

Viewpoint

Unnecessary Controversy Regarding Dietary Sodium: A Lot About a Little

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Recently, the *Journal of the American Medical Association (JAMA)* published an article by Stolarz-Skrzypek and colleagues.¹ The cohort study examined 24-hour urinary sodium excretion in relationship to blood pressure, hypertension, and fatal and nonfatal outcomes and concluded low-sodium diets increased cardiovascular disease and should not be recommended on a population basis. The investigative team was strong and indicated a lack of financial conflicts of interest. So what does this mean? In this article we review briefly the evidence supporting the link between higher dietary sodium intake and cardiovascular disease and the smaller body of work purporting that this association is not true, present an abbreviated critique of the study by Stolarz-Skrzypek et al., and add this study to a growing meta-analysis demonstrating that higher sodium intake is associated with worse cardiovascular outcomes.²

Reviews of the extensive body of evidence on health risks of high dietary sodium by respected and independent scientific and public health bodies indicate dietary sodium consumed at current levels represents one of the major risks to wellness in the world.^{3–8} In fact, reducing dietary sodium has been estimated to save very substantive health costs in developed countries^{9,10} and to be even more cost effective than interventions to reduce smoking in middle- to low-income countries.¹¹ The research base for the impact of high sodium intake spans animal and clinical studies and is summarized briefly in Table 1.^{3–8}

In contrast, a few cohort and epidemiologic studies do not confirm the association between high salt intake and hypertension or vascular disease.^{2,4,7} The fact that a few studies do not support the health risks of high sodium intake is not surprising given the limitations of epidemiologic study designs and in particular the difficulty epidemiologic studies have in addressing confounding factors. A study from Cohen et al.,¹² designed similarly to the cohort study by Stolarz-Skrzypek et al.,¹ sug-

gested that high-sodium diets were associated with less vascular disease. Inspection of Cohen's results showed those who eat less sodium tended to be less educated, less active, black, and of smaller body size, all factors also associated with low income and associated with poor outcomes. Even with the design limitation, when the cohort studies that assessed the relationship between dietary sodium and cardiovascular outcomes were put in a landmark meta-analysis by Strazzullo et al.,² increased dietary sodium was associated with increased vascular disease.

The new study by Stolarz-Skrzypek et al.¹ has the limitations of the cohort study by Cohen et al.¹² While the 24-hour collection of urine is the standard for assessing a population's sodium intake, if it is not collected correctly, there is a risk of misclassification. Further, a single 24-hour urine collection is not as accurate as multiple-day collection in classifying an individual's usual sodium intake as there is day-to-day variation in sodium intake.¹³ Of concern, data from Stolarz-Skrzypek et al.'s electronic Table 1 shows that the lowest-sodium group tended to have higher cardiovascular risk factors, including the lowest educational attainment, higher baseline systolic blood pressure, age, and total cholesterol. Further, the study population was young and hence had a low cardiovascular disease event rate, and the statistical power to detect a dietary sodium effect is low. Sodium intake covaries with caloric intake, and the physically active would tend to be in the high-sodium-intake group, as they have been in other studies.¹² The lower-sodium-excretion group (across genders and population samples) also had lower urinary creatinine, potassium, and urinary volumes not explained by differences in body mass, suggesting concurrent illness or an undercollection of the 24-hour urine, rather than consumption of less sodium. The finding in the lower-sodium-excretion group of urinary sodium values of 50 mmol/d (1150 mg/d), levels not found in typical Western populations, is also suggestive of this.^{14–16} Low adherence even to placebo is strongly associated with poor outcomes.^{17,18} A usual finding for lower sodium intakes is higher potassium intake, since the main mechanism for lower dietary sodium intake is the consumption of unprocessed foods, which are higher, not lower, in potassium.¹⁹ Thus the "inverse" association between

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See page 406 for disclosure information.

Table 1. Summary of types of studies detailing the effects of sodium on blood pressure, and major outcomes

Type of study	Details
Animal studies	Demonstrate high sodium intake increases blood pressure and causes adverse vascular outcomes both directly and through increased blood pressure
Migration studies	Show increases in blood pressure in people who migrate from areas of low to high sodium intake
Genetic diseases	Indicate that defects in the ability to retain sodium cause low blood pressure and that defects that lead to sodium retention cause hypertension
Cohort studies	Associate high dietary sodium to vascular disease (meta-analysis)
Randomized controlled trials	Demonstrate low sodium intake decreases blood pressure in newborn babies, children, and adults and reduces hypertension in adults
Limited controlled intervention studies	Show reductions in vascular disease with reduced sodium intake
National intervention studies	Demonstrate that dietary sodium can be reduced and is associated with decreased blood pressure and vascular disease
Arrays of studies on surrogate markers of outcomes	Show that lower sodium intake is associated with: (1) a reduction in intermediate cardiovascular end points such as left ventricular mass and endothelial dysfunction and (2) a reduction in bone mineral density loss, kidney stone disease, and predisposition to gastric cancer

urinary sodium-to-potassium ratio and vascular outcomes is also an unexplained paradox. These are a few of many potential confounders that could explain the paradoxical outcomes.

Regardless of whether the study was confounded, its impact must be assessed in the context of the large numbers of other cohort studies addressing the same question. To this end we updated the meta-analysis of Strazzullo et al.² with data from the new study. The results are shown in Table 2. They continue to indicate that higher sodium intake of approximately 80 mmol/d (1840 mg/d) is associated with a higher incidence of stroke. There also remained a tendency to greater cardiovascular disease event rates, consistent with the known and established pathophysiology of excess dietary sodium in animal and human studies.

In their article, Stolarz-Skrzypek et al.¹ do not sufficiently discuss why their study found unexpected results but extensively discuss the limited evidence that suggests high dietary sodium is not harmful and use conflicted and biased interpretations of the evidence that are heavily promoted by commer-

cial entities associated with profit from the sales of salt and salty foods and that have been repeatedly rebutted in the scientific literature. Several of the studies they cite were performed by investigators with ties to food processors or the Salt Institute, and at least one of the cited studies was funded by the research institute of a food processing company.^{12,20,21} Finally, the authors do not cite the extensive reviews of evidence by highly regarded scientific institutions that indicate high dietary salt is harmful and should be reduced on a population basis. In fact, the large body of evidence accrued over the past 50 years has been thoroughly and repeatedly reviewed by numerous national and international independent panels of experts. The panels of experts include those formed by the World Health Organization,⁶ the US Institute of Medicine,⁷ the Scientific Advisory Committee on Nutrition in England,⁴ as well as the Canadian Hypertension Education Program,^{3,22} to mention a few. Even when the data from Stolarz-Skrzypek et al.'s study are added to the meta-analysis of Strazzullo et al.,² the results are not changed and continue to indicate the harmful cardiovascular effects of a high-dietary-sodium intake. The strong consensus of impartial scientific bodies is that a population reduction in sodium intake from the current high levels is a health priority for the prevention of cardiovascular disease. In our opinion the approach of Stolarz-Skrzypek et al. is misleading, particularly for readers not familiar with the sodium literature, who need to be aware that the present findings are inconsistent with known evidence and are likely related to methodological flaws. Moreover, the interpretation by Stolarz-Skrzypek et al. is contrary to mainstream science.

In conclusion, excess dietary sodium is a leading risk for death and disability. In the United States, high sodium intake is estimated to be the seventh leading risk for death.²³ There is sufficient evidence to intervene to reduce dietary sodium in populations, and Japan and Finland, which have acted, have seen substantive benefits.²⁴ Although the data supporting the risks of high dietary sodium are strong, and based on an extensive array of differing types of studies, it is important that the ultimate study design, a large, long-term, well-conducted randomized controlled trial, has not been performed for dietary sodium or, for that matter, for many other important public health issues, such as for cigarette smoking, weight loss through diet, physical activity, or low saturated fats or trans fats. Although these trials are expensive, difficult to conduct, and unlikely to ever be performed, failure to conduct them should not be used as a distraction in the effort to improve population health. Rather than pursuing the question of *whether* sodium

Table 2. Pooled relative risk estimates of incident strokes and total cardiovascular events associated with 2000-mg difference in sodium intake

Participants	Events	Pooled relative risk (95% confidence interval)	Statistics
Incident strokes (15 trials) 157,963	5,379	Random-effects model: 1.20 (1.03-1.41) Fixed-effects model: 1.14 (1.05-1.24)	$z = 2.49$ $P = 0.026$ $z = 3.46$ $P = 0.003$
Incident total cardiovascular events (13 trials*) 105,677	5,128	Random-effects model: 1.14 (0.99-1.33) Fixed-effects model: 1.08 (1.02-1.15)	$z = 1.96$ $P = 0.07$ $z = 3.11$ $P = 0.009$

* Without outlier, based on sensitivity analysis. See Strazzullo et al.²

intake should be reduced to prevent cardiovascular disease, the health priority is and should remain *how* to reduce population sodium intake to save lives.

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References

1. Stolarz-Skrzypek K, Kuznetsova T, Thijs L, et al. Fatal and nonfatal outcomes, incidence of hypertension, and blood pressure changes in relation to urinary sodium excretion. *JAMA* 2011;305:1777-85.
2. Strazzullo P, D'Elia L, Kandala NB, Cappuccio FP. Salt intake, stroke, and cardiovascular disease: meta-analysis of prospective studies. *BMJ* 2009;339:b4567.
3. Khan NA, Hemmelgarn BR, Padwal R, et al. The 2007 Canadian Hypertension Education Program recommendations for the management of hypertension: part 2: therapy. *Can J Cardiol* 2007;23:539-550.
4. Scientific Advisory Committee on Nutrition. Salt and Health. Norwich, UK: Stationery Office, 2003:1-134.
5. Dickinson BD, Havas S. Reducing the population burden of cardiovascular disease by reducing sodium intake: a report of the Council on Science and Public Health. *Arch Intern Med* 2007;167:1460-8.
6. World Health Organization. Reducing salt intake in populations: report of a WHO forum and technical meeting 5-7 October 2006, Paris, France. Geneva, Switzerland: World Health Organization, 2007:1-65.
7. Panel on Dietary Reference Intakes for Electrolytes and Water, Standing Committee on the Scientific Evaluation of Dietary Reference Intakes. Dietary reference intakes for water, potassium, sodium, chloride and sulfate. Washington, DC: National Academies Press, 2004:1-640.
8. Appel LJ, Frohlich ED, Hall JE, et al. The importance of population-wide sodium reduction as a means to prevent cardiovascular disease and stroke: a call to action from the American Heart Association. *Circulation* 2011;123:1138-43.
9. Bibbins-Domingo K, Chertow GM, Coxson PG, et al. Projected effect of dietary salt reductions on future cardiovascular disease. *N Engl J Med* 2010;362:590-9.
10. Joffres M, Campbell NRC, Manns B, Tu K. Estimate of the benefits of a population-based reduction in dietary sodium additives on hypertension and its related health care costs in Canada. *Can J Cardiol* 2007;23:437-43.
11. 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;370:2044-53.
12. Cohen HW, Hailpern SM, Fang J, Alderman MH. Sodium intake and mortality in the NHANES II follow-up study. *Am J Med* 2006;119:e7-14.
13. Liu K, Cooper R, McKeever J, et al. Assessment of the association between habitual salt intake and high blood pressure: methodological problems. *Am J Epidemiol* 1979;110:219-26.
14. 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;2:1244-7.
15. Sacks FM, Svetkey LP, Vollmer WM, et al. Effects on blood pressure of reduced dietary sodium and the dietary approaches to stop hypertension (DASH) diet. *N Engl J Med* 2001;344:3-10.
16. Brown IJ, Tzoulaki I, Candeias V, Elliott P. Salt intakes around the world: implications for public health. *Int J Epidemiol* 2009;38:791-813.
17. Curtis R, Larson JC, Delzell E, et al. Placebo adherence, clinical outcomes, and mortality in the Women's Health Initiative Randomized Hormone Therapy Trials. *Med Care* 2011;49:427-35.
18. Avins AL, Pressman A, Ackerson L, Rudd P, Neuhaus J, Vittinghoff E. Placebo adherence and its association with morbidity and mortality in the studies of left ventricular dysfunction. *J Gen Intern Med* 2010;25:1275-81.
19. Committee on Public Health Priorities to Reduce and Control Hypertension in the U.S. Population, Board on Population Health and Public Health Practice, Institute of Medicine. A population-based policy and systems change approach to prevent and control hypertension. National Academy of Sciences, 2010. Available at: http://books.nap.edu/openbook.php?record_id=12819. Accessed May 19, 2011.
20. Logan AG. Dietary sodium intake and its relation to human health: a summary of the evidence. *J Am Coll Nutr* 2006;25:4F-169F.
21. Midgley JP, Matthew AG, Greenwood CM, Logan AG. Effect of reduced dietary sodium on blood pressure: a meta-analysis of randomized controlled trials. *JAMA* 1996;275:1590-7.
22. Van Vliet BN, Campbell NRC; on behalf of the Canadian Hypertension Education Program. Efforts to reduce sodium intake in Canada: why, what, and when? *Can J Cardiol* 2011;27:437-45.
23. Danaei G, Ding EL, Mozaffarian D, 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.
24. He FJ, MacGregor GA. A comprehensive review on salt and health and current experience of worldwide salt reduction programmes. *J Hum Hypertens* 2009;23:363-84.