Appendix E2.42: Evidence Portfolio

Part D. Chapter 6: Cross-Cutting Topics of Public Health Importance

What is the relationship between dietary sodium intake and blood pressure in adults?

Conclusion Statements: The DGAC concurs with the three conclusions from the 2013 AHA/ACC Lifestyle Guideline that apply to adults who would benefit from blood pressure lowering:

The DGAC concurs that adults who would benefit from blood pressure lowering should "lower sodium intake." AHA/ACC Grade: Strong

DGAC Grade: Strong

The DGAC concurs that adults who would benefit from blood pressure lowering should "Consume no more than 2,400 mg of sodium/day." The report also indicates that "Further reduction of sodium intake to 1,500 mg/d can result in even greater reduction in blood pressure"; and concludes that "Even without achieving these goals, reducing sodium intake by at least 1,000 mg/d lowers blood pressure." AHA/ACC Grade: Moderate

DGAC Grade: Moderate

The DGAC concurs that adults who would benefit from blood pressure lowering should "Combine the DASH dietary pattern with lower sodium intake." AHA/ACC Grade: Strong

DGAC Grade: Strong

Methodology

To answer this question, the Committee used the 2013 National Heart, Lung, and Blood Institute (NHLBI) *Lifestyle Interventions to Reduce Cardiovascular Risk: Systematic Evidence Review from the Lifestyle Work Group* and the associated American Heart Association (AHA)/ American College of Cardiology (ACC) *Guideline on Lifestyle Management to Reduce Cardiovascular Risk*.[1] The Committee also reviewed the 2013 Institute of Medicine (IOM) report, *Sodium Intake in Populations*[2] and the recommendations of the IOM Panel on Dietary Reference Intakes for Electrolytes and Water[3] for consistency. Although new studies examining the relationship between sodium and blood pressure have been published since the completion of the NHLBI review, including findings from the Prospective Urban Rural Epidemiology (PURE) study,[4] the Committee determined the evidence presented in the SR conducted by NHLBI, linking sodium and blood pressure, was strong and that consideration of more recent findings would not change the conclusions. Thus, the Committee did not update the review.

Review of Evidence

The 2013 AHA/ACC Lifestyle Guideline and associated NHLBI Lifestyle Report summarized strong and consistent evidence that supports dietary sodium reduction as a means to prevent and treat high blood pressure. The studies used to inform the conclusion to lower sodium intake were conducted in older and younger adults, individuals with prehypertension and hypertension, men and women, and African American and non-African American adults. The trials also documented positive effects of sodium reduction that were independent of weight change; and include behavioral interventions where individuals were counseled to reduce sodium, as well as feeding studies.

The recommendation to combine the DASH dietary pattern with lower sodium is based heavily on the results of the DASH sodium trial, which showed clinically significant lowering of blood pressure with sodium intake of 2,400 mg/day and even lower blood pressure with sodium intake of 1,500 mg/day. The goal of 2,400 or less mg/day was selected because it is the estimated average urinary sodium excretion in the DASH sodium trial.

The recommendation to reduce sodium intake by 1,000 mg/day even if goals for 2,400 mg/day or 1,500 mg/day cannot be reached comes from studies where this level of sodium reduction was beneficial for blood pressure lowering.

The differences in the evidence grade for the three conclusions related to sodium and blood pressure in adults results from the differences in the number and power of clinical trials supporting each recommendation. For example, a grade of “moderate” was assigned to the second conclusion because fewer clinical trials informed the goals of 2,400 and 1,500 mg/day than for the overall goal of sodium reduction.

Table 1. Summary of existing reports examining the relationship between dietary sodium intake and blood pressure in adults

Question/ Purpose	Outcomes and Population of Interest	Included Studies	Evidence Statements/Conclusions from Existing Reports
Lifestyle Interventions to Reduce Cardiovascular Risk-Systematic Evidence Review from the Lifestyle Work Group, (NHLBI 2013) **ACC/AHA Guideline on Lifestyle Management to Reduce Cardiovascular Risk (Eckel, 2013)**			
Critical Question 2 (CQ2): Among adults, what is the effect of dietary intake of sodium and potassium on CVD risk factors and outcomes, when compared to no treatment or to other types	**Sodium and Blood Pressure**: Part a: Overall effect of dietary intake of sodium on blood pressure	Three RCTs.	Evidence Summary 1 (ES1): In adults, 25–80 years of age with BP 120–159/80–95 mmHg, reducing sodium intake lowers BP. (Strength of evidence: High)
	Part b: Comparison of different levels of dietary intake of sodium on blood pressure	One RCT	Evidence Summary 2 (ES2): In adults, 25–75 years of age with BP 120–159/80–95 mmHg, reducing sodium intake that achieves a mean 24-hour urinary sodium excretion of approximately 2,400 mg/day, relative to approximately 3,300 mg/day, lowers BP by 2/1 mmHg, and reducing sodium intake that achieves a mean 24-hour urinary sodium excretion of approximately 1,500 mg/day, lowers BP by 7/3

of interventions?			mmHg. (Strength of evidence: Moderate)
	Counseling to reduce dietary sodium and BP reduction	Two RCTs	Evidence Summary 3 (ES3): In adults, 30–80 years of age with or without hypertension, counseling to reduce sodium intake by an average of 1,150 mg/day reduces BP by 3–4/1–2 mmHg. (Strength of evidence: High)
	Part c: Sodium and blood pressure in subpopulations: subgroups included men and women, African Americans and non-African Americans, and older and younger adults.	Three RCTs (3–6 months' duration)	Evidence Summary 4 (ES4): In adults with prehypertension or hypertension, reducing sodium intake lowers BP in women and men, African American and non-African American adults, and older and younger adults. (Strength of evidence: High)
	Sodium and blood pressure in subpopulations: adults with either prehypertension or hypertension.	Three studies	Evidence Summary 5 (ES 5): Reducing sodium intake lowers BP in adults with either prehypertension or hypertension when eating either the typical American diet or the DASH dietary pattern. The effect is greater in those with hypertension. (Strength of evidence: High)
	Part d: Sodium and blood pressure in the context of dietary pattern changes	DASH-Sodium trial.	Evidence Summary 6 (ES6): In adults, 25–80 years of age with BP 120–159/80–95 mmHg, the combination of reducing sodium intake and eating the DASH dietary pattern lowers BP more than reducing sodium intake alone. (Strength of evidence: Moderate)
	Part e. Sodium and blood pressure in the context of other minerals	No RCTs or meta-analyses met inclusion criteria that examined whether reducing sodium intake plus changing dietary intake of any other single mineral lowers BP more than reducing sodium intake alone.	Evidence Summary 7 (ES7): Evidence from RCTs is not sufficient to determine whether reducing sodium intake and changing dietary intake of any other single mineral (e.g., increasing potassium, calcium, or magnesium) lowers BP more than reducing sodium intake alone
IOM, Sodium intake in populations: Assessment of evidence, 2013			
What is the effect of reducing dietary sodium intake in all individuals compared to habitual intake on health outcomes?	Cardiovascular disease (CVD), including stroke CVD mortality and all-cause mortality, congestive heart failure (CHF), chronic kidney disease (CKD), diabetes, cancer, and "other" outcomes, such as asthma and depression.	4 RCTs; 35 observational (cohort or case-control) studies • CVD, Stroke and Mortality (4 RCTS, 22 obs. studies) • Kidney disease (2 obs. studies) • Metabolic syndrome (2 obs. studies)	Conclusion 1: Although the reviewed evidence on associations between sodium intake and direct health outcomes has methodological flaws and limitations, the committee concluded that, when considered collectively, it indicates a positive relationship between higher levels of sodium intake and risk of CVD. This evidence is consistent with existing evidence on blood pressure as a surrogate indicator of CVD risk. Conclusion 2: The committee determined that evidence from studies on direct health outcomes is inconsistent and insufficient to conclude that lowering sodium intakes below 2,300 mg per day either increases or decreases risk of CVD outcomes (including stroke and CVD mortality) or all-cause mortality in the general U.S. population.

		• Diabetes (2 obs. studies) • Gastrointestinal cancer (8 obs. studies)	
What is the effect of reducing dietary sodium intake in individuals with hypertension, pre-hypertension, those aged 51 years and older, African Americans, and individuals with diabetes, chronic kidney disease, or congestive heart failure, compared to habitual intake on health outcomes?	Cardiovascular disease (CVD), including stroke CVD mortality and all-cause mortality, congestive heart failure (CHF), chronic kidney disease (CKD), diabetes, cancer, and "other" outcomes, such as asthma and depression.	4 RCTs; 35 observational (cohort or case-control) studies • CVD, Stroke and Mortality (4 RCTS, 22 obs. studies) • Kidney disease (2 obs. studies) • Metabolic syndrome (2 obs. studies) • Diabetes (2 obs. studies) • Gastrointestinal cancer (8 obs. studies)	Conclusion 1: The committee concluded that the available evidence suggests that low sodium intakes may lead to higher risk of adverse events in mid- to late-stage CHF patients with reduced ejection fraction and who are receiving aggressive therapeutic regimens. Because these therapeutic regimens were very different than current standards of care in the United States, the results may not be generalizable. Similar studies in other settings and using regimens more closely resembling those in standard U.S. clinical practice are needed. Conclusion 2: The committee concluded that, with the exception of the CHF patients described above, the current body of evidence addressing the association between low sodium intake and health outcomes in the population subgroups considered is limited. The evidence available is inconsistent and limited in its approaches to measuring sodium intake. The evidence also is limited by small numbers of health outcomes and the methodological constraints of observational study designs, including the potential for reverse causality and confounding. The committee further concluded that, while the current literature provides some evidence for adverse health effects of low sodium intake among individuals with diabetes, CKD, or preexisting CVD, the evidence on both the benefit and harm is not strong enough to indicate that these subgroups should be treated differently from the general U.S. population. Thus, the committee concluded that the evidence on direct health outcomes does not support recommendations to lower sodium intake within these subgroups to, or even below, 1,500 mg per day.
IOM, Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate, 2005			
What is the AI for sodium intake? (*Because insufficient data from dose-response trials, an Estimated Average Requirement (EAR) could not be established, and thus a Recommended*	To ensure that the overall diet provides an adequate intake of other important nutrients and to cover sodium sweat losses	>400 citations	Adults (19-50 yrs): The AI for sodium is set for young adults at 1.5 g (65 mmol)/day (3.8 g of sodium chloride) to ensure that the overall diet provides an adequate intake of other important nutrients and to cover sodium sweat losses in unacclimatized individuals who are exposed to high temperatures or who become physically active as recommended in other DRI reports. Older adults: The AI for sodium for older adults and the elderly is somewhat less, based on lower energy intakes, and is set at 1.3 g (55 mmol)/day for men and women 50 through 70 years of age, and at 1.2 g (50 mmol)/day for those 71 years of age and older Children 1– 18 : Given that little data are available indicating that in normal children, inadequate sodium intakes result in specific identifiable markers, and that, as with adults, normal kidney function can maintain sodium balance at extremes of sodium intake, the AI is set based on meeting

Dietary Allowance could not be derived)			nutrient needs for other essential nutrients. The AI is thus extrapolated down from the adult AI of 1.5 g/day (65 mmol/day) using relative energy intake, that is, the average of median energy intake levels of the age groups for adults and for children as the basis for extrapolation.
What is the recommended UL for sodium intake?	Blood pressure, stroke and CHD; left ventricular mass; calcium excretion, bone mineral density, and kidney stones; pulmonary function; gastric cancer	>400 citations	Adults (19- 50 yrs): Because the relationship between sodium intake and blood pressure is progressive and continuous without an apparent threshold, it is difficult to precisely set a UL, especially because other environmental factors (weight, exercise, potassium intake, dietary pattern, and alcohol intake) and genetic factors also affect blood pressure. For adults, a UL for sodium of 2.3 g (100 mmol)/day is set, equivalent to a total of 5.8 g/day of sodium chloride. In dose-response trials, this level was commonly the next level above the AI that was tested. The equivalent UL for chloride is 3.5 g. It should be noted that the UL is not a recommended intake and, as with other ULs, there is no demonstrated benefit to consuming levels above the AI. Individuals who are most sensitive to the blood pressure effects of increased sodium intake (e.g., older persons, African Americans, and individuals with hypertension, diabetes, or chronic kidney disease): Their UL for sodium may well be lower. These groups also experience an especially high incidence of blood pressure-related cardiovascular disease. Individuals who are unacclimatized to prolonged physical activity in a hot environment: Their needs may exceed the UL because of sodium sweat losses Children and adolescents (1- 18 yrs) The ULs for children are extrapolated from the adult UL of 2.3g (100 mmol)/day based on these estimated energy intakes, after rounding. Since the estimated energy intake for adolescents is in the same range as adults, the ULs for this age group are the same as those for adults.

References Included in Review

1. National Heart, Lung, and Blood Institute. Lifestyle Interventions to Reduce Cardiovascular Risk: Systematic Evidence Review from the Lifestyle Work Group, 2013. Bethesda, MD: U.S. Department of Health and Human Services, National Institutes of Health, 2013. Available from: http://www.nhlbi.nih.gov/guidelines/cvd_adult/lifestyle/index.htm

   Associated Lifestyle Guideline:

   Eckel RH, Jakicic JM, Ard JD, de Jesus JM, Houston Miller N, Hubbard VS, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2014;63(25 Pt B):2960-84. PMID: 24239922. http://www.ncbi.nlm.nih.gov/pubmed/24239922

2. Institute of Medicine. Sodium intake in populations: Assessment of evidence. Washington, DC: The National Academies Press; 2013. Available from: http://www.nap.edu/catalog.php?record_id=18311

3. Institute of Medicine. Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate. Washington, DC: The National Academies Press; 2005. Available from: http://books.nap.edu/openbook.php?record_id=10925

Additional References

4. Mente A, O'Donnell MJ, Rangarajan S, McQueen MJ, Poirier P, Wielgosz A, et al. Association of urinary sodium and potassium excretion with blood pressure. N Engl J Med. 2014;371(7):601-11. PMID: 25119606. http://www.ncbi.nlm.nih.gov/pubmed/25119606.