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REVIEW

Proceedings from the workshop on estimating the contributions of sodium reduction to preventable death

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Summary
The primary goal of this workshop was to identify the most appropriate method to estimate the potential effect of reduction in sodium consumption on mortality. Difficulty controlling hypertension at the individual level has motivated international, federal, state, and local efforts to identify and implement population-wide strategies to better control this problem; reduction of sodium intake is one such strategy. Published estimates of the impact of sodium consumption on mortality have used different modeling approaches, effect sizes, and levels of sodium

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consumption, and thus their estimates of preventable deaths averted vary widely, and are not comparable. In response to this problem, the Centers for Disease Control and Prevention's Division for Heart Disease and Stroke Prevention (DHDSP) convened and facilitated a workshop to examine different methods of estimating the effect of sodium reduction on mortality. The panelists agreed that any of the methodologies presented could provide reasonable estimates, and therefore discussion focused on challenges faced by all methods. The panel concluded that future sodium modeling efforts should generate multiple estimates employing the same scenarios and effect sizes while using different modeling techniques; in addition, future efforts should include outcomes other than mortality (morbidity, costs, and quality of life). Varying reductions in sodium should be modeled at the population level over different time intervals. In an effort to better address some of the uncertainties highlighted by this workshop, the panelists are currently considering developing multiple estimates in a collaborative manner to clarify the potential impact of population-based interventions to reduce sodium consumption.

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Introduction

In the United States, high blood pressure affects approximately one-third of the adult population and is a major risk factor for cardiovascular mortality [1,2]. According to data from the National Health and Nutrition Examination Survey (NHANES) 2003—2006, over half of all American adults with hypertension did not have it under control [1]. Difficulty controlling hypertension at the individual level has motivated international, federal, state, and local efforts to identify and implement population-wide strategies to better control this problem.

Reduction of sodium intake is one such strategy, and several published articles have estimated changes in blood pressure and annual change in mortality using alternative levels of sodium intake across the population [3—5]. All the estimates showed an impact on mortality. However, they used different modeling approaches, effect sizes, and levels of sodium consumption, and thus their estimates of preventable deaths averted vary widely (Table 1) and are not comparable. The differences among these estimates have made it difficult to precisely determine the potential impact of population-based interventions to reduce sodium intake. In response to this problem, the Centers for Disease Control and Prevention's Division for Heart Disease and Stroke Prevention (DHDSP) convened and facilitated a workshop, *Estimating the Contributions of Sodium Reduction to Preventable Death*, in Atlanta, Georgia on February 24—25, 2010, to examine different methods of estimating the effect of sodium reduction on mortality. The intent was to identify models to compute a more precise estimate in order to strengthen and support policy recommendations for population-wide sodium reduction.

The primary goal of this workshop was to identify the most appropriate method to estimate the potential effect of reduction in sodium consumption on mortality. The DHDSP invited external panelists (Table 2) with expertise in modeling methodology and/or in determining the effects of reduced sodium on blood pressure and mortality to participate in the workshop. The workshop began with a brief presentation by Dr. Majid Ezzati on the methodology used in a recently published estimate of mortality attributable to excess sodium consumption [4]. This presentation served as a starting point to stimulate group discussion and debate over alternative modeling approaches, model assumptions, and choice of effect sizes. During the day-and-a-half workshop, panelists and CDC participants discussed gaps in available methods and data, reviewed the strengths and weaknesses of alternative methods, and assessed strategies to effectively communicate estimates to policy makers and the general public.

Table 1 Published changes in estimated annual mortality from population based sodium reduction.

Study	Change in Sodium	Change in Mortality
Havas et al. [5]	Reduce sodium in processed food by 50%	150,000 fewer deaths per year
Danaei et al. [4]	Reduce individual intake to minimum risk exposure level, 500 mg/day	102,000—194,000 fewer deaths per year[a]
Bibbins-Domingo et al. [3]	Reduce population intake by 1200 mg/day	44,000—92,000 fewer deaths per year[a]

[a] Range based on choice of effect sizes for the effect of sodium change on blood pressure.

Table 2 Panelists in attendance at the CDC workshop on estimating the contributions of sodium reduction to preventable death.

Name	Affiliation
Kirsten Bibbins-Domingo, PhD, MD	University of California, San Francisco
Vicki Burt, ScM, RN	National Center for Health Statistics, CDC
Nancy R. Cook, ScD	Harvard Medical School
Lester R. Curtin, PhD[a,b]	National Center for Health Statistics, CDC
Majid Ezzati, MEng, PhD[b]	Harvard School of Public Health
Johanna M. Geleijnse, MSc, PhD, FAHA	Wageningen University, Netherlands
Jack Homer, PhD	Homer Consulting
Michel Joffres, MD, PhD	Simon Fraser University, Canada
Malcolm Law, MSc, MBBS, FRCP	Queen Mary, University of London, UK
Catherine Loria, PhD, MS, MA, FAHA	National Heart, Lung, and Blood Institute

[a] Participated via teleconference.
[b] Participation limited to the first half of day one.

Modeling methodology

One of the main purposes of the workshop was to identify the modeling methodology that would produce the most realistic estimate of preventable deaths related to a given amount of sodium reduction. Several methods were discussed: (a) the approach used by Danaei and colleagues (including Dr. Ezzati) [4]; (b) the Coronary Heart Disease Policy Model used by Dr. Bibbins-Domingo and associates [3]; (c) the system dynamics approach that was used by Dr. Homer and colleagues in work with the PRevention Impacts Simulation Model (PRISM) [6]; (d) the research of Dr. Cook on the direct effects of sodium [7]; (e) ongoing projects of Dr. Joffres that involve modeling a gradual decrease in sodium consumption over time; and (f) a general discussion by Dr. Curtin about the use of population attributable fractions. The panelists agreed that any of these methodologies could provide reasonable estimates. Therefore, discussion at the workshop focused mostly on the challenges faced by all of the modeling methods, and the individual details of the different methodologies were not discussed.

Perhaps the most important issue raised by the panelists concerned the choice of whether to model the direct effect of sodium reduction on mortality (direct method) or to model the effect of reduced sodium on change in blood pressure and the subsequent effect of a change in blood pressure on change in mortality (two-step method). The two-step approach requires at least two estimates: one for the effect of sodium intake on blood pressure and the other for the effect of blood pressure on mortality. The direct method, in contrast, requires only one estimate, the effect of sodium intake on mortality. Dr. Cook stated that the advantage of the direct method is that there are fewer assumptions to make than in the two-step process, which could lead to more accurate estimates. She also indicated that the direct approach would account for potential deleterious effects of sodium intake on mortality through mechanisms other than blood pressure. All the panelists agreed that the direct method is ideal, but most believed that current data were inadequate to use this method to calculate a nationally representative estimate of change in population mortality due to sodium reduction. Even so, they concluded that estimates from the direct method could provide (a) an interesting comparison with estimates from two-step modeling or (b) validation of the two-step estimates.

Dr. Curtin suggested that the two-step process is a reasonable approach but one that has its own weaknesses; each step introduces cumulative error into the model via the confidence intervals surrounding each of the effect sizes used in each step. The cumulative error needs to be considered during the framing and communication of the estimates, and this will be discussed in more detail below. Panelists agreed that the purpose of modeling, the choices of effect sizes, other assumptions, and plausible scenarios (e.g., a 50% reduction of sodium in processed food over the next 10 years) were more important factors than the specific model used to generate estimates.

Comparison of the purposes of modeling

Dr. Bibbins-Domingo stated that when developing a model it is important to consider what question is being asked: for example, what is the proportion of current mortality attributable to a risk factor, as contrasted with what is the effect of an intervention to eliminate or reduce a risk factor? Dr. Ezzati thought it important to model the impact of very low levels of sodium consumption (500 mg/day) in each individual in the population to estimate the current mortality attributable to excess sodium consumption, which would allow direct comparisons with other risk factors, such as smoking. While this approach would allow us to demonstrate which risk factors are potentially contributing more (and which are contributing less) to the burden of disease, this approach does not demonstrate the potential impact of realistic public health interventions.

In contrast, Dr. Bibbins-Domingo described methods that model a shift in the population's mean intake of sodium, which could represent the impact of a realistic public health intervention. The majority of panelists agreed that what would be most useful currently are models that predict the decrease in mortality based on specific public health interventions to reduce sodium consumption and/or a reduction in sodium consumption across the population consistent with dietary guidelines. The modeling approach should be chosen based on the purpose of developing such estimates. An estimate of total mortality attributable to a risk factor, like that described above by Dr. Ezzati, would likely be larger than estimates based on realistic public health interventions. Although this level of sodium reduction is probably not achievable in the population, the panelists thought that the larger estimate would be more likely to draw public attention to the issue of excessive sodium intake. However, estimates that predict the potential reduction in mortality associated with a realistic public health intervention, one that reduces the population's sodium intake but does not completely eliminate excess consumption, could be more useful to policy makers as they could more easily weigh the costs and benefits of possible interventions.

Selection of effect sizes

Throughout the workshop, panelists agreed that there is no unequivocal effect size that estimates the change in blood pressure from a reduction in sodium consumption (the first step of the two-step approach). Dr. Geleijnse noted that the meta-analyses based on randomized controlled trials (RCTs) are not representative of the total population because the participants from individual studies are selected from specific subpopulations and not from the general population, and normotensives with lower blood pressures are either not represented or are greatly underrepresented. The panelists generally agreed that while there are substantial data from trials involving older, hypertensive, and prehypertensive populations, there are not enough data to determine the effect of sodium reduction in individuals with a blood pressure below 120 mm Hg systolic/80 mm Hg diastolic, or to determine the effect among specific racial and ethnic subpopulations. Furthermore, the RCTs that have been used to compute the effect sizes were conducted over a relatively short time period even in the most recent meta-analysis [8], with interventions lasting a median of 4 weeks. Although the long-term impact of sodium reduction on blood pressure cannot be estimated with available evidence, the panelists agreed that decreased sodium intake should at a minimum reduce or delay the age-related rise in blood pressure. Panelists were in favor of conducting sensitivity analyses with high and low estimates of effect size in order to demonstrate the range in the number of deaths that might be prevented.

Panelists identified the Prospective Studies Collaboration [9] and Framingham risk scores [10,11] as the best resources regarding the adequacy of evidence on the relative risk of mortality attributed to high blood pressure. The panelists noted that using some combination of effect sizes in the two-step approach would provide a realistic range of estimates but could not be used to provide a precise estimate. However, an accurate range would still be useful for policy maker as long as the lower end of the range still included tens of thousands of deaths prevented.

Other assumptions

While adding complexity to two-step models (e.g. stratification by age, sex, race, or blood pressure level or by adjusting for other risk factors) has the potential to add precision to the estimates, it also may produce estimates that are less reliable, as each level of complexity introduces the possibility of more error. Most panelists suggested that, when possible, models should stratify for the distribution of population age, the distribution of starting blood pressure level, race and/or ethnicity, and possibly sex in order to develop a more precise range of the potential effects of sodium reduction on mortality. However, several panelists (Drs. Curtin, Cook, and Joffres) noted that when more strata are added one is essentially adding more individual effect sizes and corresponding confidence intervals, which in turn increase error. Thus the estimates may be less accurate if the additional effect sizes add more error than the additional strata add precision. However, the panelists could not determine whether increased precision or increased error would predominate; therefore, they suggested presenting a range of estimates, accepting compounded error in the two-step approach, rather than trying to calculate a single precise estimate.

Scenarios to model

Dr. Bibbins-Domingo asked, ''What is the best scenario to model?'' Although most panelists agreed that the level of sodium reduction to be modeled should be based on a realistic population-based intervention, opinion varied on what was a realistic level. Therefore, panelists suggested running multiple models with several levels of population sodium intake that could include the recommended amounts in the current dietary guidelines of less than 1500 or 2300 mg/day [12] or on recommendations that may be in the forthcoming Institute of Medicine report, *Strategies to Reduce Sodium Intake in the United States*, which had not been released at the time of this workshop. One other option was to model a reduction of sodium in processed and restaurant food by a given percentage such as 50%; this reduction could be modeled across the population. These scenarios, however, were all weakened by uncertainty about the US population's baseline consumption of sodium because of concerns about the reliability of 24-h dietary recall currently used to estimate sodium consumption in the US CDC staff are currently examining ways to improve sodium surveillance, which would strengthen all estimates.

A second challenge to developing a realistic scenario that was noted by the panelists involved the timing and pace of sodium reductions. Dr. Joffres suggested that estimates based on a gradual reduction in sodium consumption would be more realistic. Many published estimates on the potential impact of sodium reduction assume a single immediate reduction in consumption, but it is very unlikely that food manufacturers and restaurants would lower salt content dramatically all at once. Gradually reducing the sodium content of all foods simultaneously so that consumers did not notice the change in their taste could help to prevent a greater use of salt at the table and could increase acceptability of sodium reductions by food manufacturers. Dr. Joffres discussed several international efforts to reduce sodium intake that are seeking to reduce consumption gradually over a period of 10 years or more. While consumers would likely not notice such a gradual change, Dr. Joffres believed that such efforts may be too slow. Therefore, future estimates should model a gradual reduction over multiple time periods in order to give policy makers several alternatives to consider.

The final issue raised throughout the workshop was the importance of modeling the impact of sodium reduction on outcomes other than mortality. Future models should also include estimates of nonfatal cardiovascular events, quality of life, and costs. The biggest challenge noted was in modeling nonfatal events in the US population. While efforts are under way to improve surveillance, currently it is not possible to accurately estimate the national baseline rate of nonfatal cardiovascular disease events, which would be necessary to estimate the impact of a change in sodium.

Communicating results

Drs. Homer and Loria suggested that to promote policy change it is important to get the attention not only of policy makers but also of the general population, which could be accomplished by providing estimates of the health benefits of consuming less sodium and by highlighting the negative health consequences of excess consumption. The messages based on these types of estimates must be honest, provide meaningful information, and be easy to understand. A theme that emerged was the distinction between lives saved and quality-adjusted life year (QALY) gained; this is because reduction of sodium intake may not save individual lives so much as extend QALY's for many. QALY, which measures both quantity and quality of life lived, is considered a preferred measure of quality of life and has been widely used in cost-effectiveness analysis. To ensure transparency, assumptions and weaknesses should be accurately described. Multiple modeling techniques using the same input scenarios could either provide convergence or produce a larger range of estimates.

Recommendations of the workshop

The complete list of workshop recommendations is in Table 3. Future sodium modeling efforts should generate multiple estimates employing the same scenarios and effect sizes while using different modeling techniques; in addition, future efforts should include outcomes other than mortality (morbidity, costs, and quality of life). Varying reductions in sodium should be modeled at the population level over different time intervals. In an effort to better address some of the uncertainties highlighted by this workshop, the panelists are currently considering developing multiple estimates in a collaborative manner to clarify the potential impact of population-based interventions to reduce sodium consumption.

Table 3 Recommendations for Future Sodium Modeling Efforts.

1. Use multiple modeling techniques with the same input scenarios and effect sizes
2. Include outcomes other than mortality (morbidity, costs, and quality of life)
3. Include estimates from the direct method to provide a comparison with two-step models
4. Conduct sensitivity analyses with high and low effect sizes of the impact of sodium intake on blood pressure
5. Present a range of potential changes in mortality instead of making only a precise estimate
6. Stratify for population age, starting blood pressure level, race and/or ethnicity, and possibly sex
7. Model a gradual reduction of sodium consumption over multiple time periods
8. Accurately describe assumptions and weaknesses relative to the modeling efforts

Additional contributions

Lester R. Curtin, PhD substantively contributed to the findings of the workshop but was unfortunately unable to participate in the writing of the manuscript. Additional CDC staff participating in the workshop were Peter Briss, MD, MPH; Shanta Dube, PhD, MPH; Deborah Galuska, MPH, PhD; David Homa, MPH, PhD; Robert Merritt, MA; Andrea Neiman, MPH, PhD; Janelle Peralez Gunn, MPH; and Cheryl Robbins, MS, PhD. We gratefully acknowledge Christopher Thomas, MS, CHES, for his assistance in planning and organizing the workshop.

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Disclaimer

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Conflicts of interest

None.

References

[1] Lloyd-Jones D, Adams RJ, Brown TM, Carnethon M, Dai S, De Simone G, et al. Heart disease and stroke statistics — 2010 update: a report from the American Heart Association. Circulation 2010;121:e46—e215.
[2] National Center for Health Statistics, Health, United States, 2009: With Special Feature on Medical Technology, Hyattsville, MD; 2010.
[3] Bibbins-Domingo K, Chertow GM, Coxson PG, Moran A, Lightwood JM, Pletcher MJ, et al. Projected effect of dietary salt reductions on future cardiovascular disease. N Engl J Med 2010;362:590—9.
[4] Danaei G, Ding EL, Mozaffarian D, Taylor B, Rehm J, Murray CJL, et al. The preventable causes of death in the United States: comparative risk assessment of dietary, lifestyle, and metabolic risk factors. PLos Med 2009;6:e1000058. doi:10.1371/journal.pmed.1000058.
[5] Havas S, Roccella EJ, Lenfant C. Reducing the public health burden from elevated blood pressure levels in the United States by lowering intake of dietary sodium. Am J Public Health 2005;94:19—22.
[6] Homer J, Milstein B, Wile K, Trogdon J, Huang P, Labarthe D, et al. Simulating and evaluating local interventions to improve cardiovascular health. Prev Chronic Dis 2010;7:A18, http://www.cdc.gov/pcd/issues/2010/jan/08_0231.htm [accessed 0712.10].
[7] Cook NR, Cutler JA, Obarzanek E, Buring JE, Rexrode KM, Kumanyika SK, et al. 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—8.
[8] He FJ, MacGregor GA. Effect of longer-term modest salt reduction on blood pressure. Cochrane Database Syst Rev 2004(1):CD004937. doi:10.1002/14651858.CD004937.
[9] Lewington S, Clarke R, Qizilbash N, Peto R, Collins RProspective Studies Collaboration. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet 2002;360:1903—13.
[10] Anderson KM, Odell PM, Wilson PW, Kannel WB. Cardiovascular disease risk profiles. Am Heart J 1991;121:293—8.
[11] D'Agostino Sr RB, Grundy S, Sullivan LM, Wilson P, CHD Risk Prediction Group. Validation of the Framingham coronary heart disease prediction scores: results of a multiple ethnic groups investigation. JAMA 2001;286:180—7.
[12] US Department of Health and Human Services and US Department of Agriculture, Dietary Guidelines for Americans, 2005. 6th ed. Washington, DC: US Government Printing Office; January 2005. http://www.health.gov/dietaryguidelines/dga2005/document/pdf/dga2005.pdf [accessed 07.12.10].