Reducing Sodium Intake to Prevent Stroke
Time for Action, Not Hesitation

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The burden of stroke is enormous and increasing. According to the Global Burden of Disease Study, stroke is the second leading cause of mortality and the third leading cause of disability-adjusted life-years worldwide. In the United States, stroke is the second leading cause of mortality and the seventh leading cause of disability-adjusted life-years. Although standardized rates of stroke seem to be decreasing somewhat, the absolute number of strokes, both ischemic and hemorrhagic, have increased during the past 2 decades. Importantly, most strokes occur in low- and middle-income countries, which are poorly equipped to deal with the vast medical, economic, and societal consequences of strokes.

The relationship of blood pressure (BP) with stroke is direct and progressive throughout the range of usual BP, starting at a level of ≈115/75 mm Hg. It has been estimated that elevated BP accounts for 54% of stroke and 47% of coronary heart disease events. It is noteworthy that about half of these events occur in persons without hypertension. Prevention of stroke in this setting will require nonpharmacological approaches, given that such persons are not candidates for antihypertensive drug therapy.

Excess salt (sodium chloride) intake has a major role in the pathogenesis of elevated BP. Supportive evidence comes from animal studies, observational studies, trials, and meta-analyses. To date, >50 clinical trials have evaluated the effects of sodium reduction on BP in adults. A recent systematic review and meta-analysis of trials testing the effects of sodium intake on BP concluded that lowering sodium intake reduces BP in adults and children and that most people will likely benefit from reducing sodium intake.

Although most studies on the health effects of sodium have been done in Western countries, several key studies have been done in Africa and Asia, where the burden of elevated BP and stroke is escalating. For example, the Kenyan Luo Migration study documented that migrants to urban areas had higher mean sodium intake and BP compared with those who remained in rural areas of Kenya. In the Northern Araki prefecture in Japan, a region with an extraordinarily high intake of sodium and one of the highest rates of stroke worldwide, a public health campaign that lowered sodium intake also reduced BP and substantially lowered stroke rates.

Some of the most convincing evidence on the effects of sodium on BP comes from tightly controlled, dose–response trials. These trials tested ≥3 sodium levels, and each documented direct, progressive, and statistically significant dose–response relationships. In each trial, the lowest level of sodium intake was ≈1500 mg/d, which is now a strategic goal of the American Heart Association. Importantly, sodium reduction was yet again reaffirmed in the recently released American Heart Association/American College of Cardiology Guidelines on Lifestyle Management to Reduce Cardiovascular Risk. Of considerable relevance to dietary recommendations is consistent evidence of a nonlinear relationship such that the decline in BP is steeper when the initial level of sodium intake is below 2300 mg/d than when the initial sodium intake is above this level.

Other research findings are especially relevant to the prevention of stroke in adults. First, older adults and blacks, 2 groups at high risk of stroke, are quite sensitive to the BP-lowering effects of sodium reduction. In the Dietary Approaches to Stop Hypertension (DASH)-Sodium trial, sodium reduction to a level of ≈1500 mg/d lowered BP more in older adults than in younger adults. Specifically, in response to a reduced sodium intake systolic BP decreased by 8.1 mm Hg in persons aged 55 to 76 years versus 4.8 mm Hg in those aged 23 to 41 years. In adults without hypertension, systolic BP decreased by 7.0 mm Hg in those >45 years compared with 3.7 mm Hg in those ≤45 years. In the same trial, sodium reduction lowered systolic BP by 8.0 mm Hg in blacks and 5.0 mm Hg in non-blacks. Second, patients with resistant hypertension seem to be especially sensitive to the BP-lowering effects of sodium reduction. In a small but well-done trial of patients with resistant hypertension on multiple antihypertensive medications, reducing sodium intake from ≥3500 to ≈1100 mg/d lowered systolic BP by a mean of 22.7 mm Hg and diastolic BP by 9.1 mm Hg.

Against this background of persuasive evidence linking excess sodium intake with BP is a recent report from the Institute of Medicine (IOM), which concluded that evidence on direct health outcomes does not support recommendations to lower sodium intake to ≈1500 mg. This report, along with subsequent misinterpretation of its findings by the press,
has created substantial and unwarranted confusion among the public, scientists, and policymakers about the health effects of sodium reduction. Subsequent communications by members of the IOM committee summarized the report’s findings in an attempt to clarify their position and to emphasize their support for reducing the amount of sodium added to processed foods.29,30

It is important to understand the context for the IOM report.21 Several recent observational studies have reported paradoxical findings, for example, a higher risk of cardiovascular outcomes in persons with an apparently low intake of sodium,22,23 in the range recommended by national and professional societies. Given these results, the Centers for Disease Control asked the IOM to convene a committee with the goal of reviewing studies, published after the last IOM report on sodium in 2003,24 that linked sodium intake with direct health outcomes, other than BP. The IOM committee was asked to focus on the health effects of sodium intake in the range of 1500 to 2300 mg/d. The level of 2300 mg/d corresponds to the recommended upper limit set for the general adult population by the 2010 US Dietary Guidelines for Americans,25 whereas the level of 1500 mg/d corresponds to the goal for individuals at high risk for BP-related cardiovascular disease (CVD) and is the goal set for all Americans by the American Heart Association.26 It is important to emphasize that the IOM report neither reviewed nor based its recommendations on the compelling body of evidence, accumulated over decades, that link excess sodium intake with elevated BP.

For CVD outcomes, the IOM committee noted that the evidence was predominantly from observational studies. In addition, there were a few clinical trials from a center in Italy that tested the effects of sodium reduction in patients with heart failure.26,27 These heart failure trials are irrelevant to recommendations for sodium intake in the general population and likely irrelevant to the treatment of patients with heart failure, given the unconventional treatment approach of the investigators.28 In the observational studies, the relationship of estimated sodium intake with CVD outcomes was extremely inconsistent: direct, inverse, J-shaped, and often null. Although some scientists have posited that the J-shaped and inverse relationships reflect a causal relationship, that is, a low sodium intake increased CVD risk,29 the most plausible explanation is that these findings resulted from methodological limitations of the studies—most importantly, inaccurate measurement of sodium intake and the potential for reverse causality.

Randomized trials have the potential to overcome the methodological limitations of observational studies. Numerous trials have documented that the relationship of sodium intake to BP is direct and progressive without a threshold. However, none have been explicitly designed to test the effects of sodium reduction on direct health outcomes, such as CVD in the general population. Importantly, 4 trials that tested the long-term effects of sodium reduction on incident hypertension and BP control did report the effects of sodium reduction on clinical outcomes.30–33 In each trial, there was a consistent trend for less CVD events and mortality in those originally assigned to a reduced sodium intervention. In a meta-analysis of these studies, assignment to a reduced sodium intervention significantly lowered the risk of CVD by 20% compared with assignment to a control group.34 To my knowledge, there is only 1 ongoing trial of sodium reduction with clinical outcomes. In rural China, where the major source of sodium is the addition of salt by individuals during food preparation rather than consumption of processed foods, a trial is testing the effects of sodium reduction on stroke.

Importantly, there is no credible evidence of harm from sodium reduction, even among older aged persons who often have multiple comorbidities.36 As discussed previously, cohort studies that reported adverse effects from sodium reduction are replete with methodological limitations and the potential for spurious results. The trials of sodium reduction in patients with heart failure had substantial design flaws.28 As concluded in a recent systematic overview, sodium reduction has no significant impact on blood lipids, catecholamine levels, and renal function.7 Sodium reduction does increase plasma renin activity, a counter-regulatory hormone that rises in response to a wide variety of BP reduction therapies that lower CVD risk, despite the rise in plasma renin activity.

A central issue, not directly addressed by the IOM report, is whether BP is an appropriate surrogate outcome on which to base policy. It is well recognized that the evidence base to support the use of most surrogate outcomes for policy making is weak.37 Nonetheless, BP is considered one of the few surrogate outcomes with a sufficiently robust body of evidence to guide policy.37 At the Food and Drug Administration, evidence that diverse antihypertensive drug therapies lower CVD risk, together with substantial data linking elevated BP with CVD events, provides the basis for their acceptance of BP as a valid surrogate outcome for policy making.

In conclusion, evidence supporting population-wide reduction in sodium intake remains compelling. In particular, the anticipated benefits of reducing sodium intake as a means to prevent CVD and stroke are substantial. Lowering sodium intake by 4% per year for 10 years is estimated to prevent between 30,000 and 83,000 deaths from stroke.38 Furthermore, there is no credible evidence that sodium reduction is harmful in the general population. Given the totality of evidence, clinicians should continue to recommend sodium reduction in their patients. More importantly, to achieve population-wide sodium reduction, policymakers should redouble their efforts to lower sodium intake in processed foods, the primary source of sodium in the United States and most other countries.

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References


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