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Potassium intake and risk of stroke in hypertensive and non-hypertensive women in the Women's Health Initiative

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Abstract

Background and Purpose—Dietary potassium has been associated with lower risk of stroke but there is little data on dietary potassium effects on different stroke subtypes or in older hypertensive and non-hypertensive women.

Methods—The study population consisted of 90,137 postmenopausal women aged 50–79 at enrollment, free of stroke history at baseline, followed prospectively for an average of 11 years. Outcome variables were total, ischemic, and hemorrhagic stroke, and all-cause mortality. Incidence was compared across quartiles of dietary potassium intake and hazard ratios were obtained from Cox proportional hazards models after adjusting for potential confounding variables, and in hypertensive and non-hypertensive women separately.

Results—Mean dietary potassium intake was 2611 mg/day. Highest quartile of potassium intake was associated with lower incidence of ischemic and hemorrhagic stroke, and total mortality. Multivariate analyses comparing highest to lowest quartile of potassium intake, indicated a hazard ratio (HR) for all-cause mortality of 0.90 (95% CI: 0.85 – 0.95), for all stroke of HR=0.88 (95% CI: 0.79 – 0.98), and for ischemic stroke of 0.84 (95% CI: 0.74 – 0.96). The effect on ischemic stroke was more apparent in non-hypertensive women among whom there was a 27% lower risk with HR of 0.73 (95% CI: 0.60 – 0.88), interaction *p*-value <.10. There was no association with hemorrhagic stroke.

Conclusions—High potassium intake is associated with a lower risk of all stroke and ischemic stroke as well as all-cause mortality in older women, particularly those who are not hypertensive.

Keywords

stroke; dietary potassium; hypertension; Women's Health Initiative

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Introduction

Stroke is the fourth leading cause of mortality in the United States, and women account for 60 percent of all US stroke cases[1]. Women also have a higher lifetime risk of stroke than men[2]. There is interest in studying lifestyle factors, such as diets rich in potassium, that may reduce stroke risk.

Evidence from prospective studies suggests that higher dietary potassium intake is associated with reduced risk of stroke[3, 4,5]. Three studies have specifically reported the effects of dietary potassium on risk of stroke in women. Khaw and Barret-Connor[3] found that women consuming less than 49mmol (1911mg) of potassium had a relative risk of 4.8 (p = 0.01) as compared to women eating more than 49mmol of potassium. Iso[6] found that women in the highest quintile of potassium intake (median of 3555mg) vs the lowest quintile (median of 2017mg) had a relative risk of 0.72 (95% CI, 0.51–1.01). Larsson[7] in the Swedish Mammography Cohort, found that women with a history of hypertension had a relative risk of 0.64 (0.45–0.92) for all stroke types when comparing highest quintile of potassium intake to lowest quintile (mean = 3,845mg vs 2,363mg). In contrast, The EPIC-NL study (European Prospective Investigation into Cancer and Nutrition – Netherlands)[8], found that potassium intake was not associated with stroke. Despite these useful contributions, it remains unclear whether higher dietary potassium intake is associated with reduced risk of all subtypes of stroke and whether these findings are especially relevant in specific population subgroups.

The Women's Health Initiative Observational Study (WHI-OS), the largest prospective cohort study of post-menopausal women with long-term follow-up, was used to assess whether higher dietary potassium consumption is associated with reduced risk of total, ischemic or hemorrhagic stroke, and all-cause mortality. We also evaluated effects on ischemic stroke subtypes as determined by the TOAST, Trial of ORG 10172 Acute Stroke Trial, classification, which previous studies have not investigated.

Subjects and Methods

Study Population

A detailed description of the WHI-OS is published[9]. Briefly, between 1993 and 1998, 93,676 women aged 50 to 79 years were recruited from 40 states and followed prospectively for a mean of 11.1 years (range = 0.14 to 16.0 years). We excluded women with history of stroke at baseline (n = 1354), women with missing information on history of stroke (N=54), those with no information on dietary potassium (n=96). Finally, we also excluded as outliers n= 2035 women in the bottom 1% of caloric intake (less than 465 calories), whose potassium intake ranged from 0.07–1790mg, and women in the top 1% of caloric intake (more than 3931 calories) whose potassium intakes ranged from 1507–31,129mg. We therefore had an analytic cohort of 90,137.

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Dietary Assessment of Potassium

Participants completed food frequency questionnaires (FFQ) at enrollment and Year 3 of follow-up. Details regarding diet assessment and the FFQs have been described elsewhere [9, 10]. Briefly, participants completed questionnaires that reflected their dietary habits over the three months prior to enrollment. The questionnaire consisted of three sections: adjustment questions, food line items, and summary questions. The nineteen adjustment questions allowed for more detailed analysis of fat intake by asking participants how foods were prepared. The list of 122 food line items specified type and frequency of various foods and food group intake according to small, medium or large portion sizes. The four summary questions asked about intake of fruits, vegetables, and fat added to foods or in cooking. The FFQ nutrient database was derived from the University of Minnesota Nutrition Coordinating Center Nutrient Data for Scientific Research (NDSR) database for women in our analytic cohort.

Measurement properties of the WHI FFQ were evaluated in a sub-cohort of WHI, and found to be similar to other dietary assessments used in the WHI, such as dietary recalls[10]. The Pearson correlation coefficient between the FFQ and 8 days of dietary intake from combined 4 days of dietary recalls plus 4 days of food records was 0.58 for dietary potassium[10]. In our own analysis, the correlation between intake at baseline and intake at year 3 in the WHI Observational study was 0.63 indicating that potassium intake is fairly stable.

Ascertainment of Health Outcome

Ascertainment of death was determined based on the death certificate, medical records, or other records such as autopsy report[11]. Mortality cause was initially adjudicated by a local physician adjudicator at the Clinical Centers for the WHI, and then centrally adjudicated by two physicians. The two central adjudicators were required to review all deaths and come to agreement before closing the case.

Stroke was initially identified through self-report at annual visits, and medical records were then requested. Stroke was defined as rapid onset of neurologic deficit lasting more than 24 hours and without evidence of other causes. Outcomes were adjudicated by a local physician adjudicator who then assigned a diagnosis based on medical records and WHI criteria, which have been defined elsewhere[12,13]. More than 95% of WHI stroke classification was based on MRI or CT findings[13]. Neurologists then centrally adjudicated locally determined strokes. A comparison of adjudicated strokes in the WHI versus stroke events defined in Medicare data showed substantial agreement between the two for all stroke (kappa=0.69)[14], suggesting that WHI stroke ascertainment is a valid measure of stroke outcome.

Stroke was classified as ischemic stroke if diagnosis revealed an occlusion of cerebral or pre-cerebral arteries with infarction (cerebral thrombosis, cerebral embolism, or lacunar infarction)[12, 13]. Central adjudicators then further classified ischemic stroke according to the TOAST (Trial of ORG 10172 Acute Stroke Trial) classification. The TOAST Classification is based on presumed underlying stroke etiology, and requires detailed investigation through brain imaging and methods described elsewhere[12, 15]. Stroke was classified as hemorrhagic

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if diagnosis revealed a subarachnoid hemorrhage, intracerebral hemorrhage, or other intracranial hemorrhage not resulting from a procedure[12, 16].

Measurements of Covariates

Participants completed demographic and lifestyle questionnaires and physical measurements during baseline visits to a WHI Clinical Center. Demographic factors included date of birth and ethnicity (categories consistent with the 1990 US Census). Body mass index (BMI) was calculated by dividing weight in kilograms by the square of the height in meters. Past smokers were those who self-reported having smoked at least 100 cigarettes and were currently not smoking. Alcohol intake was defined as number of drinks in a given time. Women were classified as hypertensive if they were either taking anti-hypertensive medications or had a systolic blood pressure ≥ 140, or a diastolic blood pressure ≥ 90. Participants who had ever taken any aspirin containing medications were classified as aspirin users. Participants who took hormone therapy (HT) for more than three months but were not currently using HT were classified as past HT users. HT was based on estrogen and progesterone pill and patches only; creams and shots were excluded. Self-report of doctor diagnosis was used for diabetes (sugar related diabetes when not pregnant), for history of myocardial infarction (MI) and for having high cholesterol requiring pills. Recreational physical activity was assessed using information about frequency, duration and intensity of activity, and organized into categories of activity as described elsewhere[9].

Statistical Methods/Analysis

Quartiles of dietary potassium were obtained. We examined the means and 95% confidence intervals (95%CI) of dietary potassium by demographic variables and by covariates that have been reported to increase the risk of stroke. All probability values for any differences across the various categories of each covariate were obtained by analysis of variance or chi-square. We also calculated the incidence of stroke and death per thousand person-years across quartiles of potassium intake and did linear trend analyses.

Hazard ratios (HRs) were estimated from Cox proportional hazards models comparing highest quartile to lowest quartile of potassium intake. We also considered an analysis of potassium per kilocalorie (K/Kcal) using quartile cutpoints of K/Kcal. However, since absolute potassium is more stably assessed with FFQ than are calories, an estimate of effect of nutrient density on stroke would not be as reliable. The correlation between potassium assessed by FFQ and 8 days of dietary records is 0.58, while the corresponding correlation for calories is 0.37 [10]. Since potassium intake may be related to blood pressure, and since hypertension may be in the pathway between potassium intake and stroke, and also because hypertension is a major risk factor for stroke, we considered hypertensive status a priori for stratified analyses. Follow up time was calculated in months from the date of enrollment to the date of first stroke, death, or end of the follow-up whichever came first. Model 1 is unadjusted, model 2 is adjusted for age, race and hypertension status, and model 3 is adjusted for model 2 variables plus smoking, recreational physical activity, history of diabetes, history of myocardial infarction (MI), hormone use, alcohol intake, aspirin use, high cholesterol requiring pills, and BMI. We examined each of these variables separately for interaction with potassium intake by including an interaction term of the variable and

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potassium intake in model 3 for ischemic stroke. When the interaction terms were significant with $p<.10$, we did stratified analyses for that variable. Statistical analyses were performed using SAS software (SAS Institute Inc, Cary, NC).

Results

The analytic cohort of 90,137 post-menopausal women with no history of stroke at baseline, had mean age 63.6 years at baseline, standard deviation (SD) 7.4 years. Mean dietary potassium intake was 2611 mg/day. Blacks, current smokers, and non-drinkers of alcohol reported lower dietary potassium intakes (Table 1). Those who reported 2 or more episodes of recreational physical activity a week had greater dietary potassium intake than those who reported limited or no activity.

Stroke Incidence

Incidence per 1000 person years was 3.10 for all stroke, 2.24 for ischemic stroke, 0.50 for hemorrhagic stroke and 11.60 for all-cause mortality. Those in the lowest quartile of estimated dietary potassium intake (<1925.5mg potassium) had higher estimated incidence than those in other quartiles across all outcomes (Table 2). There was a statistically significant linear trend for mortality (p=.0002) but the linear trend test did not reach statistical significance for the other outcomes.

Dietary Potassium and Stroke Risk

Table 3 shows a statistically significant lower risk in all quartiles of potassium intake compared to lowest quartile, for all-cause mortality, all stroke, and ischemic stroke, in unadjusted, age-race -hypertension adjusted, and multivariate adjusted models (Table 3). In a sensitivity analysis excluding those with previous MI, the hazard ratios and confidence intervals were similar to those for all stroke (data not shown). The HR in the fully adjusted model comparing highest quartile (Q4) to the lowest quartile (Q1) of potassium intake, was 0.90 (95%CI 0.85–0.95) for all-cause mortality, 0.88 (95%CI 0.79–0.98) for all stroke, and 0.84, (95% CI 0.74–0.96) for ischemic stroke. There was no association with hemorrhagic stroke.

In accordance with our a priori analysis plan we present results for all outcomes of interest stratified by hypertension status (Table 4). Among non-hypertensive women, there was a lower risk of all-cause mortality, all stroke, and ischemic stroke across increasing quartiles for potassium. In particular, there was a 27% lower risk of ischemic stroke when comparing Q4 to Q1 in model 3 (HR 0.73, 95% CI 0.60–0.88), and no association for hemorrhagic stroke. Among hypertensive women, higher potassium intake was associated with lower all-cause mortality but there was no association with any stroke outcome.

Interactions were observed for ischemic stroke between dietary potassium and hypertension ($p<.10$), diabetes ($p<.05$), high cholesterol requiring pills ($p<.01$) and BMI ($p<.05$). Figure 1 shows stratified analyses by these variables. For example, among the 35,227 women who had normal BMI, there were 727 ischemic stroke events. The HR comparing the highest quartile to the lowest quartile of potassium intake indicates that among those of normal

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weight, higher potassium intake was associated with a 30% lower risk of stroke (HR=0.70, 95% CI: 0.56–0.87).

Subtypes of Ischemic Stroke According to TOAST Classification

Cox proportional hazards models were run for the predominant Trial of Org 10172 in Acute Stroke Treatment (TOAST) classes: large artery atherosclerosis, cardioembolism, and small vessel occlusion (lacunae). We compared each subtype to a reference group of no stroke. Power to detect effects was small for these subgroups. Nevertheless, higher potassium intake was associated with a lower risk of small vessel disease among those not hypertensive. Compared to the lowest quartile, Q2, Q3 and Q4 had HRs (95% CI) of 0.43 (0.26–0.71), 0.60 (0.38–0.95) and 0.67 (0.43–1.04), respectively.

Discussion

In the largest U.S. cohort study of over 90,000 post-menopausal women, we found an inverse association between self-reported dietary potassium intake and incidence of ischemic stroke. The lower risk of stroke associated with higher intake of potassium persisted after adjusting for multiple covariates. In particular, women consuming the highest quantity of potassium in our cohort (>3193.6mg) had a 12% lower risk of all-type stroke (HR 0.88, 95% CI 0.79–0.98), and a 16% lower risk of ischemic stroke (HR 0.84, 95%CI 0.74–0.96) as compared to women consuming less than 1925.5mg of potassium.

Non-hypertensive women tended to benefit the most from consuming diets higher in potassium. Women in the highest quartile of potassium intake had a 21% reduction in risk of all-type stroke (HR= 0.79, 95% CI 0.67–0.93) and a 27% reduction in risk of ischemic stroke (HR= 0.73, 95% CI 0.60–0.88). Women with hypertension had a lower total mortality risk with higher potassium intake but no lowered risk of stroke suggesting that higher potassium intake may be of more benefit before hypertension develops. This finding supports cell culture and animal model studies that have shown that higher potassium levels improve vascular endothelial function and promote nitric oxide release, thereby improving vascular flow [17, 18] In non-hypertensive women the correlation between systolic blood pressure and potassium intake was negligible at −.008, suggesting that in our data, the beneficial effect of potassium intake among non-hypertensives was not modulated by its effect on blood pressure. Instead, this particular result may be due to habitually higher intakes of dietary potassium that prevent arterial stiffness[19]. A small study of young men and women found that habitually low potassium intake was associated with increased arterial stiffness, measured by carotid-femoral pulse wave velocity, despite normal blood pressures. This suggests that dietary potassium may have an effect on blood vessels beyond its effects on blood pressure[19]. Further research to elucidate mechanisms is needed.

The US Department of Agriculture currently recommends that women eat at least 4700 mg of potassium daily[20]. In WHI only 2.8% of women met or exceeded this level. The World Health Organization recently amended its recommendation after conducting a meta-analysis of dietary potassium intake and cardiovascular disease, and advises that women eat at least 3510mg of potassium [21] per day[22]. In the WHI OS cohort, 16.6% of women met or exceeded this level. Overall, the mean reported dietary potassium intake was only 2611mg.

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Few postmenopausal women appear to reach the recommended levels of daily potassium intake.

Further, the National Health and Nutrition Examination Survey (NHANES) comparing the period from the 1988–1994 with the 2003–2008 survey, reports that mean dietary potassium intake declined among women aged 51–70 by 87mg to 2419mg and in those over 71 by 173mg to 2234mg[23]. This decline is predicted to continue unless major changes in the food environment provide more unprocessed meats, fruits and vegetables to consumers. Some foods rich in potassium are white and sweet potatoes, bananas, and white beans. Our results illustrate that consuming more potassium, even below recommended levels, is associated with a reduced risk of all-type stroke and ischemic stroke by over 20% in non-hypertensive women. With the general decline in potassium consumption, women may be at greater risk of suffering strokes. Health care providers therefore may wish to reinforce the importance of a potassium rich diet especially among postmenopausal women.

The difference between our results and those from the Swedish Mammography Cohort (SMC) and EPIC cohort studies can be explained in several ways. Our study was substantially larger than the SMC, and our measurement of hypertension was more robust than SMC, which relied on self-reported history of hypertension without subsequent validation[7]. This influenced their finding that an increase in potassium intake is more protective for hypertensive women. Our study looked exclusively at older women, unlike the EPIC-NL study which looked at a group of 36,094 men and women with a mean age of 49[8]. The mean dietary potassium intake was also substantially lower in women from the WHI than in the EPIC-NL study participants (2611mg vs 3672mg). The generally higher potassium intakes in their analysis may have prevented them from finding an association with stroke.

There are some limitations to our study. First, this was an observational study rather than a clinical trial and therefore results must be interpreted with caution concerning causation. Secondly, our estimates of potassium intake come from food frequency questionnaires (FFQ) and may under- or over-estimate true intake. Thirdly, we only used baseline dietary potassium in assessing relationships to outcomes. WHI-OS participants also completed FFQs at Year 3 of follow up. In comparing the dietary potassium intake between baseline and year 3, there was a mean decrease in potassium intake of 79mg, with a correlation between baseline and year 3 of 0.63 Fourth, our analyses focus on potassium only, while corresponding sodium consumption may be an important covariate in determining hypertension [24] and cardiovascular disease[21] risk. However, sodium consumption is not reliably estimated by the WHI FFQ, so analyses of potassium and sodium jointly in relation to these outcomes in the WHI OS needs to rely on biomarkers for sodium consumption[25], which are not available on the entire cohort.

In summary, in the largest prospective study of older women with long-term follow-up, we found lower risk of ischemic but not hemorrhagic stroke associated with higher intakes of potassium, especially in non-hypertensive women, as well as lowered risk of all-cause mortality in all women. We also found that higher potassium intake is associated with lower risk of small vessel stroke subtype. Since dietary intake of potassium in the U.S. is well

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below the recommended intake, these findings are important in suggesting preventive dietary measures to lower the risk of stroke.

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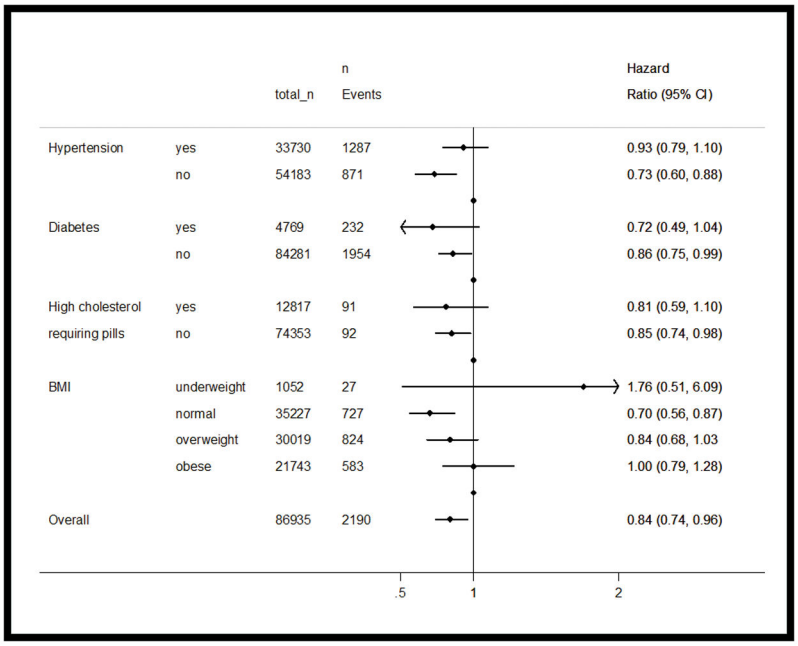

Figure 1.

Hazard ratios comparing highest to lowest quartile of potassium intake (mg) for ischemic stroke stratified by hypertension, diabetes, high cholesterol and BMI

Hazard ratios adjusted for age, race, hypertension, smoking, physical activity, history of diabetes, history of atrial fibrillation, history of myocardial infarction, hormone use, alcohol intake, aspirin use, high cholesterol, and BMI. Variables that make up the strata are omitted when running Cox regressions in that stratum.

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Table 1

Baseline potassium intake by characteristics

		Dietary Potassium (mg)	
	N	**Mean (95% CI)**	***p* value***
Whole Cohort	90137	2611 (2605 – 2618)	
Age			
50 – 59	28675	2589 (2578 – 2600)	<0.001
60 – 69	39739	2625 (2615 – 2634)	
70–79+	21723	2616 (2603 – 2629)	
Ethnicity			
White	75842	2684 (2678 – 2691)	<0.001
Black	6848	2145 (2122 – 2168)	
Hispanic	3301	2274 (2240 – 2309)	
Other	3909	2304 (2274 – 2335)	
Education			
0–8 years or Some High School	4353	2199 (2170 – 2228)	<0.001
High School diploma - Some college	47004	2519 (2511 – 2528)	
College graduate or Post-graduate	38061	2772 (2763 – 2782)	
Income			
< $20000	12897	2428 (2411 – 2446)	<0.001
$20000 – $49999	36353	2609 (2599 – 2619)	
≥ $50000	34334	2692 (2682 – 2702)	
Don’t know	2608	2506 (2467 – 2545)	
Marital Status			
Never	4232	2655 (2624 – 2685)	<0.001
Divorced or separated	13991	2537 (2520 – 2553)	
Widowed	15410	2560 (2544 – 2576)	
Presently married	54619	2642 (2634 – 2650)	

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		Dietary Potassium (mg)	
	N	Mean (95% CI)	*p* value*
Marriage like relationship	1459	2591 (2542 – 2639)	
Smoking History			
Current	5441	2362 (2337 – 2387)	<0.001
Past	38194	2646 (2637 – 2656)	
Never	45239	2613 (2603 – 2622)	
Alcohol Intake			
None/Non-drinker	9809	2429 (2409 – 2449)	<0.001
Past Drinker	16455	2527 (2511 – 2542)	
<1 drink per month	10347	2537 (2519 – 2556)	
<1 drink per week	18105	2608 (2594 – 2622)	
1 – <7 drinks per week	23371	2709 (2697 – 2721)	
7+ drinks per week	11474	2769 (2752 – 2785)	
Recreational Physical Activity			
No activity	11904	2341 (2324 – 2358)	<0.001
Some activity of limited duration	34071	2534 (2524 – 2545)	
2 – < 4 episodes/wk	16603	2679 (2665 – 2693)	
4 episodes/wk	26559	2791 (2779 – 2802)	
Hormone Use			
Current	43123	2630 (2621 – 2639)	<0.001
Past	18663	2604 (2590 – 2618)	
Never	26732	2582 (2570 – 2594)	
Weight status, Body Mass Index (BMI, kg/m^2)			
Underweight (<18.5)	1066	2550 (2491 – 2608)	0.039
Normal (18.5 – 24.9)	35638	2616 (2606 – 2626)	
Overweight (25.0 – 29.9)	30348	2606 (2596 – 2617)	
Obesity I (30.0 – 34.9)	13859	2602 (2586 – 2619)	
Obesity II (35.0 – 39.9)	5120	2628 (2600 – 2656)	

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		Dietary Potassium (mg)	
	N	Mean (95% CI)	*p* value*
Extreme Obesity III (>= 40.0)	3058	2610 (2574 – 2646)	
Systolic Blood Pressure			
≤120	36057	2633 (2623 – 2643)	<0.001
120–140	35947	2607 (2597 – 2617)	
>140	18011	2576 (2561 – 2590)	
Diastolic Blood Pressure			
<90	84347	2616 (2610 – 2623)	<0.001
≥90	5649	2538 (2512 – 2564)	
Hypertension (if self-reported treatment or BP ≥140/90)			
Yes	34277	2573 (2563 – 2583)	<0.001
No	54635	2637 (2629 – 2645)	
High Cholesterol (requiring pills ever)			
Yes	12991	2574 (2557 – 2590)	<0.001
No	75171	2620 (2613 – 2627)	
Aspirin Use (Any)			
Yes	31768	2679 (2668 – 2689)	<0.001
No	58369	2575 (2567 – 2582)	
History of Diabetes			
Yes	4855	2558 (2529 – 2587)	<0.001
No	85205	2614 (2608 – 2621)	
History of MI			
Yes	2020	2534 (2490 – 2577)	<0.001
No	88056	2613 (2607 – 2619)	
History of Atrial Fibrillation			
Yes	4089	2624 (2594 – 2655)	0.821

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		Dietary Potassium (mg)	
	N	**Mean (95% CI)**	***p* value***
No	84603	2613 (2606 – 2619)	
History of CABG/PTCA			
Yes	1602	2535 (2486 – 2583)	<0.001
No	87121	2615 (2608 – 2621)	
History of CHD			
Yes	2871	2547 (2511 – 2584)	<0.001
No	85863	2616 (2609 – 2622)	

* *p* values were obtained from chi-square tests or analyses of variance across the various categories of each covariate.

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Table 2

All-cause mortality and stroke rates by quartiles of dietary potassium intake

		All-cause mortality		Stroke (all)		Stroke (no Hx of MI)		Ischemic Stroke		Hemorrhagic Stroke	
Quartiles of Dietary Potassium (mg)	**Participant number**	**Event number**	**Annualized rate***	**Event number**	**Annualized rate***	**Event number**	**Annualized rate***	**Event number**	**Annualized rate***	**Event number**	**Annualized rate***
Q1: < 1925.5	22534	3096	13.03	793	3.40	750	3.29	574	2.48	125	0.55
Q2: ≥1925.5 – 2519.4	22534	2921	11.65	769	3.12	732	3.03	542	2.21	128	0.53
Q3:>2519.4 – 3193.6	22535	2685	10.52	719	2.86	687	2.78	530	2.12	106	0.43
Q4: >=3193.6	22534	2894	11.30	765	3.03	734	2.96	544	2.17	125	0.51
Overall	90137	11596	11.60	3046	3.10	2903	3.01	2190	2.24	484	0.50

p for trend for all cause mortality = .0002, no significance for other endpoints

*Annualized rate is defined as number of events per 1000 person years

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Table 3

Hazard Ratios for All-cause mortality and Stroke by Quartiles of Potassium

	Quartiles of Potassium (mg)			
	Q1: < 1925.5	**Q2: ≥1925.5 – 2519.4 (HR, 95% CI)**	**Q3:>2519.4 – 3193.6 (HR, 95% CI)**	**Q4: >3193.6 (HR, 95% CI)**
All-Cause Mortality				
Model (1)	1	0.87 (0.82 – 0.91)	0.77 (0.74 – 0.82)	0.83 (0.79 – 0.87)
Model (2)	1	0.87 (0.82 – 0.91)	0.78 (0.74 – 0.82)	0.83 (0.79 – 0.87)
Model (3)	1	0.91 (0.86 – 0.96)	0.84 (0.79 – 0.89)	0.90 (0.85 – 0.95)
Stroke (all)				
Model (1)	1	0.89 (0.81 – 0.99)	0.82 (0.74 – 0.91)	0.87 (0.79 – 0.96)
Model (2)	1	0.90 (0.81 – 1.00)	0.83 (0.75 – 0.92)	0.88 (0.79 – 0.97)
Model (3)	1	0.88 (0.79 – 0.98)	0.85 (0.76 – 0.94)	0.88 (0.79 – 0.98)
Ischemic Stroke				
Model (1)	1	0.88 (0.78 – 0.99)	0.84 (0.74 – 0.94)	0.85 (0.76 – 0.96)
Model (2)	1	0.88 (0.78 – 0.99)	0.85 (0.75 – 0.95)	0.85 (0.76 – 0.96)
Model (3)	1	0.85 (0.75 – 0.96)	0.85 (0.75 – 0.97)	0.84 (0.74 – 0.96)
Hemorrhagic Stroke				
Model (1)	1	0.95 (0.74 – 1.22)	0.77 (0.60 – 1.00)	0.91 (0.71 – 1.16)
Model (2)	1	0.96 (0.75 – 1.23)	0.75 (0.58 – 0.98)	0.90 (0.70 – 1.16)
Model (3)	1	0.91 (0.70 – 1.19)	0.78 (0.59 – 1.03)	0.92 (0.71 – 1.20)
TOAST subtype*				
Large artery atherosclerosis	1	0.95 (0.60 – 1.49)	0.85 (0.53 – 1.35)	0.69 (0.42 – 1.13)
Cardioembolism	1	0.91 (0.70 – 1.17)	1.01 (0.79 – 1.30)	1.04 (0.81 – 1.32)
Small Vessel occlusion (lacune)	1	0.82 (0.62 – 1.08)	0.77 (0.59 – 1.03)	0.83 (0.63 – 1.10)

Model (1) unadjusted

Model (2) adjusted for Age, Race, and Hypertension status

Model (3) adjusted for Model 2 variables plus Smoking Status, Physical Activity, History of Diabetes, History of Atrial Fibrillation, History of Myocardial Infarction, Hormone Use, Alcohol Intake, Aspirin Use, High Cholesterol, and BMI

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* All adjusted for all variables in Model (3)

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Table 4

Hazard Ratios for All-cause mortality and Stroke in Quartiles of Potassium by Hypertension Status

	Quartiles of Potassium (mg)			
	Q1: < 1925.5	**Q2: ≥1925.5 – 2519.4 (HR, 95% CI)**	**Q3:>2519.4 – 3193.6 (HR, 95% CI)**	**Q4: >3193.6 (HR, 95% CI)**
All-Cause Mortality				
hypertension	1	0.92 (0.85 – 0.99)	0.85 (0.79 – 0.92)	0.89 (0.82 – 0.96)
no hypertension	1	0.91 (0.84 – 0.98)	0.84 (0.77 – 0.91)	0.92 (0.85 – 1.00)
Stroke (all)				
hypertension	1	0.99 (0.86 – 1.13)	0.93 (0.81 – 1.07)	0.97 (0.84 – 1.12)
no hypertension	1	0.75 (0.64 – 0.89)	0.75 (0.64 – 0.89)	0.79 (0.67 – 0.93)
Ischemic Stroke				
hypertension	1	0.96 (0.82 – 1.14)	0.96 (0.81– 1.13)	0.93 (0.79 – 1.10)
no hypertension	1	0.71 (0.58 – 0.86)	0.73 (0.60 – 0.88)	0.73 (0.60 – 0.88)
Hemorrhagic Stroke				
hypertension	1	0.81 (0.56 – 1.18)	0.85 (0.59 – 1.24)	0.85 (0.58 – 1.24)
no hypertension	1	1.02 (0.70 – 1.49)	0.72 (0.48 – 1.09)	1.01 (0.69 – 1.48)
TOAST Subtype				
Large artery atherosclerosis				
Hypertension	1	1.13 (0.65 – 1.96)	0.92 (0.51 – 1.65)	0.66 (0.35 – 1.25)
No hypertension	1	0.67 (0.30 – 1.49)	0.74 (0.34 – 1.59)	0.72 (0.33 – 1.57)
Cardioembolism				
Hypertension	1	0.99 (0.71 – 1.38)	1.06 (0.76 – 1.48)	1.17 (0.85 – 1.61)
No hypertension	1	0.80 (0.54 – 1.19)	0.95 (0.65 – 1.38)	0.87 (0.60 – 1.28)
Small Vessel occlusion (lacune)				
Hypertension	1	1.11 (0.80 – 1.56)	0.90 (0.63 – 1.28)	0.95 (0.67 – 1.36)
No hypertension	1	0.43 (0.26 – 0.71)	0.60 (0.38 – 0.95)	0.67 (0.43 – 1.04)

Adjusted for Age, Race, Hypertension status, Smoking Status, Physical Activity, History of Diabetes, History of Atrial Fibrillation, History of Myocardial Infarction, Hormone Use, Alcohol Intake, Aspirin Use, High Cholesterol, and BMI

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