The Science upon Which to Base Dietary Sodium Policy¹–⁴

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ABSTRACT

Few nutrient intake recommendations become subjects of heated scientific debate, but sodium is 1 of them. In the absence of sufficient clinical trials focused on sodium intake and health outcomes, studies that used the surrogate marker of blood pressure have been used to support extreme sodium reduction. Under tightly controlled conditions, maximum achievable sodium reduction leads to a 1–6 mm Hg reduction in systolic blood pressure, which presumably leads to reduced cardiovascular disease morbidity and mortality. However, in observational cohort studies that used not blood pressure but actual health conditions as outcomes, the presumed relation between sodium intakes <2500 mg/d was not observed. Thus, the blood pressure effect of sodium restriction can no longer be accepted as a surrogate for health outcomes associated with sodium intake. Evidence that reducing sodium intakes to <2500 mg/d will improve health is needed to justify continuing efforts to modify diet. Adv Nutr 2014;5:764–769.

Introduction

Why is the debate about dietary sodium intake so heated? Perhaps it is because the stakes are so high. Many authoritative bodies recommend that 90% of the world’s population reduce their current sodium intake by one-third or more. Many also believe this dangerous diet can only be altered by changing the composition of processed food, because it is responsible for so much of what we consume. Food manufacturers are accused of promoting products designed to shorten the life of their customers. The result has been a call for dramatic behavior change by all but the most abstemious 5–10% of the world’s 6 billion people, as well as costly, untested modification of processed foods. And, if achieved, systolic blood pressure will decrease by anywhere from 1–6 mm Hg, thus preventing somewhere between 60 and 90,000 deaths in the United States each year (1–3). Ambitious, but is it justified, or even possible?

Over the past 2 decades studies linking sodium intake to actual health outcomes now stand at >2 dozen, with nearly 300,000 participants (4). However, instead of supporting the idea that virtually everyone should curb their sodium habit, the evidence has actually revealed a very different picture. One conclusion, now supported by a large and expanding body of data, is that the relation of sodium to health best fits a U or J shape (5). Thus, there is a wide range of optimal intake surrounded by potential harm associated with intakes beyond the high and low bounds of normal. This is the pattern of all other essential nutrients (6).

The purpose of this review is to briefly describe the evolution of the debate and to present the case for the “J/U” hypothesis in which intakes of sodium between ~2500 and 5000 mg/d are associated with the most favored health outcomes (4).

Methods

A literature review identified studies that linked sodium intake to subsequent morbidity and mortality. In addition, formal reviews, including meta-analyses, were examined. Of particular value were successive Cochrane Reviews and reports of Institute of Medicine (IOM) committees (7,8). Recommendations of various authoritative bodies provided a scaffold upon which to describe the evolving relation of science to policy. The resulting analysis is presented in a largely chronologic narrative. Although a detailed chronology of recommendations from 1969 to 2010 was presented elsewhere (7), this brief summary is intended to provide context for the more recent reports.

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Abbreviations used: CVD, cardiovascular disease; DGA, Dietary Guidelines for Americans; IOM, Institute of Medicine.
Results

The early years: pre-1985. By the 1970s, a substantial body of data existed that showed that unacculturated and nomadic peoples had lower blood pressure, which did not increase with age, than did residents of modern industrialized societies. Differences in sodium were believed to explain this beneficial effect.

In 1977, Professor Jeremiah Stammler, a distinguished public health authority, during Senate testimony, said, “It is essential to focus on the continuing high salt use of Americans. Precise data are nonexistent...growing concern...that somehow...salt intake sets the stage...acts as a conditioner, so to speak...for the development of hypertension.” This was already, if not soon to be, conventional wisdom and would translate into the prevention of strokes and heart attacks (9).

Indeed, >100 randomized clinical trials confirmed that a large difference in sodium intake (3.6 g) could produce a 1 to 6 mm Hg decrease in average systolic blood pressure (10). However, the normal kidney can accommodate wide variation in sodium intake without affecting blood pressure. Thus, sodium reduction produces little or no change in blood pressure for most people. In some, blood pressure actually increases in response to sodium restriction (11).

By 1980, U.S. dietary guidance extended its focus from deficiency to dietary excess. In 1980, concern about excess sodium surfaced in the Dietary Guidelines for Americans (DGA), but no specific recommendation was made until DGA 2005 (12). Nevertheless, physicians “particularly some academicians and some health authorities” were already recommending sodium restriction. For example, among patients with high blood pressure (~25% of the adult population), reducing sodium intake had become standard public health and physician practice (3).

The middle period: 1985–2010. A well-designed and executed study in Japanese immigrants to Hawaii found that sodium intake estimated by dietary recall was, in contrast to other nutrients, not associated with stroke (13). Sodium intake was similar to that of other Americans.

Seven years later, a second prospective study (14) in 8600 Taiwanese residents found a direct association of sodium intake to cardiovascular disease (CVD) events. Sodium intake was classified according to how often “salty” foods were consumed. There was no quantitative measure of sodium intake. Average sodium intakes in Taiwan mirrored those in Japan.

The third such study was published in 1995 (15). This prospective study in 3000 participants in a systematic hypertension treatment program revealed a specific, significant independent inverse association of 24-h urinary sodium and CVD events. Those in the lowest quartile of sodium intake (<2000 mg/d) were twice as likely to experience a CVD event as those in the highest quartile (>3600 mg/d) (Fig. 1).

Then, the 2005 DGA, for the first time, advised all Americans to consume <2300 mg/d, conveniently equaling 100 mmol/d (12). In addition, for all blacks, middle-aged and older adults, and all hypertensive persons (approximately half the U.S. population), the intake recommendation was set at 1500 mg/d. No evidence was presented to support actual health consequences (beyond blood pressure) of intakes at these levels. However, a Cochrane collaboration had earlier identified several other physiologic consequences of low sodium intakes (10).

In 2007, a review that was prepared from a presentation that was considered novel at the time included 14 studies of salt intakes, in which no association was found in 8, a positive association was shown in 4, and an inverse association was found in 5 studies (16). The studies spanned the gamut from having a direct association, to an inverse association with morbidity and mortality, with several detecting no association. Studies containing a substantial number of subjects with intakes <2300 mg/d generally found an inverse association. On the other hand, in studies with many subjects whose intakes were >5000 mg/d, sodium intake usually had an inverse association with outcomes. Thus, the authors hypothesized that there was a J-shaped association of sodium intake to outcome, with the optimal zone being ~2500–5000 mg/d.

By contrast, Strazzullo et al. (17) in 2009 published a meta-analysis that included many of the same studies. In a Cox regression analysis, assuming linearity of the association, they detected a positive association of sodium intake with morbidity and mortality. The positive result was accounted for by 4 of 13 studies with average sodium intakes >4500 mg/d, and which included few if any subjects with intakes <2300 mg/d. Because the Cox analysis assumed linearity of the association, the slope was essentially determined by participants with high intakes, which was extended to apply to low-sodium groups as well. In addition, the association only became significant when 1 of the studies (in hypertensive patients) was deleted from the analysis (5).

The most recent period: 2010 to the present. At this writing (May 2014), 4 additional studies have been reported. Of
these, 2 found inverse associations (18,19); 1 in larger, more diverse populations found a J-shaped relation (20); and in 1 study, there was a direct association between sodium intake and health outcomes (21). The J-shaped studies were notable in being large, based on urinary measures of sodium intake, and having accounted for potential confounders.

At the same time, there were serious reservations about these studies. For example, the northern European study (18) was met with a number of letters from respected authorities that challenged the validity of the findings (22). Several suggested that further analyses be performed, and their findings were consistent with the originally published conclusions.

In addition, other analyses drew different conclusions (23,24). For example, a 2013 Cochrane review of 14 observational studies and 5 randomized trials found a significant association of reduced sodium with lower blood pressure and decreased stroke (23). There was no association with either all-cause mortality or all-CVD mortality. No significant effects on sympathetic nerve activity or lipids were observed. Plasma renin activity was not reported.

The single study that did not find harm at the lower range of sodium intakes was carried out in 2657 largely African-American and Hispanic residents in northern Manhattan, NY (21). Sodium intake was assessed by self-report of food frequency. Surprisingly, mean and median intakes (3031 and 2787 mg/d, respectively) were far below national findings, calling into question the validity of the sodium intake assessment. Some 320 participants had intakes <1500 mg and 558 had intakes >4000 mg/d. Those who consumed <1500 mg/d survived longer than those who consumed >2500 mg/d.

The 2013 IOM review (8) reached several conclusions that challenged the recommendations of DGA 2010 (25). First, it rejected the notion that blood pressure change was a suitable surrogate for actual health outcomes associated with sodium intakes. It recognized that sodium restriction had several physiologic consequences, some beneficial (blood pressure) and others not (increased plasma renin activity, insulin resistance, and sympathetic nerve activity, as well as elevated aldosterone and TGs). In short, no single physiologic change associated with low sodium intakes could predict future cardiovascular mortality and morbidity.

Nevertheless, the 2013 IOM report concluded that “excessive” (undefined) sodium intake was harmful. They found insufficient evidence to determine whether intakes <2300 mg/d were “beneficial or harmful.” However, concern was expressed that intakes <1500 mg/d may be harmful.

In 2014, Graudal et al. (4) meta-analysis of 25 studies in 274,683 participants that concluded that both low and high sodium intakes were associated with increased mortality, consistent with a U-shaped association between sodium intake and health outcomes. To determine whether a J or U shape described the relation of sodium to outcome, mortality was determined for those within, below, and above the usual range. The groups both above and below were then compared, controlling for other relevant risk factors, with the usual-range group. In addition, within the usual range, 2 subgroups, stratified at the midpoint, were compared. Mortality did not differ within the 2564–4952 mg/d range. In contrast, those both above and below that range had significantly greater mortality than those with the usual intakes. The risk effect was more robust for those at the lower levels than those at the upper levels (Figs. 2–4). This supported the conclusion of an earlier review suggesting that a nonlinear risk curve existed (5) (Fig. 5).

Despite the new evidence, representatives of the CDC found no reason to reconsider, much less modify, their long-standing recommendations (26). An expert committee of the AHA published a critique of observational studies linking sodium intake to outcomes and implied that the superior data linking sodium intake to blood pressure should be the basis for determining sodium intake (27). This AHA document misquoted the IOM report as concluding that “evidence for the current DGA of 2300 mg/d recommendation was compelling.” The IOM actually reached the opposite conclusion: “The evidence from studies on direct health outcomes was insufficient and inconsistent about an association between sodium intake below 2300 mg/d and benefit or risk for the health outcomes of CVD, stroke, CVD mortality, or all-cause mortality in the general U.S. population.”

Discussion

Now, 30 y after the first report linking dietary sodium intake to health outcomes, the IOM report (8) and the Graudal et al. (4) meta-analysis provide a coherent understanding of how sodium intake relates to health. The net health effect cannot be predicted by the consequence on any single physiologic variable. The fact that blood pressure and mortality outcomes associated with low-sodium diets diverge (Fig. 6) confirms the IOM conclusion. The blood pressure effect of sodium restriction can no longer be accepted as a surrogate for health outcomes associated with sodium intake.

In addition, the IOM recognized that the heterogeneity between study results related to ambient or starting blood pressure. Nevertheless, they concluded, “excessive sodium intake is associated with cardiovascular risk.” However, “excessive” was not defined. The IOM also expressed concern about intakes <1500 mg/d and noted that insufficient data were available to determine whether intakes <2300 mg/d were harmful or beneficial. By implication, the IOM recognized that, like all other essential nutrients, there is an optimal or safe zone of sodium intake above and below which the risk increases. The IOM did not specify the range of that safe zone.

After release of the IOM report, several news outlets highlighted disagreement among health agencies about targets for dietary sodium intake and reported that experts disagreed about the importance of blood pressure (26,27). Moreover, several IOM committee members published a commentary that suggested a more limited interpretation...
Rather than focusing on disagreements about specific targets that currently affect <10% of the US population (i.e., sodium intake of <2300 mg/d vs. <1500 mg/d), the IOM, AHA, WHO, and DGA are congruent in suggesting that excess sodium intake should be reduced, and this is likely to have significant public health effects (28).

**FIGURE 2** All-cause mortality comparing those with usual sodium intakes to those with low sodium intakes. F, female; M, male; NH, NHANES; NW, normal weight; OW, overweight. Reproduced from reference 4 with permission.

<table>
<thead>
<tr>
<th>Study</th>
<th>Total</th>
<th>Weight</th>
<th>Hazard ratio, random (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lennie et al.</td>
<td>134</td>
<td>1.3%</td>
<td>0.44 (0.20 - 0.97)</td>
</tr>
<tr>
<td>Alderman et al.</td>
<td>1,900</td>
<td>5.4%</td>
<td>0.70 (0.52 - 0.94)</td>
</tr>
<tr>
<td>Ekinci</td>
<td>620</td>
<td>6.0%</td>
<td>0.72 (0.55 - 0.94)</td>
</tr>
<tr>
<td>Cohen et al. (NH II)</td>
<td>7,154</td>
<td>9.2%</td>
<td>0.78 (0.67 - 0.91)</td>
</tr>
<tr>
<td>Stobart-Skrypek</td>
<td>2,454</td>
<td>5.8%</td>
<td>0.82 (0.62 - 1.08)</td>
</tr>
<tr>
<td>Tunstall-Pedoe et al. (M)</td>
<td>3,453</td>
<td>6.5%</td>
<td>0.82 (0.64 - 1.05)</td>
</tr>
<tr>
<td>Cohen et al. (NH III)</td>
<td>6,525</td>
<td>9.9%</td>
<td>0.83 (0.73 - 0.94)</td>
</tr>
<tr>
<td>Thomas</td>
<td>2,105</td>
<td>1.7%</td>
<td>0.87 (0.45 - 1.68)</td>
</tr>
<tr>
<td>Alderson et al. (NH I)</td>
<td>11,346</td>
<td>10.7%</td>
<td>0.88 (0.80 - 0.97)</td>
</tr>
<tr>
<td>Gardener et al.</td>
<td>2,099</td>
<td>8.2%</td>
<td>0.89 (0.74 - 1.07)</td>
</tr>
<tr>
<td>Tuomilehto et al. F</td>
<td>1,263</td>
<td>2.8%</td>
<td>0.91 (0.56 - 1.46)</td>
</tr>
<tr>
<td>O'Donnell et al.</td>
<td>23,327</td>
<td>10.9%</td>
<td>0.92 (0.84 - 1.01)</td>
</tr>
<tr>
<td>Tunstall-Pedoe et al. (F)</td>
<td>4,700</td>
<td>5.4%</td>
<td>0.93 (0.69 - 1.25)</td>
</tr>
<tr>
<td>Yang et al. (NH III)</td>
<td>4,000</td>
<td>0.0%</td>
<td>0.93 (0.73 - 1.18)</td>
</tr>
<tr>
<td>He, et al. (NH I)</td>
<td>6,797</td>
<td>0.0%</td>
<td>0.98 (0.88 - 1.09)</td>
</tr>
<tr>
<td>Geleijns et al.</td>
<td>1,578</td>
<td>6.2%</td>
<td>1.12 (0.86 - 1.46)</td>
</tr>
<tr>
<td>Taylor et al. (Appel 43)</td>
<td>291</td>
<td>2.8%</td>
<td>1.14 (0.70 - 1.86)</td>
</tr>
<tr>
<td>Alderson et al. (F)</td>
<td>1,037</td>
<td>3.1%</td>
<td>1.17 (0.74 - 1.85)</td>
</tr>
<tr>
<td>He, et al. (NH I)</td>
<td>2,688</td>
<td>0.0%</td>
<td>1.32 (1.16 - 1.50)</td>
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<tr>
<td>Yang et al. (NH III)</td>
<td>5,200</td>
<td>0.0%</td>
<td>1.44 (1.06 - 1.96)</td>
</tr>
<tr>
<td>Lennie et al. (severe heart failure)</td>
<td>163</td>
<td>1.1%</td>
<td>2.54 (1.10 - 5.87)</td>
</tr>
<tr>
<td>Costa et al.</td>
<td>372</td>
<td>1.8%</td>
<td>2.86 (1.50 - 5.44)</td>
</tr>
<tr>
<td>Arcand</td>
<td>123</td>
<td>1.0%</td>
<td>3.54 (1.46 - 8.58)</td>
</tr>
</tbody>
</table>

**FIGURE 3** Outcomes when high usual and low usual sodium intakes are compared. ACM, all cause mortality; CVD, cardiovascular disease; F, female; M, male; NH, NHANES; OW, overweight; S, stroke. Reproduced from reference 4 with permission.
In 2014, a second critical publication defined specific dimensions of the safe zone (4). Meta-analysis of the 25 studies neatly identified a U-shaped association of sodium intake with an optimal central range of 2500–5000 mg/d, with increased mortality above and below those bounds.

Although I believe the evidence to be convincing, well-respected authorities in the field challenge this interpretation of the available evidence. The CDC and the AHA (at this writing) have not yet accepted these paradigm-shifting findings, despite an absence of conflicting evidence. In sum, they contend that methodologic limitations of observational studies preclude using such data to determine health policy. All observational studies—even those prospectively designed to address the issue at hand—do have limitations. Having suggested that this vast body of data be disregarded—the sort of studies that established blood pressure, cholesterol, tobacco, and glucose as CVD risk factors—they contend that extrapolation from blood pressure justifies current guidelines.

Ignoring evidence is a hazardous approach to policy making. The belief that changes in 1 of many conflicting variables will produce dramatic health outcomes is also a chancy business. Experience with dietary fat recommendations is instructive. In 1980, the DGA recommended that all Americans curb fat intake. Twenty years later, that directive was rescinded. The DGA also noted that the previous recommendation might have had unanticipated adverse consequences, specifically increased obesity and diabetes (29).

Reason argues that any attempt to alter the diet of 90% of the world’s population to modify intake of a single nutrient ought to be based on substantial, incontrovertible evidence. There is no scientific evidence that sodium intakes <2500 mg/d provide better health outcomes than intakes between 2500 and 5000 mg/d.

In sum, the available evidence supports a U-shaped relation of sodium intake to health outcomes. If this is correct, no change in dietary sodium intake is needed for the 90% of the world’s population who currently consume within 2500 and 5000 mg/d.

FIGURE 4 All-cause mortality when high and usual sodium intakes are compared. F, female; M, male; NH, NHANES; NW, normal weight; OW, overweight. Reproduced from reference 4 with permission.

FIGURE 5 Relation between sodium intake and morbidity and mortality in 23 observational studies. Sodium intake is shown in each box as means from the reported studies. Shown in parentheses are the minimum and maximum mean sodium intakes reported in the studies. Adapted from reference 5 with permission.

FIGURE 6 An illustration of how sodium’s effect on blood pressure diverges from its effect on CVD outcomes at low amounts of intake. The straight line represents the relation between sodium intake and SBP in normotensive persons and assumes that a decrease in sodium intake of 160 mmol (3680 mg) produces an ~1.2 mm Hg decrease in SBP (10). The curved line represents data that suggest increased CVD risk (despite lower blood pressure) at the lower end of sodium intake. CVD, cardiovascular disease; SBP, systolic blood pressure. Adapted from reference 16 with permission.

Study Total Weight Hazard Ratio Hazard Ratio (95% CI) (95% CI)
--- --- --- --- ---
Yang,30 NW 2,667 0.0% 0.86 (0.51–1.45) 1.16 (1.03–1.30)
Cohen39 (NH III) 6,525 15.5% 0.94 (0.79–1.12) 1.08 (0.96–1.24)
Tuomilehto,24 M, NW 4,604 13.7% 0.96 (0.77–1.20) 1.20 (1.11–1.30)
Stolarz-Skrzypek37 2,454 6.5% 1.14 (0.77–1.66) 1.18 (1.01–1.37)
TuomilehtoPedoe,20 F 3,525 7.3% 0.99 (0.70–1.43) 1.43 (1.01–2.02)
O’Donnell38 25,408 21.5% 1.12 (1.00–1.26) 1.16 (1.21–2.01)
Gardener16 2,337 10.0% 1.12 (1.00–1.24) 2.07 (1.35–3.17)
Thomas15 2,105 7.5% 1.43 (1.01–2.02) 1.20 (1.11–1.30)
Tuomilehto,24 M, OW 514 11.0% 1.56 (1.21–2.01) 1.20 (1.11–1.30)
Yang,30 OW 3,467 0.0% 2.07 (1.35–3.17)

Total (95% CI) 48131 100.0% 1.16 (1.03–1.30)

Heterogeneity: y^2 = 0.01; z ^ 2 = 17.61, df = 8 (P = 0.02); I^2 = 55% Test for overall effect: Z = 2.46 (P = 0.01)
Acknowledgments
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References