Extreme Sodium Reductions for the Entire Population: Zealotry or Evidence Based?

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Should Americans eat less salt? "Yes" has been the advice from several professional organizations. But are such sweeping public health recommendatations based on good science or are they based on an overzealous extrapolation of limited data? Currently, the average consumption of sodium (Na) in the United States is about 3.5 g/day. Some guidelines recommend reducing the Na consumption of the entire US population to <2.3 g/day, and some to even 1.5 g/day. Is this 35%–65% reduction in Na consumption in millions of Americans necessary, safe, and feasible?

Is there evidence that lowering Na intake from current levels (3.5 g/day) to much lower levels (<2.3 g/day or 1.5 g/day) is beneficial to health?

The crux of the argument is that the blood pressure (BP)–lowering effect of a reduction in Na intake (to low intake levels) will reduce cardiovascular disease (CVD). But is this supported by incontrovertible evidence, or is it in large part conjecture? One of the most influential studies was INTERSALT, which reported a weak relationship between Na and BP (0.94/0.03 mm Hg per gram of Na).[1] An equally well-conducted study from Scotland published side by side showed no significant association between Na excretion and BP,[2] yet received little attention, illustrating the biases with which papers are selectively emphasized. The DASH trial in 2001,[3] which has been a primary basis for the current American Heart Association guidelines and the 2010 National Dietary Guidelines, is a "proof of concept" study as to whether changes in multiple aspects of diet (including Na reduction) would lower BP under controlled situations (all meals were provided to the participants and their spouses) over 5 weeks. This trial demonstrated that large reductions in Na intake (1.8 g/day) lowered BP (by 4.9/2.6 mm Hg), but the effects were more modest (3.0/1.6 mm Hg) in those who consumed an otherwise healthy diet, which also lowers BP. Further, the average intake of potassium in the DASH participants was low (1.56 g/day) compared with the typical US diet (2.6 g/d),[4] and this may have enhanced the effects of Na reduction.[5,6] A study of 18 months of intervention (e.g., Trials of Hypertension Prevention) where foods were not replaced showed smaller reductions in Na (1.0 g/day) and a proportionately smaller reduction in systolic BP of 1.7 mmHg.[7]

But none of these studies addressed the crucial question: Does lowering Na intake reduce CVD? In the absence of reliable randomized controlled trials (RCTs), some clues can be obtained from cohort studies examining the association between Na intake and CVD. Recently, 4 cohort studies[8–11] with urinary estimates of Na consumption (which are better than dietary estimates) raised concerns that low Na intake (<3 g/day) was associated with higher (or no lower) rates of CVD/mortality compared with moderate intake. This flew in the face of conventional dogma, so the Insitute of Medicine (IOM) committee was struck to examine the data and has since made a number of recommendations, which we interpret in the context of the totality of evidence.

How do the new IOM recommendations differ from the past?

A key emphasis in the new report is the focus on the association of Na to health outcomes, rather than BP. This change in focus from surrogate outcomes to CVD events is consistent with other guidelines and prompted by results of recent clinical trials where changes in surrogates (e.g., BP, glucose) do not always translate into anticipated changes in CVD. The committee found that the evidence linking Na intake and CVD supports population-based efforts to lower "excessive" dietary Na intakes, but it is not consistent with recommendations that encourage lowering of dietary Na to <2.3 g/day.

The committee explicitly pointed out that they were not able to recommend a specific target range of dietary Na and emphasized the paucity of good data to do so. The report states people should not eat "high" amounts of Na, but the data on the health effects of Na were deemed too sparse for the committee to specify an upper limit for acceptable Na consumption.

Relevant issues regarding Na intake, BP, and CVD

What is the population distribution of Na intake? The average American consumes about 3.5 g of Na per day, and this has remained constant for the last 50 years, despite guidelines and

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population-based efforts to reduce Na intake further. In addition, data from >30 countries have reported a similar level of Na intake.[8–13] In the United States, only 9% of adults consume <2.3 g/day, and just 0.6% consume <1.5 g/day.[4] Therefore, the human experience for very low levels of Na consumption is extremely sparse. Interestingly, in countries such as the United States, there have been marked reductions in CVD rates by about 50% over the last 25 years although Na intake has remained constant.[14] So, Na reduction does not appear to be essential to reducing CVD.

What is the extent of CVD reduction that plausible reductions in Na can achieve? RCTs have reported a modest reduction in BP with lowering Na intake from moderate to low-moderate intake ranges,[15,16] which is larger (3.0 mm Hg SBP with 1 g of Na reduction) in hypertensive persons than in normotensive persons (1.6 mm Hg). A more achievable reduction in Na intake, by, say, 0.5 g of Na,[17] will translate into about a 1.5 mm Hg lower systolic BP in hypertensive persons and about a 0.8 mm Hg lower systolic BP in the general population. If real, these translate into a 5% and and 2.5% potential reduction in CVD risk in hypertensive persons and in the general population, respectively—a magnitude of benefit that is modest.[18]

Furthermore, the contention that BP reductions irrespective of the approach and the baseline level of BP will translate into CVD reductions is questionable. For instance, recent trials showed that some agents reduce BP but have no effect on clinical outcomes,[19] other agents reduce BP only modestly but have a substantial reduction in CVD,[20] and different agents reduce BP to similar extents and yet differ in their impact on CVD.[21] Further, even in high-risk individuals (e.g., diabetics), lowering systolic BP from 133.5 to 119.3 mm Hg (a 14.2 mm Hg change) was not associated with a significant reduction in CVD.[22] Therefore, the clinical benefits on health outcomes cannot be reliably predicted by a reduction in BP. Currently, apart from beta-blockers post-myocardial infarction (MI) or angiotensin-converting enzyme (ACE) inhibitors in those with CVD or other markers of high risk,[20,23–28] there is no clear evidence that BP-lowering drugs will reduce CVD in those with "normal" entry BP levels (i.e., systolic BP < 140 mm Hg). Recent European guidelines have called for large RCTs to definitively address this question.[29]

What is the relationship between Na and clinical events? In almost all cohort studies reporting an association between increased Na intake and CVD, the increased risk was only observed when Na intake was greater than approximately 5 g/day.[8,11] Below this level, there is no convincing association between Na intake and CVD with increasing intake, and some studies have reported a higher risk with Na intake below 3 g/day compared with moderate intake (3–5 g/day).[8–11] Even if we dismiss the higher CVD rates at low Na levels as due to a methodologic artefact ("reverse" causality), there is no study indicating that Na intake (measured using urinary markers) <3 g/day is associated with lower rates of CVD compared with 3–5 g/day (the US average). However, an intake of 3–5 g/day is associated with lower CVD compared with higher intake.[8,11,30]

There is a clear need for large, well-executed cohort studies with urinary measures of Na involving healthy individuals and a broad range of Na consumption, among whom a few thousand CVD events occur, so that we can reliably characterize the shape of the associations of Na intake vs. CVD.

RCTs with morbidity and mortality outcomes are the goldstandard for testing health interventions. To date, the only RCTs of reduced Na intake and mortality involved patients with heart failure, which showed an increase in mortality with very low Na intake compared with moderate Na intake,[31–33] but the validity of some of these studies has been challenged. Data from well-designed RCTs in healthier populations are currently unavailable. The Trials of Hypertension Prevention[34] was designed to assess the effect of Na reduction on BP, which it clearly demonstrated. In the extended observational follow-up, 23% of participants were lost to follow-up, and of those followed, records to document CVD were unavailable in a further third. This suggests that data on CVD may not have been available >40% of the events. A usual analysis (without "adjustment") reported no significant reduction in CVD, but a post hoc "adjusted" analysis was just "nominally statistically significant." The relative risk reduction in CVD was reported to be 25% (and 30% after adjustment), which would be 5 times larger (and therefore implausible) than that predicted from the observed systolic BP reduction of 1.7 mm Hg. Further, the mortality rate, which was available in the entire cohort, showed no significant difference. Therefore this study does not inform us reliably as to whether reduction in Na intake affects CVD or mortality.

As the IOM committee recommended, there is a particular need to conduct large RCTs with clinical outcomes as the endpoint, especially where uncertainty exists about whether the benefits outweigh harm. Such a trial could be feasible among individuals living in closed communities, such as nursing home residents, especially because the elderly are more sensitive to Na effects. As shown repeatedly in the past, well-meaning interventions based on insufficient science can mislead (e.g., hormone therapy, margarines, and total fat intake).[35–37] These examples suggest caution in recommending major public health policies based on surrogate outcomes.

Implications for dietary recommendations

The latest evidence raises several new questions: Is it wise to make dietary recommendations that affect millions when the impact of Na reduction on clinical outcomes is unproven? What is its feasibility? What are the direct and indirect costs of a wholesale change of Na content of food? If the goal is CVD reduction, are there not better proven dietary interventions (e.g., Mediterranean diet)? Is it wise to divert resources to poorly proven strategies when so much more can be achieved by interventions where the evidence is far stronger (e.g., smoking cessation, better control of hypertension through more widespread use of low-cost and safe drugs, lipid lowering)? Is targeting hypertensive persons and those with high Na intake more appropriate than a population-wide strategy?

The zeal to recommend extreme reductions in Na intake that are difficult to achieve in the entire population in the United States and other countries with moderate Na intake (e.g., <5 g/day) is a case of ideology replacing good science.

The onus is on those who advocate population-wide recommendations for extreme Na reduction to generate reliable data that widespread and substantial reduction of Na intake will reduce CVD to settle the issue definitively. As IOM committee chair Brian Strom stated: "It's not a question of studies showing benefit being better than those showing harm; there are no studies showing benefit."[38] So the answer to the question, "Should all Americans reduce their consumption of Na substantially from current average intake levels?" is "We don't know, and definitely not yet."

DISCLOSURE

The authors declared no conflict of interest.

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