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CLINICAL RESEARCH STUDY

Sodium Intake and Mortality in the NHANES II Follow-up Study

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ABSTRACT

PURPOSE: US Dietary Guidelines recommend a daily sodium intake ≤2300 mg, but evidence linking sodium intake to mortality outcomes is scant and inconsistent. To assess the association of sodium intake with cardiovascular disease (CVD) and all-cause mortality and the potential impact of dietary sodium intake <2300 mg, we examined data from the Second National Health and Nutrition Examination Survey (NHANES II).

METHODS: Observational cohort study linking sodium, estimated by single 24-hour dietary recall and adjusted for calorie intake, in a community sample (n = 7154) representing 78.9 million non-institutionalized US adults (ages 30-74). Hazard ratios (HR) for CVD and all-cause mortality were calculated from multivariable adjusted Cox models accounting for the sampling design.

RESULTS: Over mean 13.7 (range: 0.5-16.8) years follow-up, there were 1343 deaths (541 CVD). Sodium (adjusted for calories) and sodium/calorie ratio as continuous variables had independent inverse associations with CVD mortality ($P = .03$ and $P = .008$, respectively). Adjusted HR of CVD mortality for sodium <2300 mg was 1.37 (95% confidence interval [CI]: 1.03-1.81, $P = .033$), and 1.28 (95% CI: 1.10-1.50, $P = .003$) for all-cause mortality. Alternate sodium thresholds from 1900-2700 mg gave similar results. Results were consistent in the majority of subgroups examined, but no such associations were observed for those <55 years old, non-whites, or the obese.

CONCLUSION: The inverse association of sodium to CVD mortality seen here raises questions regarding the likelihood of a survival advantage accompanying a lower sodium diet. These findings highlight the need for further study of the relation of dietary sodium to mortality outcomes.

KEYWORDS: Sodium; Cardiovascular disease; Mortality; Dietary guidelines; NHANES

The US Department of Health and Human Services and the Department of Agriculture 2005 nutrition guidelines recommend that adult Americans consume less than 2300 mg of sodium (to convert sodium values to mmol, divide by 23) per day to ". . .prevent or delay the onset of high blood pressure. . ." and ". . .to lower elevated blood pressure."[1] These new guidelines, slightly below the previously recommended 2400 mg per day, also recommend that individuals with hypertension, or who are black, or middle-aged and older, consume no more than 1500 mg of sodium per day.[1]

The guidelines are largely based on the blood pressure reduction associated with lower sodium in short-term clinical trials.[2,3] However, these trials could not assess the long-term cardiovascular morbidity and mortality consequences of lower sodium. Of concern is that lower sodium intake can generate increased activity of the renin-angiotensin and sympathetic nervous systems, and possibly increased insulin resistance, and each of these could have adverse cardiovascular effects.[4-6] Morbidity and mortality outcomes will be influenced by unfavorable and favorable

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effects, as well as the unknown consequences of a diet altered to achieve lower sodium intake. In the absence of clinical trial data, several observational studies, with contradictory results, are available.[7-14]

In this setting, the second National Health and Nutrition Examination Survey[15] (NHANES II) provides a fresh opportunity to assess the relationship between dietary sodium intake and long-term mortality, by examining the experience of a representative sample of the US civilian population.

CLINICAL IMPLICATIONS

- Dietary guidelines recommend sodium restriction despite absence of clinical trial data.
- This observational study found significant associations of lower sodium with increased cardiovascular disease mortality.
- No subgroup observed to experience benefit from lower sodium diet.
- These data suggest the safety and effectiveness of lower dietary sodium merit further study.

METHODS

Study Population

Detailed methods of NHANES II, conducted by the National Center for Health Statistics, are described elsewhere.[15] Baseline interview and examination data were collected in 1976-1980 for 20 322 NHANES II participants aged 6 months to 74 years. The NHANES II Mortality study assessed vital status for 9250 NHANES II participants aged 30 to 74 years at entry.[16] To avoid confounding due to preexisting disease at entry, we excluded 1483 (16%) with self-reported history of heart disease or stroke, 344 reporting a low salt diet for medical reasons, and 21 who died with ≤6 months follow-up. To limit the influence of extreme, possibly invalid values, we excluded individuals reporting either the highest or lowest 1% of sodium or calories (n = 248). The remaining 7154 constituted the study sample.

Baseline Measurements

Baseline information included medical history, standardized physical examination, laboratory tests, anthropometric measures, and nutrient intakes computed from one 24-hour dietary recall obtained by trained interviewers. Sample mean blood pressure (BP) (127/81 mm Hg) was imputed for 18 individuals (0.25%) with missing values. Individual estimates of sodium added in cooking or at the table were not available. Energy consumption (kilocalories) will be referred to as calories in this report.

Sociodemographic characteristics included age, sex, race and education. Race was dichotomized as white and nonwhite, and education as less than high school graduate versus else. Body mass index (BMI) was calculated from height and weight (kg/m^2) and categorized as normal, overweight and obese (<25, ≥25 and <30, ≥30 kg/m^2, respectively) for subgroup analysis. Using 3-level physical activity scales, those reporting the highest "much exercise" for recreational activity or "very active" for nonrecreational activity, were coded as physically active, with all others as reference. Alcohol use was dichotomized as yes/no for regular weekly use of any alcoholic beverage and alternately as a continuous variable (drinks per week). Smoking was dichotomized as yes/no for current smoking.

Mortality Follow-up

The NHANES II Mortality Study ascertained vital status through December 31, 1992 from the National Death Index and the Social Security Administration Death Master File.[16] Those not found to be deceased were assumed alive at that date. Death certificates were ordered to resolve indeterminate matches. Underlying cause of death was coded according to the *International Classification of Disease 9th revision*[17] (ICD-9): CVD 390-459; coronary heart disease (CHD) 410-414; cerebrovascular 430-438.

Statistical Analysis

Sodium and sodium/calorie ratio were analyzed as continuous variables. Sodium was also dichotomized at 2300 mg (100 mmol), the guidelines threshold that was also close to the sample median (2360 mg). Quartiles of sodium were also created (≤1645, 1645-2359, 2360-3345, ≥3346 mg). Bivariate associations with dichotomized sodium were assessed with *t* test and chi-squared for continuous and categorical variables, respectively. Means are reported ± standard errors.

Age and sex adjusted mortality rates expressed as events per 1000 person-years for coronary heart disease (CHD), cerebrovascular cardiovascular disease (CVD) and all causes were calculated for lower and upper sodium levels.

Cox proportional hazards regression models[18] were constructed to predict time to cause-specific and all-cause mortality, simultaneously adjusting for sex, race, treatment for hypertension, smoking, history of diabetes, alcohol use, education and physical activity as indicator variables; and age, BMI, cholesterol, systolic BP, and dietary potassium as continuous variables. Adjustment for energy intake (calories) was done with three alternate methods: the standard multivariate method of adding calories as a continuous covariate to the model, the sodium density method of using sodium/calorie ratio in the model instead of sodium and calories as separate variables, and the residuals method introduced by Willett and Stampfer.[19] In the Willett and Stampfer method (designed to reduce the correlation of sodium and calories), sodium is regressed on calories, and for each observation the calculated regression residual is added to its modeled expected sodium value. The correlation of this residuals-adjusted sodium with calories was reduced to a negligible

Table 1 Baseline Characteristics by Sodium Group*

Variable	Sodium < 2300 n = 3443	Sodium ≥ 2300 n = 3711	Total n = 7154	P
Age (years)	49 ± 0.37	47 ± 0.23	48 ± 0.26	<.001
Cholesterol (mg/dL)	223 ± 1.4	220 ± 1.3	222 ± 1.1	.09
Dietary sodium intake (mg/day)†	1579 ± 9.8	3696 ± 20	2718 ± 23	<.001
Dietary calories (kcal)	1411 ± 12	2248.27 ± 22	1861 ± 15	<.001
Dietary sodium/calories (mg/kcal)	1.2 ± 0.01	1.8 ± 0.01	1.5 ± 0.01	<.001
Dietary potassium (mg/day)	1942 ± 24	2814 ± 32	2411 ± 23	<.001
Body mass index (BMI kg/m^2) (%)	25.9 ± 0.10	25.6 ± 0.08	25.7 ± 0.07	.02
BMI (%)				.07
<25 kg/m^2	49	51	50	
25-29.9 kg/m^2	34	35	35	
≥30 kg/m^2	17	14	16	
Weight (lb)	156 ± 0.69	164 ± 0.48	160 ± 0.43	<.001
Race				
White (%)	87	90	88	<.001
Black (%)	11	7	9	
Other (%)	2	3	2	
Education < high school (%)	36	29	32	<.001
Male (%)	31	60	47	<.001
Smoker (%)	34	38	36	.01
BP >140/90 mm Hg (%)	31	30	30	.79
Treatment for hypertension (%)	4.1	3.7	3.9	.44
Systolic BP (mm Hg)	127 ± 0.23	127 ± 0.67	127 ± 0.60	.52
Diastolic BP (mm Hg)	81 ± 0.55	82 ± 0.55	81 ± 0.52	.36
History of diabetes (%)	3.8	2.6	3.1	.02
Physically active (%)	38	45	42	<.001
Alcohol (%)	40	47	44	<.001

BMI = body mass index; lb = pounds; BP = blood pressure.

*Results for continuous variables are reported as mean values (with standard errors) with *P* values calculated by *t* test between the sodium categories. Categorical variables are reported as percentages with *P* values calculated by chi-square. Because of rounding, not all percentages total 100. All results take into account the complex sampling design of NHANES II.

†To convert values to mmol divide by 23.

r <0.001 (P >.99). The residuals-adjusted sodium value was also dichotomized at its median.

Interaction product terms of sodium with each covariable were created and separately tested in the full model, including main effects terms. To further assess potential heterogeneity or inadequately adjusted confounding, separate adjusted Cox models were constructed within subgroups defined by each covariable.

For all analyses, P values are 2-tailed, with alpha <0.05. Statistical analyses were performed with STATA (Version 8; StataCorp LP, College Station, Tex) and SUDAAN (Version 9; Research Triangle Institute, Research Triangle Park, NC) software, accounting for the NHANES II complex sampling design.

RESULTS

The 7154 individuals who met our preinclusion and exclusion criteria represented 78.9 million noninstitutionalized US adults aged 30-74 years at the time of study entry. During 13.7 years mean follow-up (range 0.5-16.8) there were 1343 deaths, of which 541 were for CVD, including 282 CHD and 79 cerebrovascular. Dietary sodium intake (mean = 2718 ± 23 mg) as a continuous variable was directly correlated with calories (r = 0.66, P <.001), weight (r = 0.15, P <.001), and physical activity (r = .07, P <.001) but had an inverse association with BMI (r = −0.03, P = .02).

Table 1 shows the varied CVD risk profiles of the dichotomized sodium groups. Those with sodium <2300 (n = 3443) were more likely to be older, to have history of diabetes, less education, slightly higher cholesterol and BMI and were less likely to be physically active or drink alcohol. Conversely, those with sodium ≥2300 (n = 3711) were more likely to be male, white and smokers and had substantially higher calorie and potassium intake. There were no discernable blood pressure differences.

When dietary sodium was expressed as a continuous variable (per 1000 mg), it had a statistically significant (P = .03) inverse association with CVD mortality after adjusting for calories and all above-mentioned covariables, meaning that lower sodium values were associated with greater CVD mortality (Table 2). Using the residuals-adjusted sodium as a continuous variable gave the exact same result. Sodium/calorie ratio also showed a statistically significant (P = .008) inverse association with CVD mortality. Inverse associations with all-cause mortality of continuous sodium and sodium/calorie ratio were consistent.

Those with dietary sodium ≤2300 mg had significantly higher age-sex adjusted mortality rates for CVD

Table 2 Adjusted Mortality Hazard Ratios for Dietary Sodium Measures*

Mortality Outcome	Sodium Measure	Hazard Ratio	95 % Confidence Interval	*P* Value
Cardiovascular disease	Sodium per 1000 mg†‡	0.89	0.80, 0.99	.03
	Sodium mg per calorie	0.80	0.68, 0.94	.008
	Sodium <2300 mg	1.37	1.03, 1.81	.03
	Sodium <residuals adjusted median	1.22	1.01, 1.49	.04
All-cause	Sodium per 1000 mg	0.93	0.87, 1.00	.06
	Sodium mg per calorie	0.89	0.79, 1.00	.05
	Sodium <2300 mg	1.28	1.10, 1.50	.003
	Sodium <residuals adjusted median	1.12	0.97, 1.30	.13
Coronary heart disease	Sodium per 1000 mg	0.91	0.79, 1.05	.21
	Sodium mg per calorie	0.79	0.63, 0.99	.04
	Sodium <2300 mg	1.21	0.87, 1.68	.25
	Sodium <residuals adjusted median	1.19	0.93, 1.52	.16
Cerebrovascular disease	Sodium per 1000 mg	0.95	0.75, 1.21	.68
	Sodium mg per calorie	0.91	0.60, 1.37	.63
	Sodium <2300 mg	1.78	0.89, 3.55	.10
	Sodium <residuals adjusted median	1.05	0.58, 1.88	.87

*All models adjusted for age, sex, race, smoking, alcohol use, systolic blood pressure, anti-hypertensive treatment, body mass index, education <high school, physical activity, body mass index, dietary potassium, history of diabetes, serum cholesterol. Models for sodium (continuous) and sodium <2300 mg also adjusted for calories.

†To convert values to mmol divide by 23.

‡Results for residuals adjusted sodium as a continuous variable were exactly the same as without that additional adjustment.

and all causes compared with ≥2300 mg (Figure 1). CHD mortality rates per 1000 person years for <2300 and ≥2300 mg were 3.14 and 2.74, respectively ($P = .26$). Cerebrovascular mortality rates were 0.99 and 0.66, respectively ($P = .07$). Using the residuals method calorie-adjusted median sodium, instead of 2300 mg, showed age-sex adjusted rates for CVD mortality as 6.06 and 4.97 for lower and higher sodium, respectively ($P = .03$). For all-cause, CHD, and stroke mortality, using the residuals calorie-adjusted median attenuated the differences that were not statistically significant.

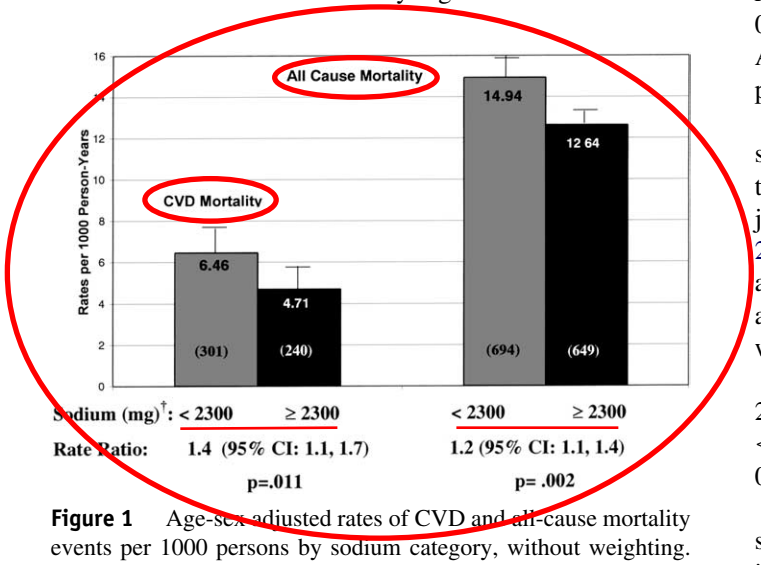

Figure 1 Age-sex adjusted rates of CVD and all-cause mortality events per 1000 persons by sodium category, without weighting. Numbers of events are in parentheses. †To convert values to mmol per day divide by 23.

Adjusting for calories and all previously mentioned CVD risk factors, sodium intake <2300 mg was associated with 37% greater risk of CVD mortality ($P = .03$) and 28% increased risk of all-cause mortality ($P = .003$) (Table 2). Residuals method, calorie-adjusted median sodium was similarly associated with CVD mortality ($P = .04$), but the association with all-cause mortality was not statistically significant ($P = .13$). For quartiles of sodium, using the highest quartile as reference, CVD mortality hazard ratios (HRs) were 1.31 (95% confidence interval [CI]: 0.90-1.89, $P = .14$), 1.39 (95% CI: 0.91-2.11, $P = .11$), 0.89 (95% CI: 0.64-1.25, $P = .49$) for quartiles 1, 2, and 3, respectively. All-cause, CHD, and stroke mortality followed a similar pattern.

There were no statistically significant interactions of sodium with any covariable. Subgroup analyses by each of the covariables separately showed consistency for the majority of subgroups in these fully adjusted models (Figure 2). However, association of sodium with CVD was not apparent among those <55 years old and was substantially attenuated for those with less than median weight and those with median or higher cholesterol.

Non-whites and the obese (BMI ≥30) were the only 2 of 26 subgroups examined whose HR for lower sodium was <1, and neither was statistically significant ($P = .70$ and 0.83, respectively).

Stratification by median calories showed a statistically significant association of lower sodium with CVD mortality in the lower calorie half (HR: 1.56; 95% CI: 1.08-2.27, $P = .02$) and a consistent, albeit attenuated and not statistically

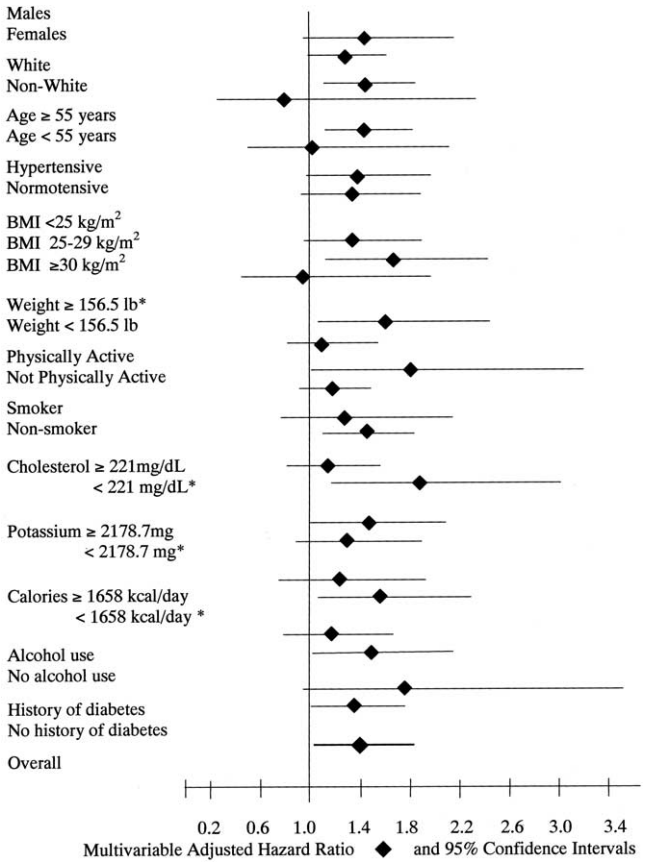

Figure 2 Hazard ratios of CVD mortality for sodium intake <2300 mg in selected subgroups estimated by Cox models adjusting for age, sex, race, smoking, alcohol use, systolic blood pressure, anti-hypertensive treatment, body mass index, education < high school, physical activity, calories, dietary potassium, history of diabetes, serum cholesterol except for the factor defining the subgroup. * Denotes median values.

significant association in the upper calorie half (HR: 1.22; 95% CI: 0.77-1.94, $P = .39$).

Sensitivity analyses for the sample without excluding any sodium or calorie values, for a subset excluding individuals with the highest or lowest 2.5% of sodium or calories, when deleting 18 cases with imputed BP, and when using a continuous rather than dichotomized alcohol measure, all gave results similar to the primary analyses. For the whole sample, alternate thresholds ranging from 1900 to 2700 mg in 100-mg increments, as well as the median 2368 mg, all showed consistent statistically significant associations of CVD risk with lower sodium and an HR range from 1.35 ($P = .03$) for 1900 mg to 1.42 ($P = .04$) for 2700 mg. Only 20% of the study sample had daily sodium intake ≤1500 mg. In a subgroup comprised of black, hypertensive or middle-aged individuals, for whom the recommended sodium threshold is 1500 mg,[1] the increased CVD mortality risk associated with that threshold (with ≥2300 mg as reference) was not statistically significant (HR: 1.16; 95% CI: 0.87-1.55, $P = .30$). This association was borderline significant, however, among the whole sample with sodium <1500 mg (HR: 1.32; 95% CI: 0.99-1.74, $P = .05$).

DISCUSSION

The principal finding in this representative sample of US adults is that sodium intake, measured as a continuous variable and adjusted for calories by each of three distinct methods, had a statistically significant and inverse association with CVD mortality, independent of known cardiovascular risk factors. Results were consistent for all-cause, CHD, and cerebrovascular-specific mortality, although these latter associations were not statistically significant. In addition, individuals reporting consumption of sodium consistent with the most recent US dietary guidelines of ≤2300 mg had 37% higher CVD mortality and 28% higher mortality from all causes, compared with those whose reported sodium intake exceeded 2300 mg.

Although an inverse association was not apparent in those <55 years old, the obese, or among non-whites, and was much attenuated in those with less than median weight and those with greater than median serum cholesterol, it was consistent in 22 of the 27 subgroups examined along with the group as a whole. Most importantly, sodium ≤2300 mg was not significantly associated with better CVD mortality outcome in any subgroup.

Eight previous observational studies examined clinical outcomes associated with sodium levels.[7-14] Sodium intake was inversely and significantly associated with higher CVD mortality for the entire sample of NHANES I,[10] with myocardial infarction among male participants in a prospective cohort study of treated hypertensives[8] and with all-cause mortality in men in the Scottish Heart Study.[9] By contrast, a statistically significant direct association of sodium with CVD and all-cause mortality was observed in a Finnish community sample,[13] among the overweight subset of NHANES I,[11] with CHD incidence among women in the Scottish study,[9] and with stroke in a community sample in Japan.[14] No statistically significant associations were reported either among Japanese-American men of the Honolulu Heart Study[7] or in the MRFIT cohort.[12]

Although the available data can best be described as inconsistent and inconclusive, some of the variability in the results may be related to differences in characteristics of the studied populations. For example, while a significant association was observed in the Finnish sample as a whole, when examined by sex the elevated hazard ratios were statistically significant for males but not females. For the Finnish males[13] and the Japanese sample as a whole,[14] mean daily sodium intake was about 5000 mg. This is considerably higher than observed for US adults in NHANES I (2022 mg),[10] this study (2642 mg), or among Chicago adults in the Intersalt study (3222 mg), the latter determined by 24-hour urinary excretion.[20] Perhaps the association of sodium with CVD differs at markedly different levels of sodium intake.

The overweight subgroup of NHANES I[11] stands out as an inconsistent finding in studies carried out in moderate sodium intake settings. In the present study, overweight and normal weight subgroups had findings similar to the group

as a whole, and obese individuals showed no association. Authors of the earlier study did not find any direct association of sodium with CVD or mortality outcomes in the 72% of their sample who were not overweight, nor in any other subgroup that could have been defined by a dozen other covariables. Perhaps subgroup multiplicity might have played a role.[21] To date, there have been no clinical trials with sufficient data to lend support one way or the other regarding the effect of sodium restriction on CVD morbidity or mortality.[22]

Study Limitations

Our study has several limitations. There was only a single sodium measure at baseline—a limitation shared by all the longitudinal studies. Also, there was no quantitative measure of table or cooking salt that might have been added. Assessments of usual dietary intake and particularly of sodium are difficult, and the 24-hour dietary recall may be an imprecise estimation of actual consumption.[23] Mean sodium intake in this study was only 18% lower than that observed among Chicago residents by the Intersalt study, which measured sodium by 24-hour urinary excretion.[20] If one assumes that table and cooking salt can add as much as 11%,[24] this difference from the Intersalt value might actually fall to about 9%.

A uniform underestimation of actual dietary intake by the 24-hour recall would not differentially bias the results. The possibility that there was a differential bias in reporting food intake according to BMI or other CVD risk factors is mitigated by sub-group analysis by BMI, statistical adjustment for the measured CVD risk factors, and by the use of four distinct methods of adjusting for calories. Adjusting for calories as a covariable, or with the density method, the residuals method, or by stratification all gave consistent results.

The *P* values for analyses using CHD and cerebrovascular disease outcomes were, for the most part, not statistically significant. However, with smaller numbers of events in these specific classifications, statistical power was substantially lower. For death certificate data, the more specific the outcome, the greater the chance of measurement error. Nonetheless, the direction and magnitude of the point estimates were consistent with CVD and all-cause outcomes. This also applied to the quartile analysis.

It is possible that those defined as consuming <2300 mg had actually consumed more or less. However, it is important to note that individuals from the general public trying to conform to sodium guidelines will not assess their sodium intake by 24-hour urinary excretion. It is much more likely they will try to apply food label values to a recall of their food intake—a method that resembles the 24-hour dietary recall of NHANES. Thus, the 2300-mg classification used in our study might be a reasonable approximation of the target that individuals would aim for when assessing their dietary intake under real life circumstances. As is usually the case in observational studies, the two main comparison groups were not balanced in baseline characteristics, including sex, potassium, and alcohol, among others. We attempted to account for the imbalance both by multivariable adjustment and by subgroup analyses, which gave consistent results for the majority of subgroups. However, we recognize that the potential problem of confounding, including from unmeasured variables, cannot be fully overcome in an observational study. Finally, we were unable to assess the impact of any genetic variability that is likely to introduce heterogeneity with regard to the impact of sodium on health outcomes.[25]

Study Strengths

This study has several important strengths. The sample is large and was constructed to represent the US civilian, noninstitutionalized population. Long follow-up resulted in a large number of endpoints. The adjusted hazard ratios of CVD and all-cause mortality per 1000 mg of sodium (0.9) was approximately the same as those observed in NHANES I.[10] The internal validity of the sodium measure is reflected in the anticipated correlation with calories, weight and physical activity.

These findings were consistent, whether sodium was assessed as a continuous or dichotomous variable and in multiple subgroups. Although we have fixed special attention on the 2300-mg threshold for comparison to recent guidelines, this happened to be very close to the median value of this sample (2360 mg) and median-based analyses yielded indistinguishable results. Further, the use of alternate thresholds ranging from 1900 to 2700 mg in 100-mg increments in sensitivity analyses all gave consistent results.

The recently revised recommendation in the US government Dietary Guidelines for Americans, 2005, is that all adults should reduce sodium intake to below 2300 mg/day.[1] It is justified primarily on the basis of well-documented effects on blood pressure[2,3] and the belief that the adverse consequences of sodium restriction pose no important safety concern.[26] There are, nevertheless, several plausible reasons to question the validity of the assumption of safety. Reduced-sodium diet stimulates the renin angiotensin system, and elevated plasma renin activity has been associated with increased risk of myocardial infarction.[4] Lower sodium has been associated with stimulation of the sympathetic nervous system[5,27] that, in turn, has been associated with adverse CVD and mortality outcomes.[28] Sodium restriction may also influence insulin resistance either directly[6,29] or indirectly through sympathetic nervous system elevation.[30,31] To what extent, if any, these potential mechanisms may mediate sodium intake and CVD outcomes is unknown and is subject to debate based on a paucity of data. Nonetheless, the possibility of such adverse effects cannot be dismissed a priori.

The close correlation between sodium intake and total energy intake suggests that sodium may also be associated with essential nutrients that were not measured.

Lower sodium may be a marker for a less than optimal overall diet.

Implications

Observational studies have inherent limitations and no single observational study can confirm a causal inference. Nor is it possible to infer from these data what might have occurred if there had been an intervention to alter sodium intake. On the other hand, basing a lower sodium recommendation primarily on intermediate effects such as blood pressure reduction is also unsatisfactory. Unintended health consequences can result from seemingly reasonable expectations. For example, earlier recommendations to restrict weight gain in pregnancy were later found to increase infant mortality.[32] In the case of sodium, extrapolations from positive effects on blood pressure may be offset by extrapolations from potentially adverse effects on the sympathetic nervous system, the renin-angiotensin system, insulin resistance, and the potential that other important nutrients might be decreased when free-living individuals alter diets to decrease sodium. In the absence of a definitive clinical trial, additional well-designed observational studies that examine clinical outcomes merit consideration.

The data here cannot sustain a conclusion that lower sodium is harmful. However, these findings, along with the inconsistent results of other epidemiologic studies, and the propensity for substantial variability among individuals, do not lend support to any universal prescription for salt intake. More likely, optimal sodium intake will vary based upon genetic, behavioral, and environmental circumstances.

In sum, the inverse associations of sodium to CVD mortality observed in this large, nationally representative sample, raise questions regarding the likelihood that a survival advantage will necessarily result from a universal recommendation for a lower dietary sodium intake. These findings highlight the need for further studies that go beyond intermediate outcomes like blood pressure, to convincingly establish the relation of dietary sodium to mortality.

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