Problems With the American Heart Association Presidential Advisory Advocating Sodium Restriction

James J. DiNicolantonio, Asfandyar K. Niazi, Carl J. Lavie, and James H. O’Keefe

Keywords: American Heart Association; blood pressure; cardiovascular; heart failure; hypertension; sodium; sodium-restricted diet.

The American Heart Association (AHA) Presidential Advisory Committee recently published a recommendation supporting population-wide sodium reduction. The advisory concluded that the available data included in studies published since 2011 support the AHA guidelines to reduce sodium intake to <1.5 g/d in all Americans. However, no systematic review of the literature was performed to obtain all appropriate meta-analyses and studies on topics of sodium reduction prior to 2011. Moreover, the severe limitation for the trials that suggest benefit for a “lowered-sodium intake” is that patients were not given the exact same diets. Rather, they were given a diet that lowers sodium (among many other variations that come along with this type of diet), for example, increased intake of fruits, vegetables, and spices and decreased intake of processed foods. Thus, trials testing a “low-sodium diet” cannot prove causation unless the exact same diets are given, with the only difference being that of a lowered sodium intake, which has not occurred. Because of the potential adverse cardiometabolic effects of a very low-sodium diet, such as increased lipids, insulin resistance, and subsequent diabetes, the AHA should reconsider the other side of this story and soften its recommendations for a population-wide dietary sodium restriction of <1.5 g/d.

The American Heart Association (AHA) Presidential Advisory Committee recently published further evidence to support its previous recommendation of reduction in sodium intake, with what we believe is a biased interpretation of the literature. Many authors of the AHA report are members of the World Action on Salt and Health (WASH), which is an advocacy group with an agenda to “improve the health of populations throughout the world by achieving a gradual reduction in salt intake.” The Centers of Disease Control and Prevention publicly funded a parallel Institute of Medicine (IOM) project, titled “Consequences of Sodium Reduction in Populations,” that was designed to mirror the efforts of the presidential advisory. Although we applaud these groups’ efforts to improve the health of the global population, we believe that both groups have underemphasized considerable evidence that does not support their recommendations.

SURROGATE MARKERS
Blood pressure, lipids, and the renin angiotensin aldosterone system

The article authors claim that reports suggest harmful effects of a reduced-sodium diet are based on observational studies and a single meta-analysis. The authors’ guidelines state that these reports have been misinterpreted; however, they fail to give any scientific basis to support their statement. In addition, they have ignored several other key pieces of evidence. The authors discuss a meta-analysis by Graudal and colleagues in their article and state that the results of this meta-analysis indicate that blood pressure (BP) is lowered with reduced sodium intake. The results of this meta-analysis showed that there was a decrease in the systolic BP (mean weighted difference [WMD] 1.27 mm Hg; 95% confidence interval [CI], 1.88, 0.66; \( P = 0.0001 \)) and diastolic BP (WMD 0.05 mm Hg; 95% CI, 0.51, 0.42; \( P = 0.85 \)) in normotensive whites and a similar decrease in mean BP (WMD 3.56 mm Hg; 95% CI, 4.07, 3.06; \( P = 0.0001 \)) of hypertensive whites. The results could be reproduced across systolic BP (WMD 4.02 mm Hg; 95% CI, 7.37, 0.68; \( P = 0.02 \)) and diastolic BP (WMD 2.01 mm Hg; 95% CI, 4.37, 0.35; \( P = 0.09 \)) in normotensive African Americans, with systolic BP (WMD 6.44 mm Hg; 95%CI, 8.85, 4.03; \( P = 0.0001 \)) and diastolic BP (WMD 2.40 mm Hg; 95%CI, 4.68, 0.12; \( P = 0.04 \)) in hypertensive African Americans; systolic BP (WMD 1.27 mm Hg; 95%CI, 3.07, 0.54; \( P = 0.17 \)) and diastolic BP (WMD 1.68 mm Hg; 95% CI, 3.29, 0.06; \( P = 0.04 \)) in normotensive Asians; and systolic BP (WMD 10.21 mm Hg; 95% CI, 16.98, 3.44; \( P = 0.003 \)) and diastolic BP (WMD 2.60 mm Hg; 95% CI, 4.03, 1.16; \( P = 0.0004 \)) in hypertensive Asians (Table 1). However, it appears that these authors ignored the remaining portion of the conclusions of this meta-analysis. Due to the opposing nature of the effects of sodium, that is, an increase in plasma renin (standardized mean difference [SMD] of sodium reduction 1.15 [95% CI, 0.99, 1.30], \( z = 14.81, P < 0.00001 \)),
Table 1. The Effects of a Low-Sodium Diet

<table>
<thead>
<tr>
<th></th>
<th>Systolic BP (Mean weighted difference [WMD]</th>
<th>Hypertensive Caucasians: the mean reduction in BP (WMD = −3.56 [95% CI: −4.07, −3.06] mmHg, P = 0.00001)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(Mean weighted difference [WMD]) = −1.27 [95% CI: −1.88, −0.66] mm Hg, P = 0.0001; WMD in trials lasting at least 4 weeks = −1.29 [−1.96, −0.62] mmHg, P = 0.0002) and diastolic BP (WMD = −0.05 [95% CI: −0.51, 0.42] mmHg, P = 0.85)</td>
<td>Hypertensive Caucasians: the mean reduction in BP (WMD = −3.56 [95% CI: −4.07, −3.06] mmHg, P = 0.00001)</td>
</tr>
<tr>
<td></td>
<td>Normotensive Caucasians: WMD in trials lasting at least 4 weeks = −0.45 [95% CI: −0.90, 0.00] mmHg, P = 0.05</td>
<td>Normotensive Caucasians: the mean reduction in BP (WMD = −3.56 [95% CI: −4.07, −3.06] mmHg, P = 0.00001)</td>
</tr>
<tr>
<td></td>
<td>Normotensive African Americans: systolic BP (WMD = −4.02 [95% CI: −7.37, −0.68] mmHg, P = 0.02) and diastolic BP (WMD = −2.01 [95% CI: −4.37, 0.35] mmHg, P = 0.09)</td>
<td>Hypertensive African Americans: systolic BP (WMD = −6.44 [95% CI: −8.85, −4.03] mmHg, P = 0.00001) and diastolic BP (WMD = −2.40 [95% CI: −4.68, 0.12] mmHg, P = 0.04)</td>
</tr>
<tr>
<td></td>
<td>Hypertensive African Americans: systolic BP (WMD = −1.27 [95% CI: −3.07, 0.54] mmHg, P = 0.17) and diastolic BP (WMD = −1.68 [95% CI: −3.29, −0.06] mmHg, P = 0.04)</td>
<td>Hypertensive Africans: systolic BP (WMD = −10.21 [95% CI: −16.98, −3.44] mmHg, P = 0.003) and diastolic BP (WMD = −2.60 [95% CI: −4.03, −1.16] mmHg, P = 0.0004)</td>
</tr>
<tr>
<td>Increase in plasma renin (Standardized mean difference [SMD] of sodium reduction 1.15 [95% CI: 0.99, 1.30], z = 14.81, P &lt; 0.00001)</td>
<td></td>
<td>Hypertensive Africans: systolic BP (WMD = −10.21 [95% CI: −16.98, −3.44] mmHg, P = 0.003) and diastolic BP (WMD = −2.60 [95% CI: −4.03, −1.16] mmHg, P = 0.0004)</td>
</tr>
<tr>
<td>Aldosterone (SMD 1.36 [95% CI, 1.15, 1.57], z = 12.79, P &lt; 0.00001), adrenaline (SMD 0.30 [95% CI, 0.13, 0.46], z = 3.58, P = 0.0003), noradrenaline (SMD 0.52 [95% CI, 0.37, 0.67], z = 6.67, P = 0.0001), plasma cholesterol (WMD increase of 5.76 mg/dL [95% CI, 2.29, 9.24], P = 0.001) and plasma triglycerides (WMD increase of 6.78 mg/dL [95% CI, 2.81, 10.75], P = 0.0008)</td>
<td></td>
<td>Hypertensive Africans: systolic BP (WMD = −10.21 [95% CI: −16.98, −3.44] mmHg, P = 0.003) and diastolic BP (WMD = −2.60 [95% CI: −4.03, −1.16] mmHg, P = 0.0004)</td>
</tr>
<tr>
<td>Aldosterone (SMD 1.36 [95% CI, 1.15, 1.57], z = 12.79, P &lt; 0.00001), adrenaline (SMD 0.30 [95% CI, 0.13, 0.46], z = 3.58, P = 0.0003), noradrenaline (SMD 0.52 [95% CI, 0.37, 0.67], z = 6.67, P = 0.0001), plasma cholesterol (WMD increase of 5.76 mg/dL [95% CI, 2.29, 9.24], P = 0.001) and plasma triglycerides (WMD increase of 6.78 mg/dL [95% CI, 2.81, 10.75], P = 0.0008), and a minor reduction in BP, the meta-analysis concluded that there appeared to be no net beneficial effect of sodium restriction in whites and that there was insufficient evidence to make a firm conclusion regarding the impact of sodium restriction in Asians and African Americans. Overall, the results of the meta-analysis conclude against the generalized recommendation of a sodium-restricted diet.</td>
<td></td>
<td>Hypertensive Africans: systolic BP (WMD = −10.21 [95% CI: −16.98, −3.44] mmHg, P = 0.003) and diastolic BP (WMD = −2.60 [95% CI: −4.03, −1.16] mmHg, P = 0.0004)</td>
</tr>
<tr>
<td>Another RCT lasting 6 weeks revealed that a low-sodium diet had no beneficial effect on measures of systemic inflammation when compared with a normal-sodium diet (0.47 mg/L; 95% CI, 1.25–0.31).</td>
<td></td>
<td>Hypertensive Africans: systolic BP (WMD = −10.21 [95% CI: −16.98, −3.44] mmHg, P = 0.003) and diastolic BP (WMD = −2.60 [95% CI: −4.03, −1.16] mmHg, P = 0.0004)</td>
</tr>
</tbody>
</table>

Insulin resistance

The benefits of dietary sodium restriction have also been challenged. It has been shown that reductions in dietary sodium intake enhance sympathetic hyperactivity (r = 0.47, P < 0.02) and impair physiological reflex mechanisms (r = 0.46, P < 0.04), which can lead to adverse cardiovascular (CV) effects. Maintenance of this low-sodium diet for several weeks, however, did not reverse the enhanced sympathetic hyperactivity. This clearly shows that sodium restriction in the general population may increase sympathetic activity and thus may actually lead to increased CV mortality. In addition to the adverse effects of a low-sodium diet on the sympathetic nervous system, it has also been shown that a low-sodium diet can lead to insulin resistance and an increased body weight in rats (P < 0.05 and P < 0.05, respectively) and insulin resistance in humans (P < 0.01), which are independent risk factors for many aspects of CV diseases.

Cardiovascular outcomes

The authors have also dismissed a recent trial on patients with heart failure (HF) that compared the effects of normal-sodium and low-sodium diets9 as having no relevance for the general population. However, 6–10% of people in the United States aged >65 years have evidence of HF,10 suggesting that the evidence regarding sodium should not be discarded in this large segment of the population. Moreover, the AHA authors explain that this trial is irrelevant because the results were potentially the result of a very aggressive treatment with furosemide (250–500 mg twice daily) in addition to a sodium-restricted diet. However, this point of view is opposed, as a later study showed similar results (reductions in mortality and HF readmissions with a low-sodium diet vs. a normal-sodium diet) in another group of HF patients who were not treated aggressively with furosemide (i.e., two-thirds of patients received 50 mg twice daily).11 The results of the earlier trial also show that in comparison with a low-sodium diet, a normal-sodium diet shows a significant reduction (P < 0.05) in readmissions, lower brain natriuretic peptide values (685 ± 255 compared with 425 ± 125 pg/ml, respectively; P < 0.0001), and lower levels of aldosterone (P = 0.039). These results suggest a worse outcome in patients with HF on dietary sodium restriction.

An increase in the all-cause mortality (P < 0.001) and CV mortality (subhazard ratio [HR] 0.65; 95% CI, 0.44–0.95; P = 0.03) was shown with a lower sodium intake in patients with type 2 diabetes mellitus (T2DM), a condition that is increasing in epidemic proportions.12 It is currently unknown whether an increased mortality rate
with a sodium-restricted diet is specific to T2DM. However, patients with T2DM represent a huge and growing segment of the US population, around 6-7% of the population, and thus it seems logical that if a sodium-restricted diet is causing harm in this group, the diet would not be advisable for the general population. In patients with type 1 diabetes mellitus (T1DM), the highest mortality rates were noted in patients with both high and low urinary sodium excretion per day compared with a normal or intermediate amount (P < 0.001), which suggests that the lowest mortality is seen in patients with T1DM who consume a moderate-sodium diet.14

Perhaps more importantly, whether or not dietary sodium restriction leads to a decrease in BP is less important than the actual effect on CV morbidity and mortality. A recent Cochrane meta-analysis concluded that dietary salt restriction only has a minor BP lowering effects (systolic BP random effects mean difference 1.1 mm Hg (95% CI, 0.1 to 2.3; \( \chi^2 = 0.05; I^2 = 67\% \)) in normotensives, fixed effect mean difference 4.1 mm Hg (95% CI, 2.4 to 5.8; \( \chi^2 = 0.64; I^2 = 0\% \)) in hypertensives; diastolic BP fixed effect mean difference 0.8 mm Hg (95% CI, 0.2 to 1.4; \( \chi^2 = 0.39; I^2 = 0\% \)) in normotensives, random effect mean difference 3.7 mm Hg (95% CI, 0.9 to 8.4; \( \chi^2 = 0.08; I^2 = 67\% \)) in hypertensives and showed no significant positive effect on the CV mortality rate (fixed effects relative risk [RR] 0.69; 95% CI, 0.45 to 1.05; 98 CV deaths; \( \chi^2 = 0.26; I^2 = 0\% \)). Additionally, overall mortality was higher in patients with HF on sodium-restricted diets. Several of the trials included in this meta-analysis used dietary counseling in place of a standardized diet or an objective measure of dietary sodium intake. All trials measuring "sodium restriction" that have shown benefit have either incorporated more fruits and vegetables, potassium, and/or anti-inflammatory spices to replace the sodium, all of which could have beneficial CV impacts independent of sodium restriction. Therefore, in summary, the benefits of "sodium restriction" advocated by this group and the AHA are not proven, as they are not directly related to the reduction in sodium intake. Unless a trial uses the exact same diets, outcomes may be related to the different constituents of the "diet containing lower sodium" (eg, less saturated fats, increased fruits and vegetables, increased potassium, increased bicarbonate) between the groups.

A recent study using predictive mathematical models to estimate the reduction in overall mortality rates per year that could be achieved with dietary sodium restriction concluded that 44,000–92,000 deaths per year could be prevented in the United States with modest dietary sodium restriction. However, the study failed to take into account all of the effects of dietary sodium restriction, especially on insulin resistance and weight gain.16 Therefore, the results of this study did not reveal the entire net effect that sodium restriction has on overall physiological mechanisms. Another study showed a J-shaped curve between the sodium excretion and CV events, implying that a high-sodium as well as a low-sodium diet may lead to an increase in CV events as compared with normal-sodium diet. A high urinary sodium excretion was associated with increased CV mortality (9.7% for 7–8 g/d; HR, 1.53; 95% CI, 1.26–1.86; and 11.2% for >8 g/d; HR, 1.66; 95% CI, 1.31–2.10), myocardial infarction (6.8%; HR, 1.48; 95% CI, 1.11–1.98 for >8 g/d), stroke (6.6%; HR, 1.48; 95% CI, 1.09–2.01 for >8 g/d), and hospitalization for chronic HF (6.5%; HR, 1.51; 1.12–2.05 for >8 g/d). Similarly, a low urinary sodium excretion was associated with increased CV mortality (8.6%; HR, 1.19; 95% CI, 1.02–1.39 for 2–2.99 g/d; 10.6%; HR, 1.37; 95% CI, 1.09–1.73 for <2 g/d) and hospitalization for patients with chronic HF (5.2%; HR, 1.23; 95% CI, 1.01–1.49 for 2–2.99 g/d). This suggests that the best possible intervention in the dietary sodium intake of the general population may be no intervention at all.

CONCLUSION

In conclusion, we believe that based on the preceding evidence, the article written in support of the AHA recommendations represented a skewed image of the current body of literature on this topic. Conclusive evidence that restricting sodium in the diet will have a positive effect on CV morbidity and mortality is lacking; in fact, it is possible that severe sodium restrictions may be harmful to specific patient populations.

Even minor adverse effects may have significant implications when observed in the whole population. Therefore, recommendations should be made on the basis of robust support of evidence and after taking into account all available literature on the subject. Because of the potential adverse effects of a very low-sodium diet, the AHA should reconsider the other side of this story and soften its recommendations for a population-wide dietary severe sodium restriction of <1.5 g/d.

DISCLAIMER
This editorial was prepared and submitted prior to the Institute of Medicine report on sodium.

DISCLOSURE
The authors declared no conflict of interest.

REFERENCES