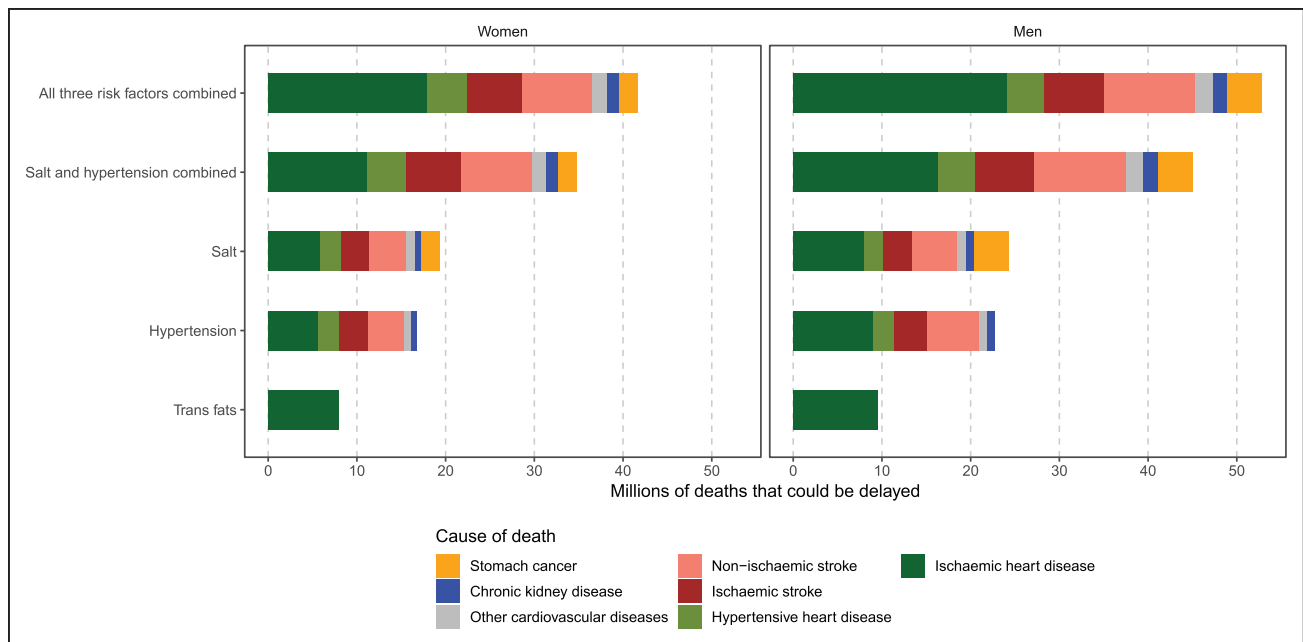


Figure 2. Deaths (million) that could be delayed by sex and cause of death.

deaths). The impact of trans fat elimination was largest in South Asia where 29.9% (28.9%–31.1%) of the 17.5 million delayed deaths between 2015 and 2040 were expected to occur.

Regional differences in avoidable deaths were substantial for major causes of death. South Asia had the largest share of projected delayed ischemic heart disease deaths at 12.2 (10.9–13.5) million (29.0% [27.9%–30.3,%]), whereas East Asia and the Pacific had the largest share of projected delayed stroke deaths at 13.6 (11.6–15.3) million (43.6% [42.1%–44.8%]).

Sub-Saharan Africa had the largest proportion of premature projected delayed deaths (those occurring at <70 years of age) at 54.2% (51.3%–57.3%; 3.6 [3.3–3.9] million) followed by South Asia at 50.9% (48.0%–53.9%; 11.5 [10.6–12.4] million). The largest sex difference in number of estimated delayed deaths was in Latin America and the Caribbean and South Asia, where 57.7% (57.1%–58.5%) and 57.5% (56.8%–58.4%) of estimated delayed deaths, respectively, were in men, and the smallest sex difference was in sub-Saharan Africa where there was an almost even split (50.5% [49.8%–51.1%] of estimated delayed deaths in men).

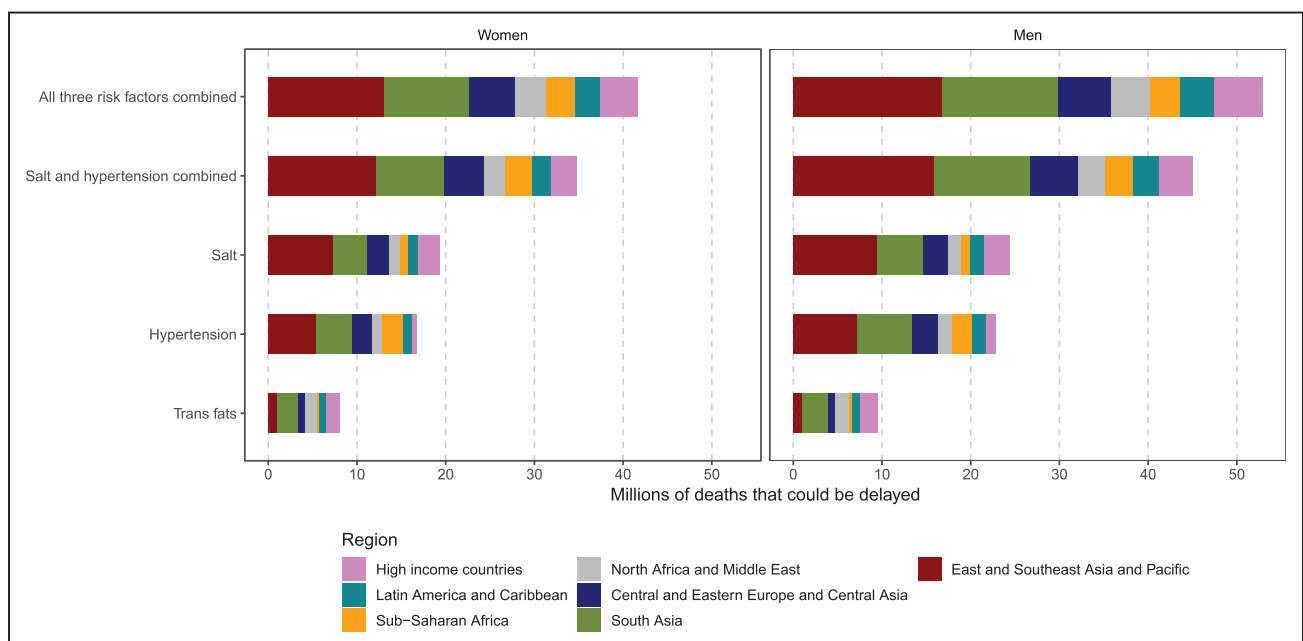


Figure 3. Deaths (million) that could be delayed by sex and region.

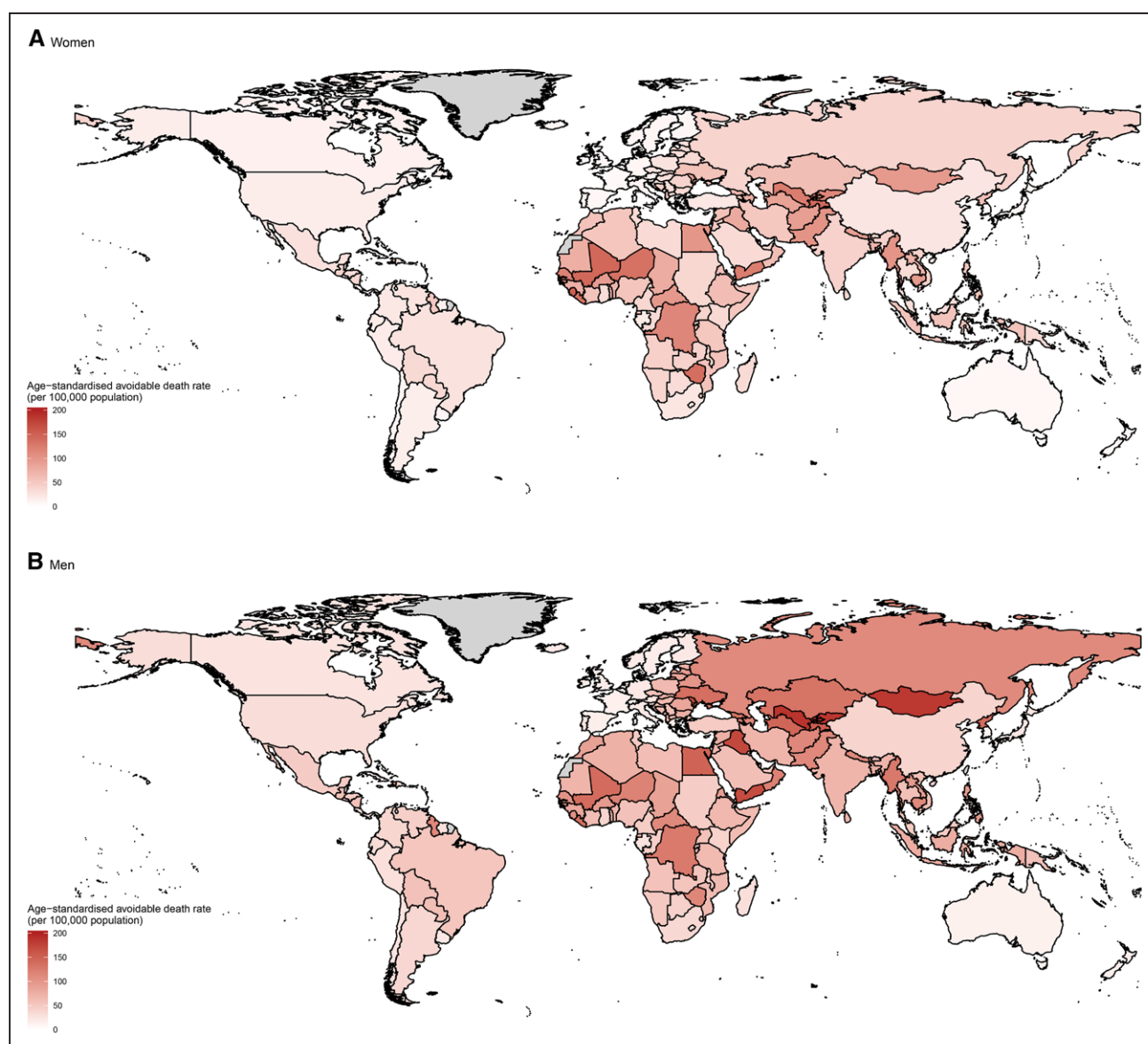


Figure 4. Age-standardized avoidable death rates by country for women (A) and men (B).

At the country level, China, India, Russia, and Indonesia contributed to the largest share of projected delayed deaths (46.5% [45.4%–47.5%] of delayed deaths). However, much less populous countries in Eastern Europe and Central Asia contributed a relatively large share to projected delayed deaths (Figure 4 and Table V in the online-only Data Supplement). For example, Uzbekistan, Kyrgyzstan, and Tajikistan all had age-standardized avoidable death rates per 100 000 population of >110 in both men and women. At the other extreme, all high-income countries (except Brunei) had <40 avoidable deaths per 100 000 population in both men and women.

The 3 interventions combined could reduce disparities in global NCD mortality. The SD of age-standardized NCD death rates across countries in 2040 declined by 9% in men and women in comparison with the

business-as-usual scenario (Table VI in the online-only Data Supplement).

DISCUSSION

We estimated that increasing the treatment of hypertension to 70% in addition to reducing sodium intake by 30% and eliminating artificial trans fat intake could delay 94.3 (85.7–102.7) million deaths globally during 25 years. More than half of all delayed deaths, and two-thirds of deaths delayed before 70 years of age, are expected to be among men, who have higher NCD death numbers globally, indicating the potential for these 3 interventions to reduce the global sex gap in NCD deaths. These sex differences are attributable to a combination of higher age-specific NCD death rates among men (which, at the same proportional reduction, leads

to more deaths delayed), and lower initial coverage of treatment for high blood pressure and slightly higher sodium intake levels among men, as well. Within regions, East Asia, the Pacific, and South Asia have the largest potential to benefit from these interventions because of a combination of high NCD death rates, lower access to hypertensive treatment, and high sodium intake. However, sub-Saharan African countries would also benefit substantially and rank fourth among the regions for benefiting from increased antihypertensive treatment because of low access to treatment. South Asian countries would have the largest share of benefit from banning trans fat, with almost one-third of delayed deaths estimated to be observed in this region because of high intake levels.

Our results are consistent with previous global impact analysis of similar interventions. A previous global analysis of NCD risk factors used similar data sources and analytical methods and showed that a 25% reduction in prevalence of raised blood pressure would prevent 20.7 million deaths between 2010 and 2025, which translates to ≈ 1.4 million deaths delayed per year²¹ (in comparison with 1.7 million deaths delayed per year in our analysis). These 2 estimates are not directly comparable, because the previous analysis quantified the impact of a 25% reduction in prevalence of raised blood pressure, whereas we modeled the impact of increasing treatment coverage to 70%. A global analysis of sodium intake between 2006 and 2015 estimated that 9.5 million deaths (1.7% of deaths from all causes during this period) would have been delayed between 2006 and 2015 had sodium intake been reduced by 15%,³⁸ which is consistent with our estimated 43 million deaths delayed for a 30% reduction (2.8% of all deaths estimated to occur in the selected 25-year period). A recent analysis of Global Burden of Disease estimated that 448 000 deaths in 2015 were attributed to trans fat intake $>1\%$ of total energy intake.⁴ This is consistent with our estimate of 17.4 million deaths postponed because of eliminating trans fat intake alone during the 25 years (from 2016 to 2040), because we used a lower optimal level of 0.5% of total energy intake.

Our results should be interpreted with several limitations in mind. We used “the number of NCD deaths delayed” as the outcome because estimates of cause-specific deaths are much more reliable than disease incidence. However, this measure does not capture how many years of life were gained for each delayed death or how many nonfatal events (myocardial infarctions and strokes) would be prevented. Information on current coverage of antihypertensive treatment was not available for each country, forcing us instead to use regional estimates. We did not consider other potential beneficial/harmful changes in diet that might result from the interventions. For example, the benefit

of sodium reduction estimated here would be reduced if manufacturers and those who prepare food increase the amounts of unhealthy nutrients such as sugar and carbohydrates as a means to reducing sodium content. In addition, we may have underestimated the effect of lowering very high blood pressure on preventing hemorrhagic stroke, because we used a more gradual decline in RR averaged over all CVDs. We did not include the potential impact of scaling up hypertension treatment on increasing control rates among treated hypertensive patients, leading to underestimating the potential impact of such programs. We may have further underestimated the effect of these interventions by not including congestive heart failure directly as an outcome. Finally, our estimates of uncertainty should be considered as a lower bound, because the uncertainties for other inputs (ie, exposure estimates and number of deaths by cause) were not available. Furthermore, the true uncertainty of the estimated delayed deaths is mostly attributable to modeling assumptions and choice of parameters rather than uncertainties around the chosen parameters.

Our analyses had several strengths. We used the most recent evidence on cause-specific death rates from WHO and projected them forward. We also used the most reliable data on blood pressure, sodium intake, and trans fat intake from global analyses of population surveys. We incorporated time trends in RRs and therefore had a more conservative estimate of delayed deaths because many conventional analyses that assume the full effect of an intervention would be realized immediately after implementation. We also allowed for multicausality (ie, each NCD death may be caused by >1 risk factor and therefore can be prevented by intervening on any of the contributing risk factors) by estimating the joint population-attributable fraction. Finally, we quantified parameter uncertainty using simulations and examined different intensities of interventions and quantified their impact on each country, age, and sex group separately.

Overall, this study indicates that these 3 interventions have enormous potential to save lives. However, scaling up these interventions to global populations is a huge challenge.

Various programs and policies targeting these interventions have been shown to be effective. Increasing coverage of hypertension treatment requires a multi-pronged program. This will require drug- and dose-specific treatment protocols,^{6,39} reliable supply of quality-assured medicines and blood pressure monitors, task sharing, patient-friendly services, and healthcare information systems that facilitate tracking and improving control rates. In addition, awareness that hypertension is a silent killer,⁴⁰ expansion of primary healthcare coverage, and effective care in the private sector will all be essential.^{41,42} To reduce sodium intake by 30%, policies need to target primary sources of sodium in each country. Packaged food and food eaten away from home

are growing contributors to sodium intake worldwide.⁴³ Evidence-based policy options include mandatory (preferred) or voluntary industry targets and front-of-pack warning labels¹⁵ and institutional food standards in schools, government offices, and other institutions.⁴⁴ In many LMICs, homemade food is the main source of sodium intake,⁴⁵ so media campaigns and public education will be crucial to reduce intake. In addition, promoting and subsidizing sodium substitutes including low-sodium salts, and reducing the sale of high-sodium foods, may be important. Finally, eliminating artificial trans fat may be the least difficult of the 3 goals to achieve. Model regulations exist in Denmark, the United States, and Canada and are the most effective route to elimination.²⁰ Twenty-three countries had regulations limiting artificial trans fat in effect by the end of 2018. In addition to passing regulations to eliminate trans fats from foods, WHO's REPLACE package recommends reviewing the sources of trans fat, promoting replacement with healthier oils, assessing time trends in trans fat in the food supply, creating awareness among industry, policy makers, and consumers, and enforcing regulations.⁴⁶

Previous cost-effectiveness analyses of the 3 selected interventions show that they are not only achievable, but they are also affordable. For example, reducing sodium intake by 15% has been estimated to cost <\$0.40 per person per year in low-income countries,³⁸ and scaling up a more comprehensive drug treatment regimen for CVD reduction would cost on average \$1.10 per person per year.⁴⁷ Previous analyses have also estimated that trans fat elimination would ultimately lead to large healthcare cost savings.^{48,49} All 3 interventions have been deemed highly cost-effective, and hypertension treatment and sodium reduction have been designated best buys by the WHO.⁵⁰

In conclusion, 3 interventions have the potential to substantially reduce NCD mortality across the world at an affordable cost. Successful global implementation would require increased investment in healthcare capacity and quality of care in the primary healthcare sector, and increased efforts to reduce sodium and eliminate trans fat intake through regulation and health promotion campaigns, as well. If countries commit resources to implement these highly cost-effective interventions, they will save lives and help achieve the targets set in the Sustainable Development Goals to reduce premature NCD deaths.

ARTICLE INFORMATION

Received September 28, 2018; accepted April 17, 2019.

The online-only Data Supplement is available with this article at <https://www.ahajournals.org/doi/suppl/10.1161/CIRCULATIONAHA.118.038160>.

Correspondence

Goodarz Danaei, ScD, Department of Global Health and Population, 655 Huntington Ave, Boston, MA 02115. Email gdanaei@hsph.harvard.edu

Affiliations

School of Public Health and MRC-PHE Centre for Environment and Health, Imperial College London, UK (V.K., M.E.). Vital Strategies, New York (L.K.C., T.R.F.). World Health Organization, Geneva, Switzerland (C.D.M.). WHO Collaborating Centre on NCD Surveillance and Epidemiology, Imperial College London, UK (M.E.). Department of Global Health and Population and Department of Epidemiology, Harvard TH Chan School of Public Health, Boston, MA (G.D.).

Sources of Funding

None.

Disclosures

Drs Kontis and Danaei received modest consulting fees from Resolve to Save Lives, an Initiative of Vital Strategies, for the conduct of this research. Resolve To Save Lives is funded by grants from Bloomberg Philanthropies, the Bill and Melinda Gates Foundation, and the Chan Zuckerberg Initiative DAF, an advised fund of Silicon Valley Community Foundation. Dr Ezzati reports a charitable grant from the AstraZeneca Young Health Program, and personal fees from Prudential, Scor, and Third Bridge, outside the submitted work. The other authors report no conflicts.

REFERENCES

- Jan S, Laba TL, Essue BM, Gheorghe A, Muhunthan J, Engalgau M, Mahal A, Griffiths U, McIntyre D, Meng Q, Nugent R, Atun R. Action to address the household economic burden of non-communicable diseases. *Lancet*. 2018;391:2047–2058. doi: 10.1016/S0140-6736(18)30323-4
- Frieden TR, Bloomberg MR. Saving an additional 100 million lives. *Lancet*. 2018;391:709–712. doi: 10.1016/S0140-6736(17)32443-1
- World Health Organization. Draft thirteenth general programme of work 2019–2023. http://apps.who.int/gb/ebwha/pdf_files/WHA71/A71_4-en.pdf?ua=1 Accessed April 20, 2019.
- GBD 2016 Risk Factors Collaborators. Global, regional, and national comparative risk assessment of 84 behavioural, environmental and occupational, and metabolic risks or clusters of risks, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet*. 2017;390:1345–1422. doi: 10.1016/S0140-6736(17)32366-8
- Mills KT, Bundy JD, Kelly TN, Reed JE, Kearney PM, Reynolds K, Chen J, He J. Global disparities of hypertension prevalence and control: a systematic analysis of population-based studies from 90 countries. *Circulation*. 2016;134:441–450. doi: 10.1161/CIRCULATIONAHA.115.018912
- Jaffe MG, Young JD. The Kaiser Permanente Northern California Story: improving hypertension control from 44% to 90% in 13 years (2000 to 2013). *J Clin Hypertens (Greenwich)*. 2016;18:260–261. doi: 10.1111/jch.12803
- Padwal RS, Bienek A, McAlister FA, Campbell NR; Outcomes Research Task Force of the Canadian Hypertension Education Program. Epidemiology of hypertension in Canada: an update. *Can J Cardiol*. 2016;32:687–694. doi: 10.1016/j.cjca.2015.07.734
- Patel P, Ordunez P, DiPette D, Escobar MC, Hassell T, Wyss F, Hennis A, Asma S, Angell S; Standardized Hypertension Treatment and Prevention Network. Improved blood pressure control to reduce cardiovascular disease morbidity and mortality: the Standardized Hypertension Treatment and Prevention Project. *J Clin Hypertens (Greenwich)*. 2016;18:1284–1294. doi: 10.1111/jch.12861
- Manjomo RC, Mwagomba B, Ade S, Ali E, Ben-Smith A, Khomani P, Bondwe P, Nkhoma D, Douglas GP, Tayler-Smith K, Chikosi L, Harries AD, Gadabu OJ. Managing and monitoring chronic non-communicable diseases in a primary health care clinic, Lilongwe, Malawi. *Public Health Action*. 2016;6:60–65. doi: 10.5588/pha.16.0003
- World Health Organization. Fact sheet on salt reduction: key facts, overview, recommendations, actions and WHO response 2016. <http://www.who.int/en/news-room/fact-sheets/detail/salt-reduction> Accessed April 20, 2019.
- Webster J, Waqanivalu T, Arcand J, Trieu K, Cappuccino FP, Appel LJ, Woodward M, Campbell NRC, McLean R. Understanding the science that supports population-wide salt reduction programs. *J Clin Hypertens (Greenwich)*. 2017;19:569–576. doi: 10.1111/jch.12994
- Cogswell ME, Mugavero K, Bowman BA, Frieden TR. Dietary sodium and cardiovascular disease risk—measurement matters. *N Engl J Med*. 2016;375:580–586. doi: 10.1056/NEJMs1607161

13. Frieden TR. Sodium reduction—saving lives by putting choice into consumers' hands. *JAMA*. 2016;316:579–580. doi: 10.1001/jama.2016.7992
14. He FJ, Pombo-Rodrigues S, MacGregor GA. Salt reduction in England from 2003 to 2011: its relationship to blood pressure, stroke and ischaemic heart disease mortality. *BMJ Open*. 2014;4:e004549. doi: 10.1136/bmjopen-2013-004549
15. World Health Organization. The SHAKE Technical Package for Salt Reduction. 2016. <http://apps.who.int/iris/bitstream/handle/10665/250135/9789241511346-eng.pdf> (accessed April 20, 2019).
16. Ghebreyesus TA, Frieden TR. REPLACE: a roadmap to make the world trans fat free by 2023. *Lancet*. 2018;391:1978–1980. doi: 10.1016/S0140-6736(18)31083-3
17. Micha R, Khatibzadeh S, Shi P, Fahimi S, Lim S, Andrews KG, Engell RE, Powles J, Ezzati M, Mozaffarian D. Global, regional, and national consumption levels of dietary fats and oils in 1990 and 2010: a systematic analysis including 266 country-specific nutrition surveys. *BMJ*. 2014;348:g2272. doi: 10.1136/bmj.g2272
18. Wang Q, Afshin A, Yakoob MY, Singh GM, Rehm CD, Khatibzadeh S, Micha R, Shi P, Mozaffarian D, Ezzati M, Fahimi S, Wirojatana P, Powles J, Elmadfa I, Rao M, Alpert W, Lim SS, Engell RE, Andrews KG, Abbott PA, Abdollahi M, Abeyá Gilardon EO, Ahsan H, Al Nsour MAA, Al-Hooti SN, Arambepola C, Fernando DN, Barennes H, Barquera S, Baylin A, Becker W, Bjerregaard P, Bourne LT, Capanzana MV, Castetbon K, Chang HY, Chen Y, Cowan MJ, Riley LM, DeHennauw S, Ding EL, Duante CA, Duran P, Barbieri HE, Farzadfar F, Hadziomeragic AF, Fisberg RM, Forsyth S, Garriguet R, Gaspoz JM, Gauci D, Calleja N, Ginnela BNV, Guessous I, Gulliford MC, Hadden W, Haerper C, Hoffman DJ, Houshiar-Rad A, Huybrechts I, Hwalla NC, Ibrahim HM, Inoue M, Jackson MD, Johansson L, Keinan-Boker L, Kim C, Koksai E, Lee HJ, Li Y, Lipoeto NI, Ma G, Mangialavori GL, Matsumura Y, McGarvey ST, Fen CM, Monge-Rojas RA, Musaiger AO, Nagalla B, Naska A, Ocke MC, Oltarzewski M, Sponar L, Orfanos P, Ovaskainen ML, Tapanainen H, Pan WH, Panagiotakos DB, Pekcan GA, Petrova S, Piasen N, Pitsavos C, Posada LG, Sánchez-Romero LM, Selamat RBT, Sharma S, Sibai AM, Sichieri R, Simmala C, Steingrimsdóttir L, Swan G, Sygnowska EH, Templeton R, Thanopoulou A, Thorgerisdóttir H, Thorsdóttir I, Trichopoulou A, Tsugane S, Turrini A, Vaask S, van Oosterhout C, Veerman JL, Verena N, Waskiewicz A, Zaghloul S, Zajkás G. Impact of nonoptimal intakes of saturated, polyunsaturated, and trans fat on global burdens of coronary heart disease. *J Am Heart Assoc*. 2016;5:e002891. doi: 10.1161/JAHA.115.002891
19. Leth T, Jensen HG, Mikkelsen AA, Bysted A. The effect of the regulation on trans fatty acid content in Danish food. *Atheroscler Suppl*. 2006;7:53–56. doi: 10.1016/j.atherosclerosis.2006.04.019
20. Downs SM, Thow AM, Leeder SR. The effectiveness of policies for reducing dietary trans fat: a systematic review of the evidence. *Bull World Health Organ*. 2013;91:262–29H. doi: 10.2471/BLT.12.111468
21. Kontis V, Mathers CD, Rehm J, Stevens GA, Shield KD, Bonita R, Riley LM, Poznyak V, Beaglehole R, Ezzati M. Contribution of six risk factors to achieving the 25x25 non-communicable disease mortality reduction target: a modelling study. *Lancet*. 2014;384:427–437. doi: 10.1016/S0140-6736(14)60616-4
22. NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in blood pressure from 1975 to 2015: a pooled analysis of 1479 population-based measurement studies with 19.1 million participants. *Lancet*. 2017;389:37–55. doi: 10.1016/S0140-6736(16)31919-5
23. Powles J, Fahimi S, Micha R, Khatibzadeh S, Shi P, Ezzati M, Engell RE, Lim SS, Danaei G, Mozaffarian D. Global, regional and national sodium intakes in 1990 and 2010: A systematic analysis of 24 h urinary sodium excretion and dietary surveys worldwide. *BMJ Open*. 2013;3:e003733. doi: 10.1136/bmjopen-2013-003733
24. World Cancer Research Fund / American Institute for Cancer Research. *Food, nutrition, physical activity, and the prevention of cancer: a global perspective*. Washington, DC: AICR; 2007.
25. Murray CJ, Kulkarni SC, Ezzati M. Understanding the coronary heart disease versus total cardiovascular mortality paradox: a method to enhance the comparability of cardiovascular death statistics in the United States. *Circulation*. 2006;113:2071–2081. doi: 10.1161/CIRCULATIONAHA.105.595777
26. Singh GM, Danaei G, Farzadfar F, Stevens GA, Woodward M, Wormser D, Kaptoge S, Whitlock G, Qiao Q, Lewington S, Di Angelantonio E, Vander Hoorn S, Lawes CM, Ali MK, Mozaffarian D, Ezzati M; Global Burden of Metabolic Risk Factors of Chronic Diseases Collaborating Group; Asia-Pacific Cohort Studies Collaboration (APCSC); Diabetes Epidemiology: Collaborative analysis of Diagnostic criteria in Europe (DECODE); Emerging Risk Factor Collaboration (ERFC); Prospective Studies Collaboration (PSC). The age-specific quantitative effects of metabolic risk factors on cardiovascular diseases and diabetes: a pooled analysis. *PLoS One*. 2013;8:e65174. doi: 10.1371/journal.pone.0065174
27. Chow CK, Thakkar J, Bennett A, Hillis G, Burke M, Usherwood T, Vo K, Rogers K, Atkins E, Webster R, Chou M, Dehbi HM, Salam A, Patel A, Neal B, Peiris D, Krum H, Chalmers J, Nelson M, Reid CM, Woodward M, Hilmer S, Thom S, Rodgers A. Quarter-dose quadruple combination therapy for initial treatment of hypertension: placebo-controlled, crossover, randomised trial and systematic review. *Lancet*. 2017;389:1035–1042. doi: 10.1016/S0140-6736(17)30260-X
28. 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:f1325. doi: 10.1136/bmj.f1325
29. World Health Organization. Projections of mortality and causes of death, 2016 to 2060. http://www.who.int/healthinfo/global_burden_disease/projections/en/ [Accessed April 20, 2019].
30. World Health Organization. *WHO methods and data sources for global burden of disease estimates 2000–2015 (Global Health Estimates Technical Paper WHO/HIS/IER/GHE/2017.1)*. Geneva: World Health Organization; 2017.
31. Di Cesare M, Bennett JE, Best N, Stevens GA, Danaei G, Ezzati M. The contributions of risk factor trends to cardiometabolic mortality decline in 26 industrialized countries. *Int J Epidemiol*. 2013;42:838–848. doi: 10.1093/ije/dyt063
32. Lin HH, Murray M, Cohen T, Colijn C, Ezzati M. Effects of smoking and solid-fuel use on COPD, lung cancer, and tuberculosis in China: a time-based, multiple risk factor, modelling study. *Lancet*. 2008;372:1473–1483. doi: 10.1016/S0140-6736(08)61345-8
33. 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. doi: 10.1136/bmj.b1665
34. Czernichow S, Zanchetti A, Turnbull F, Barzi F, Ninomiya T, Kengne AP, Lammers Heerspink HJ, Perkovic V, Huxley R, Arima H, Patel A, Chalmers J, Woodward M, MacMahon S, Neal B; Blood Pressure Lowering Treatment Trialists' Collaboration. The effects of blood pressure reduction and of different blood pressure-lowering regimens on major cardiovascular events according to baseline blood pressure: meta-analysis of randomized trials. *J Hypertens*. 2011;29:4–16. doi: 10.1097/HJH.0b013e32834000be
35. Ezzati M, Hoorn SV, Rodgers A, Lopez AD, Mathers CD, Murray CJ; Comparative Risk Assessment Collaborating Group. Estimates of global and regional potential health gains from reducing multiple major risk factors. *Lancet*. 2003;362:271–280. doi: 10.1016/S0140-6736(03)13968-2
36. Slagman MC, Waanders F, Hemmelder MH, Woittiez AJ, Janssen WM, Lammers Heerspink HJ, Navis G, Laveran GD; Holland Nephrology Study Group. Moderate dietary sodium restriction added to angiotensin converting enzyme inhibition compared with dual blockade in lowering proteinuria and blood pressure: randomised controlled trial. *BMJ*. 2011;343:d4366. doi: 10.1136/bmj.d4366
37. Di Cesare M, Khang YH, Asaria P, Blakely T, Cowan MJ, Farzadfar F, Guerrero R, Ikeda N, Kyobutungi C, Msyamboza KP, Oum S, Lynch JW, Marmot MG, Ezzati M; Lancet NCD Action Group. Inequalities in non-communicable diseases and effective responses. *Lancet*. 2013;381:585–597. doi: 10.1016/S0140-6736(12)61851-0
38. Asaria P, Chisholm D, Mathers C, Ezzati M, Beaglehole R. Chronic disease prevention: health effects and financial costs of strategies to reduce salt intake and control tobacco use. *Lancet*. 2007;370:2044–2053. doi: 10.1016/S0140-6736(07)61698-5
39. Jaffe MG, Frieden TR, Campbell NRC, Matsushita K, Appel LJ, Lackland DT, Zhang XH, Muruganathan A, Whelton PK. Recommended treatment protocols to improve management of hypertension globally: a statement by Resolve to Save Lives and the World Hypertension League (WHL). *J Clin Hypertens (Greenwich)*. 2018;20:829–836. doi: 10.1111/jch.13280
40. IOM (Institute of Medicine). *A Population-Based Policy and Systems Change Approach to Prevent and Control Hypertension*. Washington, DC: National Academies Press; 2010.
41. Zack RM, Irema K, Kazonda P, Leyna GH, Liu E, Spiegelman D, Fawzi W, Njelekela M, Killewo J, Danaei G. Determinants of high blood pressure and barriers to diagnosis and treatment in Dar es Salaam, Tanzania. *J Hypertens*. 2016;34:2353–2364. doi: 10.1097/HJH.0000000000001117
42. World Health Organization and International Bank for Reconstruction and Development / The World Bank. *Tracking universal health coverage : 2017 global monitoring report*. Washington, DC: 2017.

43. Monteiro CA, Moubarac JC, Cannon G, Ng SW, Popkin B. Ultra-processed products are becoming dominant in the global food system. *Obes Rev*. 2013;14 Suppl 2:21–28. doi: 10.1111/obr.12107
44. Lederer A, Curtis CJ, Silver LD, Angell SY. Toward a healthier city: nutrition standards for New York City government. *Am J Prev Med*. 2014;46:423–428. doi: 10.1016/j.amepre.2013.11.011
45. Anderson CA, Appel LJ, Okuda N, Brown IJ, Chan Q, Zhao L, Ueshima H, Kesteloot H, Miura K, Curb JD, Yoshita K, Elliott P, Yamamoto ME, Stamler J. Dietary sources of sodium in China, Japan, the United Kingdom, and the United States, women and men aged 40 to 59 years: the INTERMAP study. *J Am Diet Assoc*. 2010;110:736–745. doi: 10.1016/j.jada.2010.02.007
46. World Health Organization. WHO REPLACE action package. <http://www.who.int/docs/default-source/documents/replace-transfats/replace-action-package.pdf> Accessed April 20, 2019.
47. Lim SS, Gaziano TA, Gakidou E, Reddy KS, Farzadfar F, Lozano R, Rodgers A. Prevention of cardiovascular disease in high-risk individuals in low-income and middle-income countries: health effects and costs. *Lancet*. 2007;370:2054–2062. doi: 10.1016/S0140-6736(07)61699-7
48. Rubinstein A, Elorriaga N, Garay OU, Poggio R, Caporale J, Matta MG, Augustovski F, Pichon-Riviere A, Mozaffarian D. Eliminating artificial trans fatty acids in Argentina: estimated effects on the burden of coronary heart disease and costs. *Bull World Health Organ*. 2015;93:614–622. doi: 10.2471/BLT.14.150516
49. Collins M, Mason H, O'Flaherty M, Guzman-Castillo M, Critchley J, Capewell S. An economic evaluation of salt reduction policies to reduce coronary heart disease in England: a policy modeling study. *Value Health*. 2014;17:517–524. doi: 10.1016/j.jval.2014.03.1722
50. World Health Organization. Tackling NCDs 2017. https://ncdalliance.org/sites/default/files/resource_files/WHO-NMH-NVI-17.9-eng.pdf Accessed April 20, 2019).