

DIETARY SURVEYS AND NUTRITIONAL EPIDEMIOLOGY

High sodium:potassium intake ratio increases the risk for all-cause mortality: the REasons for Geographic And Racial Differences in Stroke (REGARDS) study

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Abstract

Increased dietary Na intake and decreased dietary K intake are associated with higher blood pressure. It is not known whether the dietary Na:K ratio is associated with all-cause mortality or stroke incidence and whether this relationship varies according to race. Between 2003 and 2007, the REasons for Geographic And Racial Differences in Stroke (REGARDS) cohort enrolled 30 239 black and white Americans aged 45 years or older. Diet was assessed using the Block 98 FFQ and was available on 21 374 participants. The Na:K ratio was modelled in race- and sex-specific quintiles for all analyses, with the lowest quintile (Q1) as the reference group. Data on other covariates were collected using both an in-home assessment and telephone interviews. We identified 1779 deaths and 363 strokes over a mean of 4.9 years. We used Cox proportional hazards models to obtain multivariable-adjusted hazard ratios (HR). In the highest quintile (Q5), a high Na:K ratio was associated with all-cause mortality (Q5 *v.* Q1 for whites: HR 1.22; 95 % CI 1.00, 1.47, *P* for trend = 0.084; for blacks: HR 1.36; 95 % CI 1.04, 1.77, *P* for trend = 0.028). A high Na:K ratio was not significantly associated with stroke in whites (HR 1.29; 95 % CI 0.88, 1.90) or blacks (HR 1.39; 95 % CI 0.78, 2.48), partly because of the low number of stroke events. In the REGARDS study, a high Na:K ratio was associated with all-cause mortality and there was a suggestive association between the Na:K ratio and stroke. These data support the policies targeted at reduction of Na from the food supply and recommendations to increase K intake.

Key words: Stroke: Death: Race: Sodium

Introduction

Since the turn of the twentieth century, reducing Na intake has been a key target for the prevention of hypertension, a major

risk factor for stroke^(1,2). Although Na occurs naturally in food, the excess Na ingested in Western cultures comes largely from processed food. Reduction of dietary Na is once again

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Abbreviations: HR, hazard ratio; REGARDS, REasons for Geographic And Racial Differences in Stroke.



gaining momentum with new recommendations from the United States Department of Agriculture⁽³⁾ and state organisations introducing Na reduction campaigns^(4,5). Despite abundant research suggesting that lower dietary Na would decrease hypertension and stroke⁽⁶⁾, Na intake in the USA remains well above recommended levels, with only 5.5% of Americans meeting United States Department of Agriculture targets⁽⁷⁾. Also, dietary Na may contribute to the higher rates of stroke and stroke mortality observed in black Americans compared with white Americans⁽⁸⁾.

In contrast with Na, increased dietary K may reduce the burden of hypertension and stroke. Increased K has been shown to lower blood pressure and this beneficial effect may be greater in the setting of a high-Na diet^(9–12). In fact, US veterans switching from regular salt to a K-enriched salt experienced reduced CVD mortality⁽¹³⁾. Dietary K may also contribute to racial differences in stroke and stroke mortality because black Americans have a lower K intake than white Americans⁽¹⁴⁾.

Taken together, the dietary Na:K ratio may explain demographic differences in stroke and stroke mortality in the USA. Using the ratio provides a means of balancing the detrimental effects of Na and beneficial effects of K in one measure. Recent analyses using mortality follow-up from the National Health and Nutrition Examination Survey demonstrated that the dietary Na:K ratio was more strongly associated with CVD mortality than Na alone, but lacked power to examine this association by race⁽¹⁵⁾. Very little is known about the question whether the dietary Na:K ratio is associated with all-cause mortality and stroke incidence and whether these relationships differ across racial groups.

The primary hypothesis of this study was that an increased dietary Na:K ratio is associated with greater risk of death and incident stroke and that this association will be stronger in blacks than in whites. To test this hypothesis, we utilised the data from participants of the REasons for Geographic And Racial Differences in Stroke (REGARDS) study, a large population-based prospective cohort study of black and white US adults aged 45 years or older⁽¹⁶⁾.

Experimental methods

Participants

The design and objectives of the REGARDS study have been described previously⁽¹⁶⁾. By design, the study oversampled blacks and included an approximately equal representation of men and women. Enrolment began in January 2003 and ended in October 2007. Approximately half of the participants were recruited from the 'Stroke Belt' (states of North Carolina, South Carolina, Georgia, Tennessee, Alabama, Mississippi, Arkansas and Louisiana). The REGARDS study participants were identified using a commercial, nation-wide list of over 250 million individuals in the USA (Genesys Incorporated). A trained interviewer contacted households by telephone, and one resident per household aged 45 years or older was randomly screened for eligibility. The response rate (the percentage agreeing to be interviewed among known eligible

candidates contacted after adjustment for those of unknown eligibility) was 41%, which is similar to other research studies that initially contacted participants by telephone^(17,18). Exclusion criteria were: race other than black or white; active treatment for cancer; medical conditions preventing long-term participation; cognitive impairment as subjectively judged by the telephone interviewer; staying in, or on a waiting list for, a nursing home; and inability to communicate in English. This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human subjects/patients were approved by the Institutional Review Boards at the University of Alabama Birmingham. Written informed consent was obtained from all subjects/patients.

Data collection and covariates

Data were collected during a telephone interview, an in-home visit and via self-administered questionnaires that were left for participants to complete following the in-home visit. Of relevance to the present analysis, the telephone interview included information on age, race, sex, education, household income, current smoking status and a prior diagnosis of hypertension, diabetes mellitus and myocardial infarction. During the in-home study visit, weight, height and waist circumference were measured by following a standardised protocol. BMI was calculated as weight in kilograms divided by height in metres squared. Using the mean of two blood pressure measurements, hypertension was defined as a systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg or self-reported use of anti-hypertensive medication. Participants were asked to fast for 10–12 h prior to the in-home study visit. A blood sample was collected, centrifuged, refrigerated and shipped overnight to the REGARDS central laboratory at the University of Vermont. Total cholesterol, HDL-cholesterol, TAG, serum glucose and serum creatinine were measured by colorimetric reflectance spectrophotometry using the Ortho Vitros Clinical Chemistry System 950IRC instrument (Johnson & Johnson Clinical Diagnostics) and LDL-cholesterol was calculated by the Friedewald equation for individuals with TAG < 10 mmol/l. Dyslipidaemia was defined as a total cholesterol ≥ 6.2 mmol/l, LDL-cholesterol ≥ 4.1 mmol/l, HDL-cholesterol < 1.0 mmol/l for men or < 1.3 mmol/l for women, or lipid-lowering medication use. Diabetes mellitus was defined as fasting glucose ≥ 7.0 mmol/l, ≥ 11.0 mmol/l for participants who did not fast, or self-reported current use of anti-diabetes medication.

Nutritional assessment

At the end of the in-home study visit, participants were asked to complete additional questionnaires which included the Block 98 FFQ (www.Nutritionquest.com). The Block FFQ has been validated for most nutrients, including Na and K, using multiple diet records⁽¹⁹⁾. Different versions of this questionnaire have been studied extensively and validated in diverse populations⁽²⁰⁾. The Block 98 version developed by Block Dietary Data Systems and distributed by NutritionQuest is



an eight-page paper-and-pencil form with more than 150 multiple-choice questions based on 107 food items that can be completed in about 30–40 min. In the REGARDS study, the FFQ was self-administered and participants were asked to report on diet over the past year. Pictures were provided to help identify portion sizes. FFQ, compared with diary techniques, tend to underestimate micronutrient intake and overestimate total energy intake; however, this measurement error is usually uniformly distributed across study subpopulations^(21,22). Therefore, it is generally recommended that estimated nutrient intakes from FFQ should be reported and analysed as either ranked values (i.e. quintiles, etc.) or ratios of two different nutrients rather than absolute values per individual⁽²²⁾. Thus, race- and sex-specific quintiles of dietary Na (mg) and the Na:K ratio were used in all analyses.

Outcome assessment for incident stroke and death

Every 6 months, the REGARDS study ascertains all hospitalisations by participant or proxy interview using methods described elsewhere⁽²³⁾. Personnel specifically pursue medical records for all hospitalisations related to stroke, transient ischaemic attack, stroke symptoms and deaths. Medical records for strokes that occurred before baseline are not pursued. For all participants who have died, study personnel interview the next of kin or other proxy to probe for information relating to the death, inquiring if a stroke not previously reported antedated the death; any hospitalisations prior to death are collected. Once the records are received, they are first reviewed by a trained neurological nurse to verify that the record is complete, and then the information is forwarded to a team of stroke neurologists for review. In the case of deaths, the interview with next of kin or proxy and death certificate or National Death Index data are included. A stroke was defined as focal neurological symptoms lasting greater than 24 h or imaging positive for a new stroke. For this analysis, adjudicated stroke events were available to 1 February 2011 and we included only incident strokes. The REGARDS study is notified of a participant's death by proxies either through the mail or on the telephone during the routine 6-month telephone calls and also uses the Social Security Death Index to look for participants who may have died and for whom we do not have a proxy report of death. For this analysis, death events were available to 1 April 2011. We used all-cause mortality as an outcome in addition to adjudicated stroke.

Statistical analysis

As the association of dietary Na with CVD has been reported to differ by race, we decided *a priori* to stratify analyses for black and white participants. The distribution of participant characteristics was determined for blacks and whites separately. The prevalence and multivariable-adjusted hazard ratios (HR) for incident stroke associated with race- and sex-specific quintiles of the Na:K ratio were calculated using Cox proportional hazards models. Lastly, the prevalence and multivariable-adjusted HR for all-cause mortality were

calculated by sex-specific quintile of the Na:K ratio. Multivariable-adjusted HR were calculated in three steps. In the first step we adjusted for age, race, sex and total energy intake. In the second step we additionally adjusted for BMI, hypertension, diabetes, dyslipidaemia, history of heart disease, smoking, income and education. In the third step, which was only for analyses with stroke as an outcome, we further adjusted for bias in medical record retrieval and extraction⁽²⁴⁾. For the mortality analysis, we performed a sensitivity analysis excluding those who died within 6 months of the baseline visit (as a proxy for terminal illness) and all participants who reported a history of stroke at baseline. As a secondary analysis, the multivariable-adjusted HR for incident stroke and all-cause mortality associated with quintiles of Na were calculated. Additionally, we considered the Na:K ratio as a continuous variable for secondary analyses and examined the HR associated with 1 SD increase in the Na:K ratio. Analyses were performed with SAS version 9.2 software (SAS Institute, Inc.).

Results

Participant characteristics

The REGARDS cohort enrolled 30 239 participants. We excluded 8603 participants because they were missing FFQ data (n 6000) or answered less than 85 % of the FFQ (n 1557) or who had extreme energy intakes (<3347.2 kJ or $>20\,920$ kJ/d for males (n 689) and <2092 kJ or $>18\,828$ kJ/d for females (n 357) (4.184 kJ = 1 kcal)). Compared with blacks (58 %), whites (81 %) were more likely to return the FFQ ($P < 0.001$). College graduates (77 %) were also more likely than non-graduates (55 %) to return the FFQ ($P < 0.001$). Participants who did not return the FFQ had a slightly higher BMI (30.0 (SD 6.4) *v.* 29.1 (SD 3.1) kg/m², $P < 0.001$). Age was not associated with the likelihood of returning the FFQ.

The median Na intake was higher in blacks (median = 0.92 ; interquartile range = 0.43) than in whites (median = 0.83 ; interquartile range = 0.32). Regardless of race, participants with higher dietary Na:K ratios were more likely to be hypertensives, younger, current smokers, obese and to reside in the Southeast (Table 1). Median energy intake increased across quintiles of Na:K ratio as did the total Na intake.

Results on risk of death associated with increasing dietary sodium:potassium ratio

Compared with participants in the lowest quintile of Na:K intake, those in the highest quintile were at increased risk of death (Table 2). In age-, race-, sex- and energy-adjusted models, the HR for death comparing quintile 5 (Q5) to quintile 1 (Q1) of dietary Na:K intake was 1.52 (95% CI 1.31 , 1.76). Adjustment for BMI, hypertension, diabetes, heart disease, smoking, income and education attenuated the association (HR 1.26 ; 95 % CI 1.08 , 1.47). We also examined the dietary Na:K ratio as a continuous variable. For each standard deviation (0.28 mg Na per mg K) increase in the dietary



Table 1. Characteristics of participants by race and quintile (Q) of sodium:potassium ratio in the REasons for Geographic And Racial Differences in Stroke (REGARDS) study*
(Number of participants, percentages, medians, interquartile ranges (IQR) and ranges)

	Q1		Q2		Q3		Q4		Q5	
	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%	<i>n</i>	%
Black participants										
<i>n</i>	1429		1431		1430		1431		1430	
Na:K ratio										
Median	0.56		0.76		0.92		1.09		1.36	
IQR	0.13		0.09		0.09		0.10		0.23	
Range (men)	0.24–0.74		0.74–0.90		0.90–1.05		1.05–1.24		1.24–2.92	
Range (women)	0.16–0.64		0.64–0.81		0.81–0.97		0.97–1.17		1.17–2.49	
Na intake (mg/d)										
Median	1346		1716		2015		2297		2586	
IQR	788		1049		1250		1516		1745	
Energy intake (kJ/d)										
Median	5342		6008		6386		6930		7265	
IQR	3034		3494		4173		4580		4693	
Age 65 years and older	726	51	677	47	626	44	579	40	539	38
Southeast	708	50	695	49	755	53	761	53	796	56
Women	944	66	945	66	944	66	945	66	944	66
Obese	643	45	666	47	715	50	716	50	731	51
History of stroke	104	7.3	83	5.8	92	6.4	94	6.6	96	6.7
History of CAD	213	15	201	14	192	13	169	12	208	15
History of HTN	994	70	1015	71	1017	71	999	70	1043	73
Current smoker	195	14	213	15	213	15	290	20	316	22
White participants										
<i>n</i>	2848		2848		2850		2848		2848	
Na:K ratio										
Median	0.57		0.72		0.83		0.96		1.18	
IQR	0.11		0.07		0.07		0.08		0.19	
Range (men)	0.29–0.69		0.69–0.81		0.81–0.93		0.93–1.08		1.08–2.64	
Range (women)	0.07–0.62		0.62–0.74		0.74–0.86		0.86–1.02		1.02–2.52	
Na intake (mg/d)										
Median	1583		2004		2187		2413		2731	
IQR	817		1025		1077		1213		1585	
Energy intake (kJ/d)										
Median	5803		6574		6859		7232		7613	
IQR	2791		3494		3293		3545		4270	
Age 65 years and older	1718	60	1566	55	1460	51	1428	50	1269	45
Southeast	1529	54	1627	57	1668	59	1743	61	1749	61
Women	1446	51	1446	51	1447	51	1446	51	1446	51
Obese	637	22	750	26	825	29	952	33	1126	40
History of stroke	137	4.8	127	4.5	137	4.8	126	4.4	144	5.1
History of CAD	539	19	537	19	541	19	486	17	533	19
History of HTN	1366	48	1377	48	1405	49	1439	51	1494	52
Current smoker	246	8.6	275	9.7	341	12	360	13	459	16

CAD, coronary artery disease; HTN, hypertension.

* Quintiles are race and sex specific.

Na:K ratio, the risk of death increased by 11 % (HR 1.11; 95 % CI = 1.05, 1.16). Although the *P* value for interaction was not statistically significant, we further examined this association stratified by race based on our *a priori* hypothesis. The risk of each standard deviation increase in dietary Na:K ratio was similar in blacks (HR 1.12; 95 % CI 1.04, 1.21) and whites (HR 1.09; 95 % CI 1.02, 1.16) (Table 2).

Results on risk of incident stroke associated with increasing dietary sodium:potassium ratio

Over a mean of 4.9 years of follow-up, we accumulated 363 stroke events. Although there was a suggestion for increased risk of stroke among individuals in Q5 compared with Q1 of dietary Na:K ratio, this association was not statistically

significant (Table 3) in analysis before or after stratifying by race. In the fully adjusted model comparing Q5 with Q1 of dietary Na:K ratio, the HR of incident stroke was 1.29 (95 % CI 0.94, 1.78). For a 1 SD increase in dietary Na:K ratio, the HR of incident stroke was 1.08 (95 % CI 0.98, 1.20). Similar to the results for death, there was no statistically significant difference by race. In blacks, all quintiles of dietary Na:K intake had a higher risk of incident stroke compared with Q1. This association was not linear. In whites, the association between dietary Na:K intake and incident stroke was fairly flat across quintiles with a slight increase in Q5 *v.* Q1 (HR 1.29; 95 % CI 0.88, 1.90). In a sensitivity analysis limited to those who survived at least 6 months beyond the baseline visit and who did not have a history of stroke at baseline, the results were similar (data not shown).



Table 2. Risk of death associated with increasing sodium:potassium ratio in the REasons for Geographic And Racial Differences in Stroke (REGARDS) study (Hazard ratios (HR) and 95% confidence intervals)

	Quintiles of Na:K ratio*										1 sd increment	
	Q1		Q2		Q3		Q4		Q5		HR	95 % CI
	HR	95 % CI	HR	95 % CI	HR	95 % CI	HR	95 % CI	HR	95 % CI		
Number of deaths	355		327		355		332		410		–	
Mortality rate (per 1000 person-years)	16.6		15.3		16.8		15.7		19.8		–	
Model 1†	1	Reference	0.98	0.85, 1.14	1.15	0.99, 1.33	1.13	0.97, 1.31	1.52	1.31, 1.76	1.19	1.14, 1.25
Model 2‡	1	Reference	0.99	0.85, 1.16	1.10	0.94, 1.29	1.04	0.88, 1.22	1.26	1.08, 1.47	1.11	1.05, 1.16
Stratified analysis <i>P</i> for interaction = 0.447											0.297	
In blacks§	1	Reference	1.15	0.88, 1.50	1.25	0.95, 1.63	1.23	0.94, 1.62	1.36	1.04, 1.77	1.12	1.04, 1.21
In whites§	1	Reference	0.93	0.77, 1.13	1.02	0.84, 1.24	0.92	0.76, 1.13	1.22	1.00, 1.47	1.09	1.02, 1.16

* Quintiles are race and sex specific.

† Model 1 – age, race, sex, total energy intake.

‡ Model 2 – age, race, sex, energy, BMI, hypertension, diabetes, history of heart disease, dyslipidaemia, smoking, income, education and use of statins.

§ For the models stratified by race, model 2 adjustments were used and race was not included in the model.

Results on risk of death and risk of incident stroke associated with increasing dietary sodium

Increasing the dietary Na had a weak, non-linear association with risk of death that was attenuated after adjustment for BMI, hypertension, diabetes, dyslipidaemia, history of heart disease, smoking, income and education (Supplementary Table 1). Comparing Q5 with Q1 of dietary Na, the risk of death associated with increasing dietary Na was stronger for the black participants (HR 1.62; 95 % CI 1.03, 2.55) than for the white participants (HR 0.94; 95 % CI 0.67, 1.30). Dietary Na was associated with incident stroke in a pattern similar to that observed for the dietary Na:K ratio (Supplementary Table 2). Again, a weak non-linear association was observed. Comparing Q5 with Q1 of dietary Na, the risk of stroke associated with increasing dietary Na was stronger for the black participants (HR 2.13; 95 % CI 0.88, 5.13) than for the white participants

(HR 1.30; 95 % CI 0.66, 2.57), though these estimates were not statistically different from one another.

Food groups and dietary sodium:potassium ratio

As we did not observe racial differences in the Na:K ratio, we also wanted to investigate whether there were differences in food choice contributing to both high and low Na:K ratios. We used Pearson's correlation to compare grams of food from each food group with the Na:K ratio. The foods were largely similar across races. In blacks and whites, high fruit and fruit juice intakes correlated with a lower Na:K ratio (Table 4). Processed meats, bread and non-fried chicken were each correlated with a higher Na:K ratio. In whites, high liquor consumption was correlated with a higher Na:K ratio, while coffee consumption was associated with a lower

Table 3. Risk of stroke associated with increasing sodium:potassium ratio in the REasons for Geographic And Racial Differences in Stroke (REGARDS) study (Hazard ratios (HR) and 95% confidence intervals)

	Quintiles of Na:K ratio*										1 sd increment	
	Q1 (low)		Q2		Q3		Q4		Q5 (high)		HR	95 % CI
	HR	95 % CI	HR	95 % CI	HR	95 % CI	HR	95 % CI	HR	95 % CI		
Number of strokes	80		64		80		64		75		–	
Incidence rate (per 1000 person-years)	4.0		3.2		4.0		3.2		3.9		–	
Model 1†	1	Reference	0.87	0.63, 1.22	1.17	0.86, 1.60	1.00	0.71, 1.39	1.27	0.92, 1.75	1.07	0.96, 1.19
Model 2‡	1	Reference	0.86	0.61, 1.21	1.16	0.84, 1.61	0.97	0.68, 1.37	1.22	0.87, 1.71	1.05	0.94, 1.18
Model 3§	1	Reference	0.85	0.62, 1.17	1.22	0.90, 1.66	1.01	0.73, 1.41	1.29	0.94, 1.78	1.08	0.98, 1.20
Stratified analysis <i>P</i> for interaction = 0.301											0.913	
In blacks	1	Reference	1.13	0.65, 1.98	1.83	1.09, 3.07	1.43	0.81, 2.53	1.39	0.78, 2.48	1.11	0.95, 1.29
In whites	1	Reference	0.76	0.51, 1.13	0.99	0.68, 1.46	0.86	0.57, 1.28	1.29	0.88, 1.90	1.06	0.92, 1.22

* Quintiles are race and sex specific.

† Model 1 – age, race, sex, energy.

‡ Model 2 – age, race, sex, energy, BMI, hypertension, diabetes, history of heart disease, dyslipidaemia, smoking, income, education.

§ Model 3 – age, race, sex, energy, BMI, hypertension, diabetes, history of heart disease, dyslipidaemia, smoking, income, education, bias in retrieving and extraction of medical records.

|| For the models stratified by race, model 3 adjustments were used and race was not included.



Table 4. Pearson's correlations of food groups (g/d) with sodium:potassium ratio by race in the REasons for Geographic And Racial Differences in Stroke (REGARDS) study*

Black participants		White participants	
Food group	<i>r</i>	Food group	<i>r</i>
Non-fried chicken	0.93	Non-fried chicken	0.64
Processed meats	0.43	Liquor	0.50
Bread	0.41	Processed meats	0.42
Added fats (lard, crisco, gravy)	0.33	Bread	0.39
Fried chicken or fish	0.28	Added fats (lard, crisco, gravy)	0.29
Low-fat milk	-0.16	Coffee	-0.20
Cruciferous vegetables	-0.18	Low-fat milk	-0.23
Other vegetables	-0.23	Other vegetables	-0.25
Fruit juice	-0.36	Fruit juice	-0.28
Fruit	-0.37	Fruit	-0.35

* For simplicity only the top five and bottom five correlations are shown. All $P < 0.001$.

Na:K ratio. In blacks, added fats such as lard and gravy were correlated with a higher Na:K ratio, while cruciferous vegetables were associated with a lower Na:K ratio.

Discussion

Among middle-aged and older adults, a high dietary Na:K ratio was associated with an increased risk of death. This association was observed in blacks and whites and persisted after adjustment for several demographic, socioeconomic and other health factors. Although a similar trend was present for the risk of incident stroke, this association was not statistically significant, which most probably is due to the lower event rate for stroke compared with all-cause mortality. Our findings on higher risk of death with increasing dietary Na:K ratio are consistent with previous research showing that a higher dietary Na:K ratio, as measured in either urine or diet, is associated with a higher risk of death⁽²⁵⁾. Compared with the results for dietary Na:K ratio, the direction of the association between Na intake and the outcomes was similar but the magnitude of the association was weaker.

Based on previous bench and population research, we hypothesised that the association of the Na:K ratio and both stroke and death would be higher in blacks than whites^(26,27). Salt sensitivity has been found to be highly correlated with specific phenotypic and metabolic characteristics, particularly for blacks in the USA^(28,29). In contrast with whites, salt sensitivity is prevalent in both normotensive and hypertensive blacks^(27,30,31). Diets that are high in K and low in Na (e.g. the Dietary Approaches to Stop Hypertension diet) effectively lower blood pressure in whites, but do so to a greater degree in blacks⁽³²⁾. Therefore, we were surprised that we did not find racial differences in the effect of the Na:K ratio (or Na alone) on stroke or mortality in this study. Inclusion of hypertension as a covariate may have dampened the observed association as it may lie in the causal pathway between higher Na intake and either death or stroke. Our findings suggest that an increased Na:K ratio in the diet is harmful regardless of race.

Separating individual nutrients from overall diet quality is challenging. Therefore, it is possible that the association of a higher Na:K ratio with increased risk of all-cause mortality that we observed is due to an improvement in overall diet quality. In fact, we observed that lower Na:K ratio values were correlated with greater intakes of fruit, low-fat milk and vegetable intake. A lower dietary Na:K ratio is associated with a greater intake of whole grains, low-fat dairy products, fruits, vegetables and lean meats, all of which have been associated with better health⁽³³⁾. However, in our study, the association between a higher Na:K ratio and increased risk of all-cause mortality persisted even after adjustment for alcohol, whole grain, fruit and vegetable intake. In addition to the fact that diet quality itself is associated with improved cardiovascular health, diet quality is also strongly correlated with socioeconomic status⁽³⁴⁾. Although a possibility for residual confounding by socioeconomic status still exists, we controlled for two major indicators of socioeconomic status: income and education.

The present study has potential limitations. We are unable to assess causality due to the study's observational design. Na and K intake were estimated by assessing diet rather than multiple 24-h urine collections, which are known to more accurately reflect Na:K intake, and we did not have the ability to capture salt added to food by the participant. Although individuals may erroneously report nutritional intake on FFQ, dietary questionnaires provide an acceptable classification of nutrient intake on a population level and are widely accepted in cohort studies with large sample sizes such as the REGARDS study^(35,36). Participants may under-report their Na intake and inflate their intake of more healthful foods. This potential bias would reduce the ability to detect significant associations between the Na:K ratio and outcomes in the present study. Participants who returned the FFQ were more likely to be college educated than those who did not return the FFQ. Although we controlled for education and income in our analyses, individuals of lower socioeconomic status were less represented in our study. Although the REGARDS study has a strong surveillance system, we did not have complete ascertainment of death. Despite this potential bias, we found a significant association between dietary Na:K ratio and mortality. In addition, we did not know the cause of death and were unable to study CVD mortality. Previous studies have demonstrated stronger associations of the Na:K ratio with CVD mortality than all-cause mortality, so we would expect our findings to be strengthened with the addition of these data⁽¹⁵⁾. Despite these limitations, the REGARDS study also has several notable strengths. These strengths include the enrolment of a large sample of whites and blacks from all over continental USA, physician adjudication of strokes using medical records, and the collection of dietary data using a standardised and validated FFQ.

In the present study, individuals with a reported diet high in Na and low in K had a greater risk of death. Although the physiological mechanisms are not fully understood, diets high in K may mediate the adverse effects of dietary Na, resulting in lower blood pressures and a decreased risk of stroke and stroke mortality. Data from this study reinforce recommendations to lower dietary Na intake and increase K



intake as a means of lowering mortality in the general population, but do not support specific recommendations for different race groups. Thus, our data suggest that the implementation of strategies to reduce Na in the US food supply has similar implications for whites and blacks.

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Supplementary material

The supplementary material for this article can be found at <http://www.journals.cambridge.org/jns>

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