Hypertension

ORIGINAL ARTICLE

Delayed Finalization of Sodium Targets in the United States May Cost Over 250 000 Lives by 2031

Jing Song, Mhairi K. Brown, Laura K. Cobb, Michael F. Jacobson, Nicole Ide, Graham A. MacGregor, Feng J. He

BACKGROUND: The US Food and Drug Administration (FDA) proposed 2- and 10-year voluntary sodium-reduction targets for >150 packaged- and prepared-food categories in 2016 and finalized the short-term targets in 2021.

METHODS: We modeled the health benefits of implementing the newly finalized sodium targets, and the net health losses because of the 4.3-year delay in finalizing the sodium targets in different compliance scenarios in adults aged ≥30, using the National Health and Nutrition Examination Survey (NHANES) 2015 to 2016 cycle. The health impact was estimated by multiplying the projected reduction in population sodium intake by the annual health benefits resulting from every 1000-mg reduction in daily sodium intake.

RESULTS: Under certain assumptions, the FDA's finalization of the short-term targets in Oct 2021 and possible finalization of the long-term targets by April 2024 is projected to save up to 445 979 (95% CI, 17 349–787 352) lives in the coming 10 years. The net number of unnecessary deaths because of FDA's delay is projected to be as high as 264 644 (95% CI, 10 295–467 215) according to our prediction.

CONCLUSIONS: These findings highlight the enormous health costs due to the FDA's delay in finalizing the sodium-reduction targets, and the great potential health benefits of industry compliance with the FDA's finalization of its short- and long-term targets in the coming 10 years. **(*Hypertension*. 2022;79:798–808. DOI: 10.1161/HYPERTENSIONAHA.121.18475.)**

• **Supplemental Material**

Key words: adult ■ cardiovascular diseases ■ coronary disease ■ sodium ■ stroke.

Cardiovascular disease is one of the leading causes of deaths and disability in the United States and many other countries.[1,2] Excessive sodium intake, mostly from sodium chloride, is one of the most important risk factors for CVD worldwide.[3,4] Globally, population sodium intake is far higher than the World Health Organization's recommended limit of 2000 mg/day.[5,6] A diverse body of evidence, including animal studies, natural experiments, epidemiological studies, population-based interventions, and numerous randomized controlled trials demonstrates a linear relationship between sodium intake and blood pressure.[7–10] Intervention trials and prospective studies also found that lower sodium intake is associated with reduced CVD risk and mortality in the long term.[3,11–13] Conflicting results showing a *J*- or *U*-shaped relationship between sodium intake and CVD risks have been proved to be attributed to the erroneous methods of measuring the sodium intake.[14–17] The reduced risk is mediated through lower blood pressure or other pathways independent of blood pressure.[3,11–13] In addition, there is evidence of potential direct benefits from reducing sodium intake on kidney disease, gastric cancer, and osteoporosis.[11]

See Editorial, pp 809–812

Currently, the average American adult consumes about 3400 mg of sodium per day, and only 10% of the population consumes the <2300 mg/day limit recommended in

Correspondence to: Jing Song, Wolfson Institute of Population Health, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, London EC1M 6BQ, United Kingdom. Email jing.song@qmul.ac.uk

Supplemental Material is available at https://www.ahajournals.org/doi/suppl/10.1161/HYPERTENSIONAHA.121.18475.
For Sources of Funding and Disclosures, see page 807.

Hypertension is available at www.ahajournals.org/journal/hyp

NOVELTY AND SIGNIFICANCE

What Is New?

The Food and Drug Administration (FDA) finalization of its 2.5-year targets in October 2021 could save as many as 446 000 deaths in the coming 10 years, depending on when the 10-year targets will be finalized and to what degree the sodium targets be achieved.

The net number of preventable deaths resulting from the FDA's 4.3-year delay in finalizing the short-term targets could be up to 265 000 between 2017-2031.

What Is Relevant?

Setting stepwise sodium-reduction targets for packaged and prepared foods could reduce the sodium content in the US diet and the population sodium intake, thus lowering average blood pressure and reducing the incidence of cardiovascular disease.

Clinical/Pathophysiological Implications?

FDA's delay in finalizing its sodium-reduction targets has had and will continue to have huge health consequences for Americans.

It is vital for the FDA to take actions to maximize industry compliance with the short-term sodium targets and finalize the long-term targets as soon as possible.

Nonstandard Abbreviations and Acronyms

CHD	coronary heart disease
COVID-19	coronavirus disease 2019
CVD	cardiovascular disease
FDA	Food and Drug Administration
NHANES	National Health and Nutrition Examination Survey
QALY	quality-adjusted life year
RCT	randomized controlled trial

the federal government's Dietary Guidelines for Americans 2020 to 2025.[18–20] More than 70% of the sodium in the average US diet comes from sodium added in processed (ie, packaged food sold in retail settings) and prepared foods (ie, food prepared for consumption outside the home),[21] indicating that reformulation to reduce levels of sodium in these sources, or replacement of higher-sodium with lower-sodium products, would play a critical role in sodium reduction.

Setting sodium-reduction targets for packaged foods has been shown to have the potential to both spur industry to lower the sodium content in processed foods and reduce the population sodium intake in some countries.[22,23] For example, beginning in 2006, the United Kingdom established progressively lower voluntary sodium (mostly from sodium chloride) targets for over 80 food categories, provided clear timetables to encourage ongoing food reformulation, and monitored the progress of sodium reduction by industry. As a result, population sodium intake measured by 24-hour urinary excretion declined by 10% between June 2005 (geometric mean [95% CI, 2989 (1013–8822)] mg/d; arithmetic mean [95% CI, 3304 (69–6539)] mg/d) and 2011 (2714 [1020–7221] mg/d; 2989 [494–5484] mg/d). Most of the reductions (60%) occurred between June 2005 and September 2008.[23] This fall in population sodium intake was associated with ≈6000 fewer CVD deaths per year.[24] Another example is South Africa's mandatory maximum sodium targets for certain processed foods implemented since 2016, which was associated with a decline of 460 mg/d in mean population sodium intake over the following 2 years (measured by 24-hour urinary excretion).[22]

In 2016, the US Food and Drug Administration (FDA) published a draft guidance for Voluntary Sodium Reduction Goals, which proposed progressively lower sodium targets for > 150 food categories to be attained in 2 and 10 years.[25] The FDA estimated that full compliance with the draft guidance would reduce sodium intake by about 11% in the first 2 years and 32% in 10 years, ultimately resulting in average intake of about 2300 mg/d. The guidance was not finalized until October 2021, when the FDA released the modified, voluntary, short-term (2.5 year) sodium-reduction targets that, if fully implemented by industry, would reduce sodium intake by 12%.[26] The FDA has not announced when it will finalize the long-term (10-year) guidance but has indicated that it will release additional intermediate targets. In this study, we projected the potential health benefits in the coming 10 years (October 2021 to October 2031) resulting from industry response to the finalized short-term targets and possibly finalized long-term targets from Oct 2021 to Oct 2031. We also projected the total health losses (mid-2017 to Oct 2031) that is likely to be caused by the FDA's 4.3-year delay in implementing its voluntary sodium targets.

METHODS

Data Sources

All data and materials have been made publicly available by the US Centers for Disease Control and Prevention and can be accessed at https://wwwn.cdc.gov/nchs/nhanes/Default.aspx.

The details of the data collection and study population of the National Health and Nutrition Examination Survey (NHANES) have been described elsewhere.[27] We used the 2015 to 2016 cycle and included 4745 participants aged 30 and above who completed 2 24-hour dietary recalls (Supplemental Methods). The survey was approved by NCHS's Ethical Review Board, and all participants provided written informed consent.

Policy Scenarios

We considered 4 policy scenarios in our analyses (see Figure 1): (1) Base scenario: no sodium targets were implemented during mid-2017 to October 2031, and therefore no changes occur in population daily sodium intake and health outcomes of interest. (2) Minimal Compliance scenario: the 2-year drafted targets were implemented in mid-2017 (assuming a 1-year time frame for FDA to finalize its proposed guidelines) and 50% achieved by mid-2019 with the lower sodium levels continuing into the future, while the 10-year targets were never finalized (Drafted Targets); or the 2.5-year finalized targets were implemented in Oct 2021 and 50% achieved by April 2024 with the lower sodium levels remaining constant into the future because the 10-year targets were never finalized (Finalized Targets). (3) Medium Compliance scenario: the 2-year drafted targets were finalized by mid-2017 and 50% achieved by mid-2019, while the 10-year targets were finalized by mid-2019 and 50% achieved by mid-2027 with the lower sodium levels continuing into the future (Drafted Targets); or the 2.5-year finalized targets were implemented in October 2021 and 50% achieved by April 2024, while the 10-year targets were finalized by April 2024 and 50% achieved by October 2031 (Finalized Targets). (4) Full compliance scenario: the 2-year drafted targets were finalized by mid-2017 and fully achieved by mid-2019, while the 10-year targets were finalized by mid-2019 and fully achieved by mid-2027 with the lower sodium levels continuing into the future (Drafted Targets); or the 2.5-year finalized targets were implemented in October 2021 and fully achieved by April

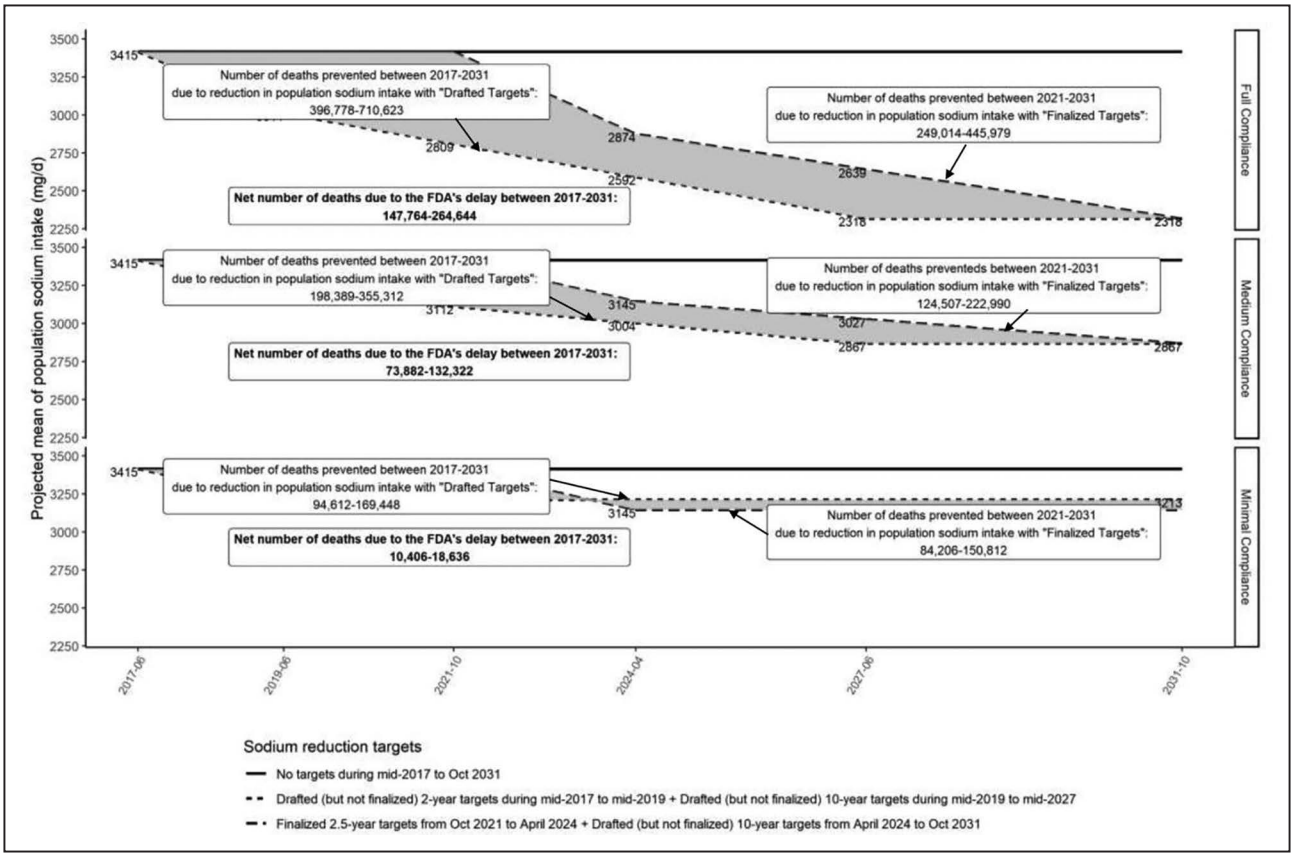

Figure 1. Schematic of the time frames and scenario assumptions in the study.
The figure indicates the sodium reductions for the full, medium and minimal compliance scenarios compared to the base scenario, and the health losses due to the Food and Drug Administration's (FDA) delay in finalizing its sodium targets. The health losses that could have been and continue to be saved over 14.3 y (mid-2017 to October 2031) were projected based on several counterfactual assumptions: the FDA had finalized its short-term (2-y) sodium-reduction targets in mid-2017 and implemented them until mid-2019 to a varying degree; the drafted long-term (10-y) sodium-reduction targets were implemented beginning in mid-2019 and continued through mid-2027; and the population sodium intake after mid-2027 would continue unchanged into the future ("Drafted Targets"–dotted lines). We also projected the health benefits for the coming 10 y considering that the FDA finalized short-term (2.5-y) targets in October 2021, which will continue in effect through April 2024; the FDA would finalize the long-term (10-y) targets before April 2024 and they would be achieved to varying degree by October 2031 ("Finalized Targets"–dashed lines). The difference between the number of deaths prevented over 14.3 y with the "Drafted Targets" and the number of deaths prevented over 10 y with the "Finalized Targets" is estimated as the net number of deaths because of the FDA's 4.3-y delay (proportional to gray area between dotted lines and dashed lines).

2024, while the 10-year targets were finalized by April 2024 and fully achieved by October 2031 (Finalized Targets). We assumed the declines of population sodium intake would be linear across each of the time intervals.

For the Finalized Targets under each scenario of compliance, we projected the changes in population sodium intake (Figure 1 dashed lines) and health benefits in the coming 10 years, given the current reality that the short-term (2.5 year) sodium targets were recently finalized in October 2021 and are scheduled to be achieved to varying degrees by April 2024, and that the long-term (10-year) sodium targets may be finalized by April 2024 and achieved to varying degrees by October 2031.

For the Drafted Targets under each scenario of compliance, we projected the reduction in population sodium intake (Figure 1 dotted lines) and the unnecessary health losses in a total of 14.3 years (mid-2017 to October 2031) if the 2-year targets were finalized by mid-2017 and achieved to varying degrees by mid-2019, and the 10-year targets were finalized by mid-2019 and achieved to varying degrees by mid-2027 with the benefits from reduced sodium intakes continuing through October 2031. The total projected health losses were further separated into 2 segments: the potential health loss that could have been saved in the past 4.3 years (mid-2017 to October 2021 when the FDA released the finalized short-term targets); and the potential health loss that could continue to be saved in the coming 10 years.

To estimate the net health losses because of the 4.3-year delay in reducing the population sodium intake levels, we compared the potential health losses that could be saved in the coming 10 years if the FDA had implemented the Drafted Targets in 2017, to the potential health benefits in the coming 10 years of implementing the Finalized Targets, and then added these differences to the potential health losses that could have been saved in the past 4.3 years if the FDA had implemented the Drafted Targets in 2017 (Figure 1 gray area).

For all the analyses, we compared the health impact estimated under Full Compliance, Medium Compliance, or Minimal Compliance scenarios with that estimated under the Base scenario during the time periods. All the comparisons were based on the assumptions that there was no lag between sodium reduction and the resultant beneficial impact on health,[28,29] that sodium intake declined linearly during the relevant intervals, and that a linear relationship exists between the decline of sodium intake and the reduction of disease burden.

Potential Changes in Population Sodium Intake

The potential changes in population sodium intake were estimated for both Drafted Targets and Finalized Targets under different scenarios using a 3-step method similar to that by Cogswell et al.[30] To examine the methodological robustness, we also compared our estimates of projected reduction in sodium intake resulting from the Drafted Targets to results derived from 2 modeling studies evaluating the projected 10-year health impact of the US 2- and 10-year sodium-reduction targets proposed in 2016 (Supplemental Methods).[31,32]

Health Outcomes

Because of the well-documented association between sodium intake and CVD burden, we assessed the projected CVD events and deaths that could have been prevented in the past 4.3 years and could be prevented in the coming 10 years. In addition, we projected the all-cause deaths that might have been averted and Quality-Adjusted Life Years (QALYs) gained in the past 4.3 years and might continue to be prevented or gained in the following 10 years.

The assessment of health impact was applied in both the primary and complementary analyses based on the projected reductions in population sodium intake (Supplemental Methods). To project the cumulative health impact over the years because of reductions in sodium intake, the estimated changes in sodium intake per day under different scenarios were multiplied by the estimated annual health benefits resulting from every 1000 mg reduction in daily sodium intake for each outcome (Table S1)[10,12,33–38] and then summed up as the cumulative health losses over the years (Figure 2).

Statistical Analyses

To account for the unequal probability of sampling across demographic groups, the mean baseline sodium intake was calculated using survey weights (base probabilities of selection with nonresponse and post-stratification adjustments created by the National Center for Health Statistics) to match the population reported from the Census Bureau. The 95% CIs were calculated for the lower and higher estimates of each health outcome. All analyses were carried out using R v4.0.0 software.

RESULTS

Projected Health Benefits of Implementing the Finalized Targets From October 2021 to October 2031

The characteristics of the study population are shown in Table S2.[20,39] We first projected the health benefits in the following 10 years given that the FDA finalized short-term (2.5 year) targets in October 2021 and are expected to be achieved by April 2024, by which time we assumed a long-term (10 year) guidance would be finalized and expected to be achieved by October 2031 (Finalized Targets) (Tables 1 and 2). Under the Full Compliance scenario, the average population sodium intake is projected to decline to 2318 mg/d, which we project would result in 642 945 (95% CI of the low estimate: 506 125–779 765) to 1 047 082 (95% CI of the high estimate: 823 850–1 270 314) fewer major CVD events, 161 757 (72 459–250 544) to 416 384 (16 329–735 304) fewer major CVD deaths, and 249 014 (150 020–348 007) to 445 979 (17 349–787 352) fewer total deaths as well as 1 375 902 (1 059 059–1 692 746) to 2 204 383 (1 678 711–2 730 055) gained QALYs, by October 2031.

Even with the Minimal Compliance, we estimate that lower sodium intake would prevent 217 418 to 354 081 major CVD events, 54 699 to 140 804 major CVD deaths, and 84 206 to 150 812 total deaths, as well as gain 465 274 to 745 433 QALYs, by 2031 (see confidence intervals for both low and high estimates in Tables 1 and 2).

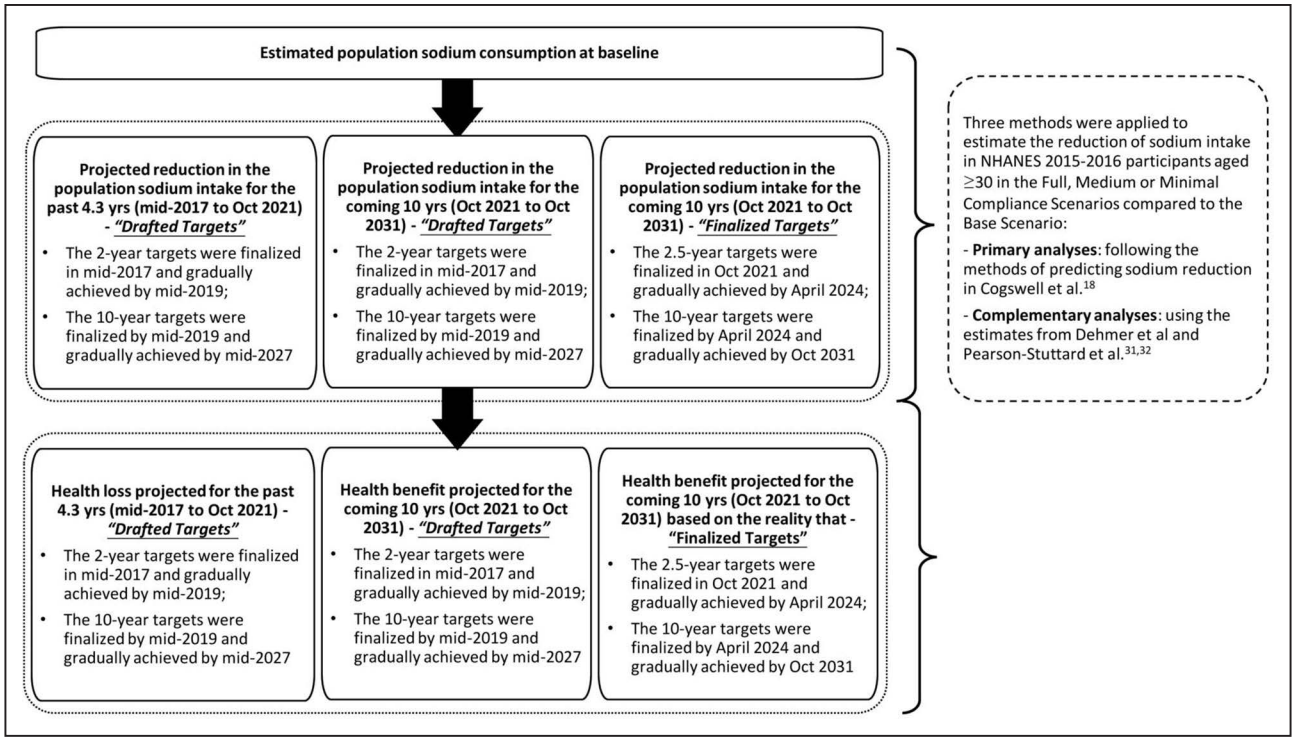

Figure 2. Flow chart of the analyses in the study.
CHD indicates coronary heart disease; NHANES, National Health and Nutrition Examination Survey.

Projected Health Losses Supposing That the Drafted Targets Would Be Implemented From Mid-2017 to Mid-2027

Tables S3 and S4 show the projected health losses that could have been saved in the past 4.3 years and could continue to be saved in the coming 10 years, if the 2-year targets had been implemented in mid-2017 and the 10-year targets had been finalized by mid-2019 (Drafted Targets). Under the Full Compliance scenario, the average population sodium intake could have decreased to 2809 mg/day by October 2021 and would continue to decline to 2318 mg/day by 2027.[40] As a result, 164 035 to 267 143 major CVD events, 41 269 to 106 232 major CVD deaths, and 63 531 to 113 783 total deaths were projected to have been saved, as well as 351 035 to 562 406 QALYs gained, by October 2021. In the coming 10 years, 860 433 to 1 401 276 more major CVD events, 216 474 to 557 233 more major CVD deaths, and 333 247 to 596 840 more total deaths are projected to be prevented, and 1 841 327 to 2 950 056 additional QALYs could be gained. In total, over the 14.3 years, 1 024 468 to 1 668 419 major CVD events, 257 743 to 663 465 major CVD deaths, and 396 778 to 710 623 total deaths could be prevented, and 2 192 362 to 3 512 462 QALYs could be gained (see confidence intervals for both low and high estimates in Table S3 and S4).

Note that under the Minimal Compliance scenario, population sodium intake was projected to have declined only slightly to 3213 mg/day in the past 4.3 years and then continue at that level into the future. Even then, 67 693 to 110 243 major CVD events, 17 030 to 43 839 major CVD deaths, and 26 218 to 46 955 total deaths were projected to have been prevented, and 144 863 to 232 091 QALYs could have been gained in the past 4.3 years. By October 2031, we estimated that an additional 176 591 to 287 591 more major CVD events, 44 428 to 114 364 more major CVD deaths, and 68 394 to 122 493 more total deaths might be prevented, and 377 905 to 605 455 QALYs might continue to be gained. In total, over the 14.3 years, 244 284 to 397 834 major CVD events, 61 458 to 158 203 major CVD deaths, and 94 612 to 169 448 total deaths could be prevented, and 522 768 to 837 546 QALYs could be gained if the FDA had implemented the Drafted Targets from mid-2017 to mid-2031 (see confidence intervals for both low and high estimates in Tables S3 and S4).

In the complementary analyses, the estimated reduction in population sodium intake and health impact of the Drafted Targets were similar to those in the primary analyses (Tables S5 through S8).[33,34]

Net Health Losses From Mid-2017 to October 2031 Because of FDA's 4.3-Year Delay

The net number of unnecessary deaths because of FDA's delay in finalizing the proposed targets would be projected as 147 764 to 264 644 from mid-2017 to October 2031 under the Full Compliance scenario. Even under the Minimal Compliance scenario, a total of 10 406 to 18 636 deaths are estimated to be attributed to the delay (see confidence intervals for both low

Table 1. CVD Events Projected to Be Prevented and QALYs to Be Gained in the Coming 10 y (October 2021 to October 2031), Considering That the FDA Finalized 2.5-y Targets in October 2021, and if it Finalized the 10-y Targets by April 2024 (Following Cogswell's Method of Predicting Sodium Reduction)

Scenario	Projected sodium consumption by 2031 (mg/d)	Projected sodium reduction by 2031 (mg/d)	Preventable incident CHDs (95% CI)		Preventable incident strokes (95% CI)		Preventable incident major CVDs (CHDs+strokes) (95% CI)		Gained QALYs (95% CI)	
			Low estimate (based on a meta-analysis of RCT+CHD policy model)*	High estimate (based on 2 high-quality RCTs+CHD policy model)*	Low estimate (based on a meta-analysis of RCT+CHD policy model)*	High estimate (based on 2 high-quality RCTs+CHD policy model)†	Low estimate (based on a meta-analysis of RCT+CHD policy model)†	High estimate (based on 2 high-quality RCTs+CHD policys model)†	Low estimate (based on a meta-analysis of RCT+CHD policy model)*	High estimate (based on 2 high-quality RCTs+CHD policy model)†
Full compliance	2318	1097	404 137 (332 127–476 147)	679 685 (560 868–798 501)	238 808 (173 999–303 617)	367 397 (262 983–471 811)	642 945 (506 125–779 765)	1 047 082 (823 850–1 270 314)	1 375 902 (1 059 059–1 692 746)	2 204 383 (1 678 711–2 730 055)
Medium compliance	2867	548	202 068 (166 064–238 073)	339 842 (280 434–399 250)	119 404 (87 000–151 808)	183 699 (131 491–235 906)	321 472 (253 062–389 882)	523 541 (411 927–635 155)	687 951 (529 529–846 373)	1 102 191 (839 355–1 365 027)
Minimal compliance	3145	270	136 663 (112 312–161 013)	229 842 (189 663–270 021)	80 755 (58 839–102 671)	124 239 (88 930–159 547)	217 418 (171 152–263 684)	354 081 (278 594–429 568)	465 274 (358 131–572 418)	745 433 (567 672–923 194)

The estimates of incident CHD, stroke, major CVD, and QALYs were calculated based on Bibbins-Domingo et al. CVD indicates cardiovascular disease; CHD, coronary heart disease; FDA, Food and Drug Administration; QALY, quality-adjusted life year; and RCT, randomized controlled trial.

*The modeling study used the dose-response effect of salt reduction on systolic blood pressure summarized in a large meta-analysis and then applied the projected reduction in systolic blood pressure in the CHD Policy Model, to model the low estimate of prevented incidence and QALYs.

†This study also used the dose-response relation between salt reduction and systolic blood pressure observed in 2 high-quality clinical trials and then applied the projected reduction in systolic blood pressure in the CHD Policy Model, to model the high estimates of prevented incidence and QALYs.

and high estimates in Table 4). The net numbers of CVD events and deaths, and QALYs because of the FDA's 4.3-year delay were shown in Tables 3 and 4.

DISCUSSION

In this study, we projected that up to 446 000 lives might be saved in the coming 10 years now that the FDA finalized the short-term targets (2.5 year) in October 2021 that are expected to be gradually achieved by April 2024, as well as the 10-year targets that finalized by April 2024 and gradually achieved by October 2031. However, because of FDA's 4.3-year delay in finalizing the short-term targets, the net losses of lives between 2017 and 2031 is projected to be as high as 265 000. The majority of attributable deaths are because of the CVD burden related to excessive sodium intake from packaged and prepared foods.

The US government, several public health organizations, and some food companies have made numerous efforts to reduce sodium intake since the 1980s, including mandatory sodium content labeling on packaged foods, public education initiatives to reduce sodium intake, population sodium intake recommendations, and voluntary reductions.[40] However, sodium intake has not declined over the past 30 years,[41,42] indicating that the previous efforts were inadequate.[19] Previous evidence showed that downstream interventions directed at consumers, such as education programs, are much less effective than upstream interventions at the manufacturer/restaurant level, such as gradual, unobtrusive reformulation to reduce sodium content in foods, which do not require behavior change on the part of consumers.[43] Multifaceted strategies including both downstream and upstream measures are considered to be much more powerful than single interventions because of potential synergistic effects and thus are needed to increase the effectiveness of sodium-reduction efforts and reduce the health burden caused by excessive sodium intake.[44,45]

In 2009, a national coalition led by the New York City health department and supported by >100 health organizations and health authorities launched the National Salt Reduction Initiative in the United States. National Salt Reduction Initiative which was modeled after the UK's successful salt-reduction program, established stepwise voluntary sodium reductions for 2012 and 2014 for >80 packaged and restaurant food categories.[24,46] The targets aimed to reduce sodium by 25% in packaged and prepared foods and reduce the population sodium intake by 20% by 2014.[30] However, only a small number of companies made public commitments to meet the National Salt Reduction Initiative targets, and the observed sodium content of the food supply by 2014 was far from meeting the targets. However, National Salt Reduction Initiative's development of targets served as a model for the FDA.

In 2016, the FDA released a draft guidance with voluntary short-term (2-year) and long-term (10-year) targets for sodium content in >150 categories of packaged and prepared foods. The guidance was in response to both the 2010 Institute of Medicine report on strategies for reducing sodium in the US food supply (including mandatory limits) and a lawsuit by the Center for Science in the Public Interest.[25,47,48] The targeted food categories

Table 2. CVD and All-Cause Deaths Projected to Be Prevented in the Coming 10 y (October 2021 to October 2031), Considering That the FDA Finalized 2.5-y Targets in October 2021, and If it Finalized the 10-y Targets by April 2024 (Following Cogswell's Method of Predicting Sodium Reduction)

Scenario	Projected sodium consumption by 2031 (mg/d)	Projected sodium reduction by 2031 (mg/d)	Preventable CHD deaths (95% CI)		Preventable stroke deaths (95% CI)		Preventable major CVD deaths (95% CI)		Preventable all-cause deaths (95% CI)	
			Low estimate (based on 2 meta-analysis of RCT)*	High estimate (based on TOHP)†	Low estimate (based on a meta-analysis of RCT+CHD Policy Model)‡	High estimate (based on TOHP)†	Low estimate§	High estimate§	Low estimate (based on a meta-analysis of RCT+CHD Policy Model)‡	High estimate (based on TOHP)†
Full compliance	2318	1097	134 712 (56 130 – 213 294)	342 394 (13 267 – 604 674)	27 045 (16 329 – 37 250)	73 990 (3062 – 130 630)	161 757 (72 459 – 250 544)	416 384 (16 329 – 735 304)	249 014 (150 020 – 348 007)	445 979 (17 349 – 787 352)
Medium compliance	2867	548	67 356 (28 065 – 106 647)	171 197 (6634 – 302 337)	13 522 (8164 – 18 625)	36 995 (1531 – 65 315)	80 878 (36 229 – 125 272)	208 192 (8165 – 367 652)	124 507 (75 010 – 174 003)	222 990 (8675 – 393 676)
Minimal compliance	3145	270	45 554 (18 981 – 72 128)	115 784 (4486 – 204 476)	9145 (5522 – 12 596)	25 020 (1035 – 44 174)	54 699 (24 503 – 84 724)	140 804 (5521 – 248 650)	84 206 (50 731 – 117 682)	150 812 (5867 – 266 251)

The estimates of CHD, stroke, and all-cause mortality were calculated based on 2 modeling studies and one randomized controlled trial (RCT) nested in Coxson et al. CVD indicates cardiovascular disease; CHD, coronary heart disease; and FDA, Food and Drug Administration.

*The first modeling study used the dose-response effect of salt reduction on systolic blood pressure summarized in a large meta-analysis, and another meta-analysis of RCTs evaluating the association between blood pressure reduction and CHD mortality change in hypertensive persons, to model the low estimate of CHD mortality.

†The high estimates of CVD deaths and total deaths were derived from an RCT of sodium-reduction interventions in individuals with high-normal diastolic blood pressure (TOHP).

‡The second modeling study used the dose-response effect of salt reduction on systolic blood pressure summarized in a large meta-analysis and then applied the projected reduction in systolic blood pressure in the CHD Policy Model to model the low estimate of stroke mortality.

§The estimates of major CVD deaths were calculated as the sums of CHD and stroke deaths.

Table 3. Net Numbers of CVD Events and QALYs Lost Between Mid-2017 and October 2031 Projected to Be Caused by the FDA's 4.3-y Delay in Finalizing the Proposed Sodium Reduction Targets (Following Cogswell's Method of Predicting Sodium Reduction)

Scenario	Projected sodium consumption by 2031 (mg/d)	Projected sodium reduction by 2031 (mg/d)	Attributable incident CHDs (95% CI)		Attributable incident strokes (95% CI)		Attributable incident major CVDs (CHDs+strokes) (95% CI)		Attributable QALYs (95% CI)	
			Low estimate (based on a meta-analysis of RCT+CHD policy model)*	High estimate (based on 2 high-quality RCTs+CHD policy model)*	Low estimate (based on a meta-analysis of RCT+CHD policy model)*	High estimate (based on 2 high-quality RCTs+CHD policy model)†	Low estimate (based on a meta-analysis of RCT+CHD policy model)†	High estimate (based on 2 high-quality RCTs +CHD policy model)†	Low estimate (based on a meta-analysis of RCT +CHD policy model)*	High estimate (based on 2 high-quality RCTs +CHD policy model)†
Full compliance	2318	1097	239 814 (197 084 – 282 545)	403 324 (332 819 – 473 830)	141 709 (103 251 – 180 166)	218 013 (156 054 – 279 973)	381 523 (300 336 – 462 710)	621 337 (488 874 – 753 800)	816 460 (628 445 – 1 004 473)	1 308 079 (996 146 – 1 620 012)
Medium compliance	2867	548	119 908 (98 541 – 141 273)	201 663 (166 410 – 236 915)	70 854 (51 625 – 90 084)	109 006 (78 027 – 139 986)	190 762 (150 169 – 231 355)	310 669 (244 437 – 376 901)	408 230 (314 223 – 502 237)	654 040 (498 073 – 810 006)
Minimal compliance	3213	202	16 887 (13 878 – 19 897)	28 401 (23 437 – 33 366)	9979 (7271 – 12 687)	15 352 (10 989 – 19 716)	26 866 (21 149 – 32 583)	43 753 (34 423 – 53 083)	57 494 (44 254 – 70 734)	92 113 (70 147 – 114 079)

The estimates of incident CHD, stroke, major CVD, and QALYs were calculated based on Bibbins-Domingo et al.CVD indicates cardiovascular disease; CHD, coronary heart disease; FDA, Food and Drug Administration; QALY, quality-adjusted life year; and RCT, randomized controlled trial.

*The modeling study used the dose-response effect of salt reduction on systolic blood pressure summarized in a large meta-analysis, and then applied the projected reduction in systolic blood pressure in the CHD Policy Model, to model the low estimate of prevented incidence and QALYs.

†This study also used the dose-response relation between salt reduction and systolic blood pressure observed in 2 high-quality clinical trials and then applied the projected reduction in systolic blood pressure in the CHD Policy Model, to model the high estimates of prevented incidence and QALYs.

contribute 90% of total dietary sodium intake, and food safety and technical feasibility were taken into account.[25] The most commonly consumed foods from the top restaurant chains were also included as these foods usually have nationally uniform nutrient levels, have a higher sodium density than food prepared at home, and provide Americans with more than one-third of their sodium intake.[25] The guidance did not make recommendations for specific methods for reducing sodium, allowing industry to reformulate products however they wanted

Table 4. Net Numbers of CVD and All-Cause Deaths Between Mid-2017 and October 2031 Projected to Be Caused by FDA's 4.3-y Delay in Finalizing the Proposed Sodium Reduction Targets (Following Cogswell's Method of Predicting Sodium Reduction)

Scenario	Projected sodium consumption by 2031 (mg/d)	Projected sodium reduction by 2031 (mg/d)	Attributable CHD deaths (95% CI)		Attributable stroke deaths (95% CI)		Attributable major CVD deaths (95% CI)		Attributable all-cause deaths (95% CI)	
			Low estimate (based on 2 meta-analysis of RCT)*	High estimate (based on TOHP)†	Low estimate (based on a meta-analysis of RCT+CHD policy model)‡	High estimate (based on TOHP)†	Low estimate§	High estimate§	Low estimate (based on a meta-analysis of RCT+CHD policy model)‡	High estimate (based on TOHP)†
Full Compliance	2318	1097	79 938 (33 308 – 126 569)	203 176 (7873 – 358 814)	16 048 (9689 – 22 104)	43 905 (1816 – 77 516)	95 986 (42 997 – 148 673)	247 081 (9689 – 436 330)	147 764 (89 023 – 206 507)	264 644 (10 295 – 467 215)
Medium Compliance	2867	548	39 969 (16 654 – 63 285)	101 588 (3936 – 179 407)	8024 (4845 – 11 052)	21 953 (908 – 38 758)	47 993 (21 499 – 74 337)	123 541 (4844 – 218 165)	73 882 (44 511 – 103 254)	132 322 (5147 – 233 607)
Minimal Compliance	3213	202	5629 (2345 – 8912)	14 307 (555 – 25 268)	1130 (682 – 1557)	3092 (128 – 5458)	6759 (3027 – 10 469)	17 399 (683 – 30 726)	10 406 (6269 – 14 542)	18 636 (725 – 32 900)

The estimates of CHD, stroke, and all-cause mortality were calculated based on 2 modeling studies and one randomized controlled trial (RCT) nested in Coxson et al. CVD indicates cardiovascular disease; CHD, coronary heart disease; and FDA, Food and Drug Administration.

*The first modeling study used the dose-response effect of salt reduction on systolic blood pressure summarized in a large meta-analysis, and another meta-analysis of RCTs evaluating the association between blood pressure reduction and CHD mortality change in hypertensive persons, to model the low estimate of CHD mortality.

†The high estimates of CVD deaths and total deaths were derived from an RCT of sodium-reduction interventions in individuals with high-normal diastolic blood pressure (TOHP).

‡The second modeling study used the dose-response effect of salt reduction on systolic blood pressure summarized in a large meta-analysis, and then applied the projected reduction in systolic blood pressure in the CHD Policy Model to model the low estimate of stroke mortality.

§The estimates of major CVD deaths were calculated as the sums of CHD and stroke deaths.

in order not to substantially change flavors, texture, shelf life, and safety. For example, a previous randomized controlled trial suggested that reducing the sodium content of bread (the most important contributor to population sodium intake in many countries, including the United States and United Kingdom) modestly (<25%) in a short time period did not lead to a detectable change in consumers' sense of flavor and liking of the product.[49] There is also evidence suggesting that the judicious use of salt substitutes (eg, potassium-enriched salt) does not substantially change the flavor or deter the consumption of many foods.[50] The proposed sodium-reduction targets were intended to encourage reformulation and thereby help Americans eat healthier diets with the same pleasure by 2031 as before and also meet the sodium intake of <2300 mg/day recommended by the 2020 to 2025 Dietary Guidelines for Americans.

Two previous modeling studies suggested that full achievement of the 10-year sodium targets would reduce the prevalence of hypertension by 22%, prevent about 225 000 to 900 000 CVD events and over 250 000 CVD deaths, and save $20 to 50 billion in 10 years.[33,34] Our study addresses limitations in, and extends, those studies. First, both previous studies focused solely on CVD outcomes, thus neglecting other causes (eg, kidney disease) and possibly understating the total health burden related to sodium intake.[11] Second, one of the previous studies merely evaluated the health benefits of reducing the population sodium intake to the recommended level (2300 mg/day) rather than reducing the sodium content of the food supply as per the guidance (which set targets for many food categories).[32] Additionally, those results may not be indicative of the real-world setting because they assumed that industry would fully comply with the targets.[51,52]

To address these limitations, we estimated not only CVD burden, but also total mortality and QALYs. We also estimated the health losses caused by the FDA's delayed implementation of its targets. Additionally we assessed several different assumptions of the degree of compliance with the voluntary targets by the food industry so as to provide estimates of health losses and benefits closer to the likely real-world outcomes. Furthermore, in consideration of the final 2.5-year sodium-reduction targets released by the FDA in October 2021, we also estimated the health benefits for the coming 10 years if the 2.5-year targets were implemented in October 2021 and achieved to varying extents by April 2024, with the long-term targets finalized by April 2024 and achieved by October 2031 (Finalized Targets). These findings are particularly timely considering that the United States government has not announced a timetable for finalizing the long-term guidance. Indeed, according to our estimation, full industry compliance with the finalized 2.5-year targets would only reduce population sodium intake to 2874 mg/day (data not shown), far short of the recommended 2300 mg/day. Therefore, we recommend that the FDA finalize its long-term targets before the April 2024 (end date of

the 2.5-year targets) so that industry could align its products with them. In addition, FDA should adopt intermediate targets, such as for the 5- and 7.5-year points. The delay or failure to finalize such incremental targets, and for industry to meet those targets, by 2031 will lead to potentially huge health losses.

The limitations of our study include: (1) compared with previous studies utilizing the microsimulation model, our method did not account for the dynamic characteristics of the study population over the years (eg, aging, changes of hypertension status, and body weight), which could modify the blood pressure change in response to sodium reduction.[31–33,53] For example, older people, Black, or hypertensive individuals have greater reductions in blood pressure than the average person given the same sodium reduction. That could result in an underestimate of the health impact to some degree. (2) We estimated the health outcomes using parameters based on the general population instead of the estimates specific to race/ethnicity, hypertension status, and age group. Thus, population heterogeneity was not accounted for. However, the parameters that we used in evaluation equations were derived from the former cycles of NHANES data including participants within the similar age range (≥30 or 35 years old)[33,34]; thus, the distributions of race/ethnicity, hypertension status, and age group were similar to our data source, as were the population average estimates of health effects in response to every unit change of sodium intake. (3) In this study, we mapped the target food categories to the NHANES 2009 to 2010 data first[54] and then applied the percentage of sodium-intake changes to participants in the NHANES 2015 to 2016 cycle, assuming that the sodium levels and the amount consumed of each applicable food category remained unchanged between 2010 and 2016.[19] This method is similar to a validated method applied in a previous study, but the risk of overestimating the reduction in population sodium intake in response to FDA's targets cannot be excluded because of a possible previous decline in the sodium content of some food categories in US supermarkets and restaurants.[55–57] (4) The FDA's delay might lead to more health losses than we projected due to the complexity of the health and marketplace reality. For example, we did not consider the CVD benefits of lower sodium intake independent of the lowered BP for most of our estimates; the additional health benefits of increased potassium intake resulting from the use of potassium-enriched salt substitutes in reformulations or new products[58]; or the increase in the CVD case fatality rate because of the coincidence of FDA's delay in finalizing the sodium targets with the coronavirus disease 2019 (COVID-19) pandemic.[59]

Our study projected the total health losses because of the FDA's delay in finalizing its voluntary sodium targets, based on the assumption that voluntary reformulation of prepackaged processed foods and foods consumed away from home would reduce population sodium intake.[43] However, we were aware that some have questioned whether the voluntary reformulation approach is capable of reducing the population sodium intake to the recommended level.[60] Based on the initial success of the UK's salt-reduction programme, the key to a successful voluntary governmental programme lies with the compliance of the food industry. That could be facilitated in the United States by (1) government and public pressure on companies; (2) a strict and transparent monitoring system with annual reporting of the sodium content in packaged and restaurant foods and regular surveys of 24-hour urinary sodium excretion in a nationally representative sample of the population; (3) mounting a well-funded public education campaign to improve consumers' understanding of the harm from excessive sodium intake and encourage shoppers to switch to lower-sodium foods; (4) providing technical guidance to small companies to help them reduce sodium; and (5) publicly applauding major companies for their progress and criticizing those failing to lower sodium.[51,52,61] (6) Participation of the out-of-home sector (restaurants, cafeterias, etc) in sodium reduction will be essential for accustoming consumers to lower-sodium foods and would help establish a level playing field throughout the food industry. (7) A more effective voluntary programme could be achieved if the FDA established intermediate goals, as suggested above, between the current 2.5- and 10-year goals (eg, at the 5- and 7.5-year points) to promote gradual reductions and to maintain government and industry interest in sodium reduction.[51] All of those actions might maximize industry compliance with the guidance and lead to a substantial, gradual reduction in population sodium intake. FDA should prepare to undertake further actions, such as mandatory limits and front-of-pack labels on foods to indicate excessive sodium content, if industry does not respond adequately to the voluntary programme. At this stage, however, the top priority should be to finalize and implement further stepwise voluntary sodium guidelines and reformulations considering the complexity of obtaining new laws or regulations.[60]

Perspectives

The FDA proposed voluntary 2- and 10-year sodium-reduction targets in 2016, but only finalized the short-term targets (2.5-year) after a 4.3-year delay in October 2021; it has not yet finalized its more ambitious 10-year targets. We projected that up to 446 000 deaths might be prevented in the coming 10 years, depending on whether the long-term targets will be finalized by April 2024 and to what degree the sodium reduction targets will be achieved. The net number of deaths because of the FDA's 4.3-year delay in finalizing the sodium reduction targets might be as high as 265 000 between 2017 and 2031. These findings indicate that the FDA's delay in the past 4.3 years has imposed and will continue to

impose a huge burden on population health. It would be important for the FDA and all stakeholders to maximize industry compliance with the short-term targets and finalize and encourage industry to implement the long-term targets as soon as possible.

ARTICLE INFORMATION

Received October 1, 2021; accepted December 25, 2021.

Affiliations

Wolfson Institute of Population Health, Barts and The London School of Medicine and Dentistry, Queen Mary University of London, United Kingdom (J.S., M.K.B., G.A.M., F.J.H.). Resolve to Save Lives, An Initiative of Vital Strategies, New York City (L.K.C., N.I.). Consultant, Washington, DC (M.F.J.).

Sources of Funding

None.

Disclosures

J. Song is funded, and G.A. MacGregor and F.J. He are partially funded by the National Institute for Health Research (NIHR) (16/136/77) using UK aid from the UK Government to support global health research. M.F. Jacobson is the co-founder of the Center for Science in the Public Interest (CSPI). G.A. MacGregor is the unpaid Chair of Consensus Action on Salt, Sugar and Health (CASSH) and Blood Pressure UK. F.J. He is an unpaid member of Action on Salt and WASSH. All other authors report no conflicts of interest. The views expressed in this publication are those of the authors and not necessarily those of the NIHR or the UK Department of Health and Social Care, or CSPI.

Supplemental Material

Supplemental Methods
Tables S1–S8
Supplemental References

REFERENCES

1. GBD 2019 Diseases and Injuries Collaborators. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. *Lancet*. 2020;396:1204–1222. doi: 10.1016/S0140-6736(20)30925-9
2. Micha R, Peñalvo JL, Cudhea F, Imamura F, Rehm CD, Mozaffarian D. Association between dietary factors and mortality from heart disease, stroke, and type 2 diabetes in the United States. *JAMA*. 2017;317:912–924. doi: 10.1001/jama.2017.0947
3. Strazzullo P, D'Elia L, Kandala NB, Cappuccio FP. Salt intake, stroke, and cardiovascular disease: meta-analysis of prospective studies. *BMJ*. 2009;339:b4567. doi: 10.1136/bmj.b4567
4. National Academies of Sciences, Engineering, and Medicine. *Dietary Reference Intakes for Sodium and Potassium*. : National Academies Press
5. Mozaffarian D, Fahimi S, Singh GM, Micha R, Khatibzadeh S, Engell RE, Lim S, Danaei G, Ezzati M, Powles J; Global Burden of Diseases Nutrition and Chronic Diseases Expert Group. Global sodium consumption and death from cardiovascular causes. *N Engl J Med*. 2014;371:624–634. doi: 10.1056/NEJMoa1304127
6. Powles J, Fahimi S, Micha R, Khatibzadeh S, Shi P, Ezzati M, Engell RE, Lim SS, Danaei G, Mozaffarian D, Global Burden of Diseases Nutrition and Chronic Diseases Expert Group (NutriCoDE). 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
7. Aburto NJ, Ziolkovska A, Hooper L, Elliott P, Cappuccio FP, Meerpohl JJ. Effect of lower sodium intake on health: systematic review and meta-analyses. *BMJ*. 2013;346:f1326. doi: 10.1136/bmj.f1326
8. Poulter NR, Khaw KT, Hopwood BE, Mugambi M, Peart WS, Rose G, Sever PS. The Kenyan Luo migration study: observations on the initiation of a rise in blood pressure. *BMJ*. 1990;300:967–972. doi: 10.1136/bmj.300.6730.967
9. Denton D, Weisinger R, Mundy NI, Wickings EJ, Dixson A, Moisson P, Pingard AM, Shade R, Carey D, Ardaillou R. The effect of increased salt intake on blood pressure of chimpanzees. *Nat Med*. 1995;1:1009–1016. doi: 10.1038/nm1095-1009
10. He FJ, MacGregor GA. Effect of longer-term modest salt reduction on blood pressure. *Cochrane Database Syst Rev*. 2004:CD004937. doi: 10.1002/14651858.CD004937.pub2
11. He FJ, MacGregor GA. Reducing population salt intake worldwide: from evidence to implementation. *Prog Cardiovasc Dis*. 2010;52:363–382. doi: 10.1016/j.pcad.2009.12.006
12. Cook NR, Cutler JA, Obarzanek E, Buring JE, Rexrode KM, Kumanyika SK, Appel LJ, Whelton PK. Long term effects of dietary sodium reduction on cardiovascular disease outcomes: observational follow-up of the trials of hypertension prevention (TOHP). *BMJ*. 2007;334:885–888. doi: 10.1136/bmj.39147.604896.55
13. Newberry SJ, Chung M, Anderson CAM, Chen C, Fu Z, Tang A, Zhao N, Booth M, Marks J, Hollands S, et al. *Sodium and Potassium Intake: Effects on Chronic Disease Outcomes and Risks. Comparative Effectiveness Review No. 206*. Agency for Healthcare Research and Quality. 2018. doi: 10.23970/AHRQEPCCER206.
14. Mente A, O'Donnell M, Rangarajan S, Dagenais G, Lear S, McQueen M, Diaz R, Avezum A, Lopez-Jaramillo P, Lanas F, et al; PURE, EPIDREAM and ONTARGET/TRANSCEND Investigators. Associations of urinary sodium excretion with cardiovascular events in individuals with and without hypertension: a pooled analysis of data from four studies. *Lancet*. 2016;388:465–475. doi: 10.1016/S0140-6736(16)30467-6
15. Graudal N, Jürgens G, Baslund B, Alderman MH. Compared with usual sodium intake, low- and excessive-sodium diets are associated with increased mortality: a meta-analysis. *Am J Hypertens*. 2014;27:1129–1137. doi: 10.1093/ajh/hpu028
16. He FJ, Campbell NRC, Ma Y, MacGregor GA, Cogswell ME, Cook NR. Errors in estimating usual sodium intake by the Kawasaki formula alter its relationship with mortality: implications for public health. *Int J Epidemiol*. 2018;47:1784–1795. doi: 10.1093/ije/dyy114
17. He FJ, Ma Y, Campbell NRC, MacGregor GA, Cogswell ME, Cook NR. Formulas to estimate dietary sodium intake from spot urine alter sodium-mortality relationship. *Hypertension*. 2019;74:572–580. doi: 10.1161/HYPERTENSIONAHA.119.13117
18. Cogswell ME, Zhang Z, Carriquiry AL, Gunn JP, Kuklina EV, Saydah SH, Yang Q, Moshfegh AJ. Sodium and potassium intakes among US adults: NHANES 2003-2008. *Am J Clin Nutr*. 2012;96:647–657. doi: 10.3945/ajcn.112.034413
19. Clarke LS, Overwyk K, Bates M, Park S, Gillespie C, Cogswell ME. Temporal trends in dietary sodium intake among adults aged ≥19 Years - United States, 2003-2016. *MMWR Morb Mortal Wkly Rep*. 2021;70:1478–1482. doi: 10.15585/mmwr.mm7042a4
20. US Department of Agriculture, Department of Health and Human Services. Dietary Guidelines for Americans, 2020-2025 (9th Edition). https://www.dietaryguidelines.gov/sites/default/files/2020-12/Dietary_Guidelines_for_Americans_2020-2025.pdf. Published 2020. Accessed Aug 9, 2021.
21. Harnack LJ, Cogswell ME, Shikany JM, Gardner CD, Gillespie C, Loria CM, Zhou X, Yuan K, Steffen LM. Sources of sodium in US adults from 3 geographic regions. *Circulation*. 2017;135:1775–1783. doi: 10.1161/CIRCULATIONAHA.116.024446
22. Charlton KE, Corso B, Ware L, Schutte AE, Wepener L, Minicuci N, Naidoo N, Kowal P. Effect of South Africa's interim mandatory salt reduction programme on urinary sodium excretion and blood pressure. *Prev Med Rep*. 2021;23:101469. doi: 10.1016/j.pmedr.2021.101469
23. Public Health England. NDNS: assessment of dietary sodium in adults in England, 2014. https://www.gov.uk/government/statistics/national-diet-and-nutrition-survey-assessment-of-dietary-sodium-in-adults-in-england-2014. Published 2012. Accessed October 21, 2021.
24. National Institute for Health and Care Excellence. Cardiovascular disease Prevention - Public health guideline. https://www.nice.org.uk/guidance/ph25/resources/cardiovascular-disease-prevention-pdf-1996238687173. Published 2010. Accessed October 21, 2021.
25. US Department of Health and Human Services, Food and Drug Administration, and Center for Food Safety and Applied Nutrition. Voluntary sodium reduction goals: target mean and upper bound concentrations for sodium in commercially processed, packaged, and prepared foods: guidance for industry. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/draft-guidance-industry-target-mean-and-upper-bound-concentrations-sodium-commercially-processed. Published 2016. Accessed August 9, 2021.

26. US Food and Drug Administration. Guidance for Industry: Voluntary Sodium Reduction Goals. https://www.fda.gov/regulatory-information/search-fda-guidance-documents/guidance-industry-voluntary-sodium-reduction-goals. Published 2021. Accessed October 21, 2021.
27. US Centers for Disease Control and Prevention National Center for Health Statistics. NHANES 2015-2016 Overview. https://wwwn.cdc.gov/nchs/nhanes/continuousnhanes/default.aspx?BeginYear=2015. Accessed August 9, 2021.
28. Capewell S, O'Flaherty M. Can dietary changes rapidly decrease cardiovascular mortality rates? *Eur Heart J*. 2011;32:1187–1189. doi: 10.1093/eurheartj/ehr049
29. Cobiac LJ, Vos T, Veerman JL. Cost-effectiveness of interventions to reduce dietary salt intake. *Heart*. 2010;96:1920–1925. doi: 10.1136/hrt.2010.199240
30. Cogswell ME, Patel SM, Yuan K, Gillespie C, Juan W, Curtis CJ, Vigneault M, Clapp J, Roach P, Moshfegh A, et al. Modeled changes in US sodium intake from reducing sodium concentrations of commercially processed and prepared foods to meet voluntary standards established in North America: NHANES. *Am J Clin Nutr*. 2017;106:530–540. doi: 10.3945/ajcn.116.145623
31. Pearson-Stuttard J, Kypridemos C, Collins B, Mozaffarian D, Huang Y, Bandosz P, Capewell S, Whitsel L, Wilde P, O'Flaherty M, et al. Estimating the health and economic effects of the proposed US Food and Drug Administration voluntary sodium reformulation: microsimulation cost-effectiveness analysis. *PLoS Med*. 2018;15:e1002551. doi: 10.1371/journal.pmed.1002551
32. Dehmer SP, Cogswell ME, Ritchey MD, Hong Y, Maciosek MV, LaFrance AB, Roy K. Health and budgetary impact of achieving 10-year u.s. sodium reduction targets. *Am J Prev Med*. 2020;59:211–218. doi: 10.1016/j.amepre.2020.03.010
33. Bibbins-Domingo K, Chertow GM, Coxson PG, Moran A, Lightwood JM, Pletcher MJ, Goldman L. Projected effect of dietary salt reductions on future cardiovascular disease. *N Engl J Med*. 2010;362:590–599. doi: 10.1056/NEJMoa0907355
34. Coxson PG, Cook NR, Joffres M, Hong Y, Orenstein D, Schmidt SM, Bibbins-Domingo K. Mortality benefits from US population-wide reduction in sodium consumption: projections from 3 modeling approaches. *Hypertension*. 2013;61:564–570. doi: 10.1161/HYPERTENSIONAHA.111.201293
35. Sacks FM, Svetkey LP, Vollmer WM, Appel LJ, Bray GA, Harsha D, Obarzanek E, Conlin PR, Miller ER 3rd, Simons-Morton DG, et al; DASH-Sodium Collaborative Research Group. Effects on blood pressure of reduced dietary sodium and the dietary approaches to stop hypertension (DASH) diet. DASH-Sodium Collaborative Research Group. *N Engl J Med*. 2001;344:3–10. doi: 10.1056/NEJM200101043440101
36. MacGregor GA, Markandu ND, Sagnella GA, Singer DR, Cappuccio FP. Double-blind study of three sodium intakes and long-term effects of sodium restriction in essential hypertension. *Lancet*. 1989;2:1244–1247. doi: 10.1016/s0140-6736(89)91852-7
37. Psaty BM, Lumley T, Furberg CD, Schellenbaum G, Pahor M, Alderman MH, Weiss NS. Health outcomes associated with various antihypertensive therapies used as first-line agents: a network meta-analysis. *JAMA*. 2003;289:2534–2544. doi: 10.1001/jama.289.19.2534
38. Weinstein MC, Coxson PG, Williams LW, Pass TM, Stason WB, Goldman L. Forecasting coronary heart disease incidence, mortality, and cost: the Coronary Heart Disease Policy Model. *Am J Public Health*. 1987;77:1417–1426. doi: 10.2105/ajph.77.11.1417
39. Veldheer S, Yingst J, Zhu J, Foulds J. Ten-year weight gain in smokers who quit, smokers who continued smoking and never smokers in the United States, NHANES 2003-2012. *Int J Obes (Lond)*. 2015;39:1727–1732. doi: 10.1038/ijo.2015.127
40. US Department of Health and Human Services, Food and Drug Administration. Approaches to reducing sodium consumption; establishment of dockets: request for comments, data, and information. https://www.federalregister.gov/documents/2011/11/30/2011-30865/approaches-to-reducing-sodium-consumption-establishment-of-dockets-request-for-comments-data-and. Published 2011. Accessed August 9, 2021.
41. Brouillard AM, Kraja AT, Rich MW. Trends in dietary sodium intake in the United States and the impact of USDA guidelines: NHANES 1999-2016. *Am J Med*. 2019;132:1199–1206 e5. doi: 10.1016/j.amjmed.2019.04.040
42. Pfeiffer CM, Hughes JP, Cogswell ME, Burt VL, Lacher DA, Lavoie DJ, Rabinowitz DJ, Johnson CL, Pirkle JL. Urine sodium excretion increased slightly among U.S. adults between 1988 and 2010. *J Nutr*. 2014;144:698–705. doi: 10.3945/jn.113.187914
43. Hyseni L, Elliot-Green A, Lloyd-Williams F, Kypridemos C, O'Flaherty M, McGill R, Orton L, Bromley H, Cappuccio FP, Capewell S. Systematic review of dietary salt reduction policies: evidence for an effectiveness hierarchy? *PLoS One*. 2017;12:e0177535. doi: 10.1371/journal.pone.0177535
44. Webb M, Fahimi S, Singh GM, Khatibzadeh S, Micha R, Powles J, Mozaffarian D. Cost effectiveness of a government supported policy strategy to decrease sodium intake: global analysis across 183 nations. *BMJ*. 2017;356:i6699. doi: 10.1136/bmj.i6699
45. Barberio AM, Sumar N, Trieu K, Lorenzetti DL, Tarasuk V, Webster J, Campbell NRC, McLaren L. Population-level interventions in government jurisdictions for dietary sodium reduction: a cochrane review. *Int J Epidemiol*. 2017;46:1551–1405. doi: 10.1093/ije/dyw361
46. Curtis CJ, Clapp J, Niederman SA, Ng SW, Angell SY. US food industry progress during the national salt reduction initiative: 2009-2014. *Am J Public Health*. 2016;106:1815–1819. doi: 10.2105/AJPH.2016.303397
47. Center for Science in the Public Interest. FDA Sued for its Failure to Regulate Salt. https://cspinet.org/news/fda-sued-its-failure-regulate-salt-20151008. Published 2015. Accessed September 27, 2021.
48. Boon CS, Taylor CL, Henney JE (eds). *Strategies to Reduce Sodium Intake in the United States*. National Academies Press.
49. Girgis S, Neal B, Prescott J, Prendergast J, Dumbrell S, Turner C, Woodward M. A one-quarter reduction in the salt content of bread can be made without detection. *Eur J Clin Nutr*. 2003;57:616–620. doi: 10.1038/sj.ejcn.1601583
50. NuTek Food Science. Re: Docket No. FDA-2014-D-0055 for "Voluntary Sodium Reduction Goals: Target Mean and Upper Bound Concentrations for Sodium in Commercially Processed, Packaged, and Prepared Foods," 81 F.R. 35363. Published 2016. https://www.regulations.gov/comment/FDA-2014-D-0055-0521. Accessed October 21, 2021.
51. He FJ, Brinsden HC, MacGregor GA. Salt reduction in the United Kingdom: a successful experiment in public health. *J Hum Hypertens*. 2014;28:345–352. doi: 10.1038/jhh.2013.105
52. MacGregor GA, He FJ, Pombo-Rodrigues S. Food and the responsibility deal: how the salt reduction strategy was derailed. *BMJ*. 2015;350:h1936. doi: 10.1136/bmj.h1936
53. Huang L, Trieu K, Yoshimura S, Neal B, Woodward M, Campbell NRC, Li Q, Lackland DT, Leung AA, Anderson CAM, et al. Effect of dose and duration of reduction in dietary sodium on blood pressure levels: systematic review and meta-analysis of randomised trials. *BMJ*. 2020;368:m315. doi: 10.1136/bmj.m315
54. US Food and Drug Administration. FNDDS Mapping File Request 082516. https://www.regulations.gov/document/FDA-2014-D-0055-0410. Published 2016. Accessed August 9, 2021.
55. Muth MK, Karns SA, Mancino L, Todd JE. How much can product reformulation improve diet quality in households with children and adolescents? *Nutrients*. 2019;11:E618. doi: 10.3390/nu11030618
56. Poti JM, Dunford EK, Popkin BM. Sodium reduction in US households' packaged food and beverage purchases, 2000 to 2014. *JAMA Intern Med*. 2017;177:986–994. doi: 10.1001/jamainternmed.2017.1407
57. Wolfson JA, Moran AJ, Jarlenski MP, Bleich SN. Trends in sodium content of menu items in large chain restaurants in the U.S. *Am J Prev Med*. 2018;54:28–36. doi: 10.1016/j.amepre.2017.08.018
58. Neal B, Tian M, Li N, Elliott P, Yan LL, Labarthe DR, Huang L, Yin X, Hao Z, Stepien S, et al. Rationale, design, and baseline characteristics of the Salt Substitute and Stroke Study (SSaSS)-A large-scale cluster randomized controlled trial. *Am Heart J*. 2017;188:109–117. doi: 10.1016/j.ahj.2017.02.033
59. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, Xiang J, Wang Y, Song B, Gu X, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. *Lancet*. 2020;395:1054–1062. doi: 10.1016/S0140-6736(20)30566-3
60. Kurtz TW, Pravenec M, Dicarlo SE. Strategies are needed to prevent salt-induced hypertension that do not depend on reducing salt intake. *Am J Hypertens*. 2020;33:116–118. doi: 10.1093/ajh/hpz173
61. Collins B, Kypridemos C, Pearson-Stuttard J, Huang Y, Bandosz P, Wilde P, Kersh R, Capewell S, Mozaffarian D, Whitsel LP, et al; Food-PRICE Investigators. FDA sodium reduction targets and the food industry: are there incentives to reformulate? Microsimulation cost-effectiveness analysis. *Milbank Q*. 2019;97:858–880. doi: 10.1111/1468-0009.12402