

# Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

**eTable 1. Hazard Ratios and 95% Confidence Intervals of Composite Cardiovascular Disease, Congestive Heart Failure, Myocardial Infarction, and Stroke According to Quartile of 24-Hour Urinary Sodium Excretion**

Variable	N	Urinary Sodium Excretion, mg/24 hours				P for trend
		<2,686	2,687 – 3,532	3,533 – 4,473	≥4,474	
No. of Participants		940	939	939	939	
<b>Composite CVD<sup>a</sup></b>						
Events		198	180	218	208	
Person-years		5,484	5,659	5,676	5,707	
Cumulative Incidence <sup>b</sup> , % (95% Confidence Interval) at median 6.8 years follow-up		17.7 (15.3, 20.0)	18.3 (15.9, 20.7)	23.8 (21.0, 26.5)	27.9 (24.5, 31.2)	<0.001
Hazard Ratio (95% Confidence Intervals)						
Model 1	3,736	1.0	1.05 (0.85, 1.29)	1.43 (1.16, 1.76)	1.74 (1.38, 2.18)	<0.001
p-value			0.67	<0.001	<0.001	
Model 2	3,528	1.0	0.92 (0.74, 1.15)	1.30 (1.04, 1.63)	1.28 (1.00, 1.63)	0.008
p-value			0.46	0.02	0.05	
Model 3	3,528	1.0	0.94 (0.75, 1.17)	1.32 (1.06, 1.65)	1.35 (1.05, 1.72)	0.002
p-value			0.58	0.01	0.02	
<b>Congestive Heart Failure</b>						
Events		147	124	153	151	
Person-years		5,659	5,855	5,954	5,920	
Cumulative Incidence <sup>b</sup> , % (95% Confidence Interval) at median 6.8 years follow-up		12.9 (10.9, 15.0)	12.7 (10.6, 14.8)	17.0 (14.5, 19.4)	21.3 (18.0, 24.4)	<0.001

Variable	N	Urinary Sodium Excretion, mg/24 hours				P for trend
		<2,686	2,687 – 3,532	3,533 – 4,473	≥4,474	
Hazard Ratio (95% Confidence Intervals)						
Model 1	3,741	1.0	0.98 (0.77, 1.26)	1.37 (1.07, 1.75)	1.78 (1.36, 2.32)	<0.001
p-value			0.90	0.01	<0.001	
Model 2	3,533	1.0	0.84 (0.64, 1.09)	1.17 (0.90, 1.52)	1.17 (0.88, 1.57)	0.08
p-value			0.19	0.24	0.28	
Model 3	3,533	1.0	0.86 (0.66, 1.12)	1.18 (0.91, 1.54)	1.25 (0.94, 1.67)	0.03
p-value			0.27	0.20	0.12	
<b>Myocardial Infarction</b>						
Events		76	70	77	82	
Person-years		5,949	6,015	6,109	6,202	
Cumulative Incidence <sup>b</sup> , % (95% Confidence Interval) at median 6.8 years follow-up		7.2 (5.5, 8.9)	7.4 (5.7, 9.1)	8.5 (6.6, 10.4)	10.9 (8.4, 13.3)	0.01
Hazard Ratio (95% Confidence Intervals)						
Model 1	3,751	1.0	1.03 (0.74, 1.44)	1.20 (0.85, 1.69)	1.55 (1.07, 2.23)	0.01
p-value			0.86	0.31	0.02	
Model 2	3,540	1.0	0.91 (0.63, 1.31)	1.14 (0.78, 1.65)	1.25 (0.84, 1.88)	0.16
p-value			0.61	0.50	0.27	
Model 3	3,540	1.0	0.92 (0.64, 1.32)	1.14 (0.79, 1.66)	1.30 (0.87, 1.95)	0.11
p-value			0.65	0.49	0.20	

Variable	N	Urinary Sodium Excretion, mg/24 hours				P for trend
		<2,686	2,687 – 3,532	3,533 – 4,473	≥4,474	
<b>Stroke</b>						
Events		36	39	39	34	
Person-years		6,045	6,202	6,262	6,320	
Cumulative Incidence <sup>b</sup> , % (95% Confidence Interval) at median 6.8 years follow-up		2.8 (1.8, 3.8)	3.8 (2.6, 5.0)	4.7 (3.2, 6.2)	5.5 (3.5, 7.4)	0.008
Hazard Ratio (95% Confidence Intervals)						
Model 1	3,753	1.0	1.39 (0.87, 2.20)	1.75 (1.07, 2.85)	2.02 (1.18, 3.47)	0.008
p-value			0.17	0.03	0.01	
Model 2	3,542	1.0	1.25 (0.77, 2.02)	1.74 (1.04, 2.91)	1.88 (1.07, 3.33)	0.02
p-value			0.37	0.03	0.03	
Model 3	3,542	1.0	1.24 (0.77, 2.01)	1.73 (1.04, 2.89)	1.91 (1.08, 3.33)	0.02
p-value			0.38	0.04	0.03	

Model 1: Adjusted for age, sex, race, clinic site and urinary creatinine excretion; Model 2: Model 1 plus education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, use of antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, and urinary creatinine excretion; Model 3: Model 2 plus adjustment for baseline eGFR.

<sup>a</sup>Composite CVD is defined as congestive heart failure, stroke, and myocardial infarction; <sup>b</sup>Adjusted for age, sex, race, clinic site and urinary creatinine excretion

**eTable 2. Hazard Ratios and 95% Confidence Intervals of Composite Cardiovascular Disease, Congestive Heart Failure, Myocardial Infarction, and Stroke Associated with a 1,000 mg difference in Calibrated 24-Hour Urinary Sodium Excretion with Additional Adjustment for Total Calorie Intake and Systolic Blood Pressure**

Subgroups	Calibrated Urinary Sodium Excretion <sup>a</sup> per 1,000 mg/24 hours											
	Composite CVD <sup>b</sup>			Congestive Heart Failure			Myocardial Infarction			Stroke		
	N	HR (95% CI)	P value	N	HR (95% CI)	P value	N	HR (95% CI)	P value	N	HR (95% CI)	P value
Model 1	3,528	1.10 (1.05, 1.16)	<0.001	3,533	1.09 (1.02, 1.15)	0.005	3,540	1.07 (0.98, 1.16)	0.11	3,542	1.16 (1.05, 1.28)	0.003
Model 2	2,726	1.11 (1.05, 1.17)	<0.001	2,729	1.09 (1.02, 1.17)	0.01	2,736	1.04 (0.95, 1.15)	0.37	2,738	1.17 (1.06, 1.30)	0.002
Model 3	3,528	1.10 (1.04, 1.15)	<0.001	3,533	1.08 (1.02, 1.14)	0.01	3,540	1.06 (0.98, 1.15)	0.16	3,542	1.15 (1.04, 1.27)	0.006

Multivariable model 1: Adjusted for age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, LDL-cholesterol, glucose, history of CVD, use of antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, and baseline eGFR; Multivariable model 2: Model 1 plus adjustment for caloric intake; Multivariable model 3: Model 1 plus adjustment for systolic blood pressure

<sup>a</sup>Calibrated to mean urinary creatinine excretion of 1,569 mg/24 hours in men and 1,130 mg/24 hours in women; <sup>b</sup>Composite CVD is defined as congestive heart failure, stroke, and myocardial infarction

**eTable 3. Characteristics of 3,757 Patients with Chronic Kidney Disease According to Quartile of Calibrated 24-Hour Urinary Potassium Excretion, the Chronic Renal Insufficiency Cohort Study**

Variable	Calibrated Urinary Potassium Excretion <sup>a</sup> , mg/24 hours				p value
	<1,608 (N=940)	1,608 – 2,107 (N=939)	2,108 – 2,750 (N=938)	≥2,751 (N=940)	
Age, years	55.0 ± 11.5	56.9 ± 11.2	58.8 ± 10.3	60.4 ± 9.8	<0.001
Men, N (%)	346 (36.8%)	485 (51.7%)	570 (60.8%)	687 (73.1%)	<0.001
Race/Ethnicity, N (%)					
White	189 (20.1%)	377 (40.1%)	532 (56.7%)	678 (72.1%)	<0.001
Black	696 (74.0%)	464 (49.4%)	275 (29.3%)	122 (13.0%)	
Other	55 (5.9%)	98 (10.4%)	131 (14.0%)	140 (14.9%)	
High School Graduate, N (%)	715 (76.1%)	745 (79.3%)	762 (81.3%)	788 (83.8%)	<0.001
Current Smoking N (%)	159 (16.9%)	141 (15.0%)	103 (11.0%)	77 (8.2%)	<0.001
Weekly Alcohol Drinking, N (%)	196 (20.9%)	239 (25.5%)	263 (28.0%)	270 (28.7%)	<0.001
Physical Activity, METs/week	208.8 ± 163.5	204.2 ± 151.7	196.7 ± 136.1	186.9 ± 122.9	0.006
Hypertension, N (%)	823 (87.6%)	817 (87.0%)	808 (86.1%)	785 (83.5%)	0.06
Diabetes, N (%)	372 (39.6%)	461 (49.1%)	468 (49.9%)	494 (52.6%)	<0.001
History of CVD, N (%)	290 (30.9%)	306 (32.6%)	274 (29.2%)	369 (39.3%)	<0.001
Antihypertensive Medication, N (%)	866 (92.6%)	858 (92.3%)	852 (91.5%)	850 (91.1%)	0.62
Diuretics	555 (59.4%)	572 (61.5%)	537 (57.7%)	540 (57.9%)	0.31
RAS Blocking Agents	647 (69.2%)	664 (71.4%)	641 (68.9%)	615 (65.9%)	0.09
Other Antihypertensive Medications	642 (68.7%)	657 (70.6%)	646 (69.4%)	682 (73.1%)	0.16
Lipid-lowering Medication, N (%)	483 (51.7%)	557 (59.9%)	576 (61.9%)	621 (66.6%)	<0.001
Antidiabetic Medication, N (%)	324 (34.7%)	419 (45.1%)	424 (45.5%)	445 (47.7%)	<0.001
Systolic Blood Pressure, mmHg	128.0 ± 22.3	127.3 ± 21.0	128.3 ± 21.3	128.7 ± 22.7	0.57

Variable	Calibrated Urinary Potassium Excretion <sup>a</sup> , mg/24 hours				p value
	<1,608 (N=940)	1,608 – 2,107 (N=939)	2,108 – 2,750 (N=938)	≥2,751 (N=940)	
Diastolic Blood Pressure, mmHg	72.9 ± 13.5	71.6 ± 12.5	71.2 ± 12.5	70.2 ± 12.3	<0.001
Waist Circumference, cm	106.3 ± 18.4	106.7 ± 18.0	105.7 ± 16.8	104.0 ± 16.3	0.005
Body Mass Index, kg/m <sup>2</sup>	33.2 ± 8.5	32.4 ± 7.6	31.6 ± 7.1	30.5 ± 6.8	<0.001
Lean Body Mass Index, kg/m <sup>2</sup>	20.6 ± 4.0	21.0 ± 4.2	21.1 ± 4.2	21.2 ± 4.2	0.006
Daily Total Calorie Intake, kcal	1,820 ± 857	1,838 ± 855	1,834 ± 823	1,834 ± 734	0.98
LDL Cholesterol, mg/dL	107.6 ± 38.0	101.3 ± 34.6	102.8 ± 36.0	97.9 ± 32.5	<0.001
HDL Cholesterol, mg/dL	48.5 ± 16.3	47.3 ± 14.8	47.1 ± 15.1	47.0 ± 15.6	0.13
Triglycerides, mg/dL	148.6 ± 112.7	163.0 ± 136.0	158.0 ± 112.3	156.3 ± 101.0	0.06
Glucose, mg/dL	109.4 ± 45.9	116.0 ± 51.8	116.1 ± 52.0	116.9 ± 50.3	0.004
HbA1c, %	6.5 ± 1.5	6.7 ± 1.6	6.7 ± 1.5	6.7 ± 1.5	0.13
Urinary Creatinine, mg/24 hr	1,429 ± 499	1,403 ± 488	1,378 ± 454	1,285 ± 407	<0.001
Urinary Sodium, mg/24 hr	3,450 ± 1,295	3,676 ± 1,391	3,802 ± 1,440	3,876 ± 1,594	<0.001
Urinary Potassium, mg/24 hr	1,420 ± 469	1,891 ± 540	2,321 ± 623	3,012 ± 1,130	<0.001
Calibrated Sodium Excretion, mg/24 hr	3,237 ± 1,099	3,668 ± 1,092	3,994 ± 1,314	4,564 ± 1,853	<0.001
Calibrated Potassium Excretion, mg/24 hr	1,300 ± 226	1,861 ± 144	2,399 ± 182	3,495 ± 937	<0.001
Urinary Protein, g/24 hr	0.16 (0.07, 0.76)	0.19 (0.07, 0.95)	0.17 (0.07, 0.86)	0.21 (0.08, 1.11)	0.02
eGFR, ml/min/1.73 m <sup>2</sup>	44.5 ± 15.8	44.1 ± 14.9	44.7 ± 14.2	44.7 ± 14.7	0.80

Values are percentage of participants, mean ± standard deviation, or median (interquartile range). CVD = cardiovascular disease; RAS = renin-angiotensin system; LDL = low-density lipoprotein; HDL = high-density lipoprotein; HbA1c = glycated hemoglobin; and eGFR = estimated-glomerular filtration rate.

<sup>a</sup>Calibrated to mean urinary creatinine excretion of 1,569 mg/24 hours in men and 1,130 mg/24 hours in women.

**eTable 4. Hazard Ratios and 95% Confidence Intervals of Composite Cardiovascular Disease, Congestive Heart Failure, Myocardial Infarction, and Stroke According to Quartile of Calibrated 24-Hour Urinary Potassium Excretion**

Variable	N	Calibrated Urinary Potassium Excretion <sup>a</sup> , mg/24 hours				P for trend
		<1,608	1,608 – 2,107	2,108 – 2,750	≥2,751	
No. of Participants		940	939	938	940	
<b>Composite CVD<sup>b</sup></b>						
Events		185	203	177	239	
Person-years		5,833	5,628	5,654	5,410	
Cumulative Incidence <sup>c</sup> , % (95% Confidence Interval) at median 6.8 years follow-up		17.2 (14.7, 19.6)	20.5 (17.9, 23.0)	20.2 (17.4, 22.8)	28.2 (24.8, 31.4)	<0.001
Hazard Ratio (95% Confidence Intervals)						
Model 1	3,736	1.0	1.22 (1.00, 1.50)	1.20 (0.96, 1.51)	1.80 (1.43, 2.27)	<0.001
p-value			0.05	0.11	<0.001	
Model 2	3,528	1.0	1.02 (0.82, 1.27)	1.00 (0.79, 1.26)	1.20 (0.93, 1.54)	0.15
p-value			0.82	0.98	0.17	
Model 3	3,528	1.0	1.04 (0.84, 1.29)	1.02 (0.81, 1.30)	1.26 (0.98, 1.63)	0.06
p-value			0.72	0.84	0.07	
<b>Congestive Heart Failure</b>						
Events		134	141	131	169	
Person-years		6,025	5,844	5,879	5,640	
Cumulative Incidence <sup>c</sup> , % (95% Confidence Interval) at median 6.8 years follow-up		11.9 (9.9, 14.0)	14.3 (12.1, 16.5)	15.2 (12.7, 17.6)	21.1 (18.0, 24.2)	<0.001



Variable	N	Calibrated Urinary Potassium Excretion <sup>a</sup> , mg/24 hours				P for trend
		<1,608	1,608 – 2,107	2,108 – 2,750	≥2,751	
Hazard Ratio (95% Confidence Intervals)						
Model 1	3,741	1.0	1.22 (0.96, 1.56)	1.30 (1.00, 1.70)	1.91 (1.45, 2.51)	<0.001
p-value			0.11	0.05	<0.001	
Model 2	3,533	1.0	0.95 (0.73, 1.23)	1.01 (0.77, 1.34)	1.16 (0.86, 1.57)	0.23
p-value			0.68	0.92	0.34	
Model 3	3,533	1.0	0.96 (0.74, 1.24)	1.40 (0.79, 1.38)	1.23 (0.91, 1.66)	0.12
p-value			0.76	0.76	0.18	
<b>Myocardial Infarction</b>						
Events		66	77	72	90	
Person-years		6,279	6,067	6,072	5,857	
Cumulative Incidence <sup>c</sup> , % (95% Confidence Interval) at median 6.8 years follow-up		7.2 (5.4, 9.1)	8.3 (6.4, 10.0)	7.9 (6.1, 9.6)	9.7 (7.6, 11.8)	0.12
Hazard Ratio (95% Confidence Intervals)						
Model 1	3,751	1.0	1.15 (0.82, 1.61)	1.09 (0.76, 1.57)	1.36 (0.93, 1.99)	0.12
p-value			0.43	0.65	0.11	
Model 2	3,540	1.0	1.07 (0.74, 1.54)	0.95 (0.64, 1.41)	0.99 (0.65, 1.52)	0.86
p-value			0.71	0.81	0.98	
Model 3	3,540	1.0	1.08 (0.75, 1.56)	0.98 (0.66, 1.45)	1.04 (0.68, 1.58)	0.99
p-value			0.66	0.90	0.87	

Variable	N	Calibrated Urinary Potassium Excretion <sup>a</sup> , mg/24 hours				P for trend
		<1,608	1,608 – 2,107	2,108 – 2,750	≥2,751	
<b>Stroke</b>						
Events		38	39	30	41	
Person-years		6,354	6,233	6,218	6,024	
Cumulative Incidence <sup>c</sup> , % (95% Confidence Interval) at median 6.8 years follow-up		3.1 (2.0, 4.2)	3.7 (2.5, 4.9)	3.6 (2.3, 4.9)	5.7 (3.7, 7.6)	0.02
Hazard Ratio (95% Confidence Intervals)						
Model 1	3,753	1.0	1.18 (0.75, 1.86)	1.14 (0.68, 1.91)	1.86 (1.09, 3.16)	0.02
p-value			0.48	0.62	0.02	
Model 2	3,542	1.0	1.01 (0.63, 1.64)	1.03 (0.60, 1.75)	1.38 (0.78, 2.43)	0.24
p-value			0.95	0.92	0.26	
Model 3	3,542	1.0	1.03 (0.64, 1.66)	1.04 (0.61, 1.77)	1.41 (0.80, 2.48)	0.22
p-value			0.91	0.88	0.24	

Multivariable model 1: Adjusted for age, sex, race and clinic site; Multivariable model 2: Model 1 plus education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, glucose, LDL-cholesterol, history of CVD, use of antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, and urinary creatinine excretion; Multivariable model 3: Model 2 plus baseline eGFR.

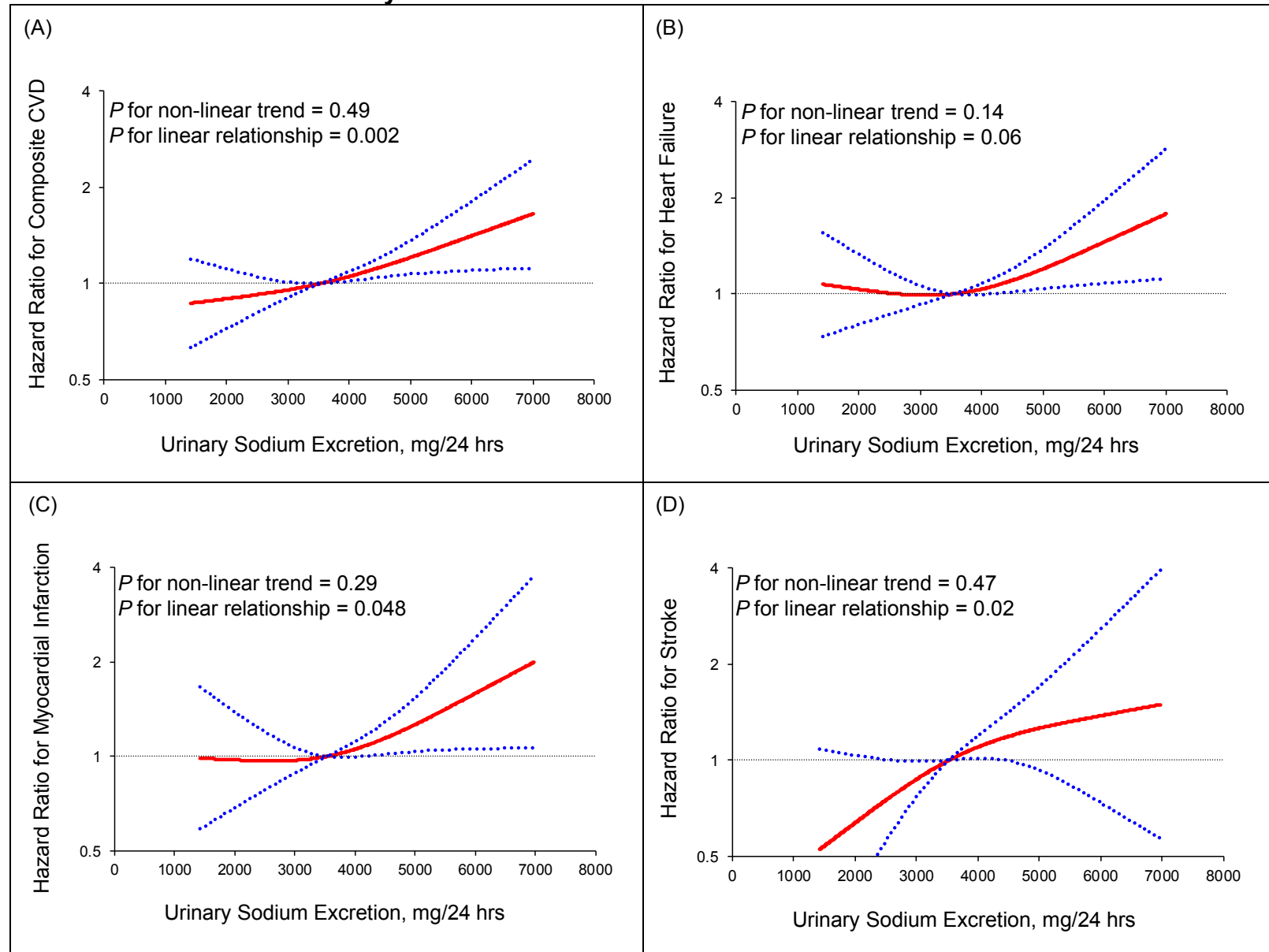
<sup>a</sup>Calibrated to mean urinary creatinine excretion of 1,569 mg/24 hours in men and 1,130 mg/24 hours in women; <sup>b</sup>Composite CVD is defined as congestive heart failure, stroke, and myocardial infarction; <sup>c</sup>Adjusted for age, sex, race and clinic site.

**eTable 5. P-values for Non-linear and Linear Associations between 24-hour Urinary Sodium Excretion and Cardiovascular Disease: Restricted Cubic Spline Regression using Alternate Numbers of Knots and Middle Knot Locations**

Spline Model	Composite CVD		CHF		MI		Stroke	
	P for non-linearity	P for linearity	P for non-linearity	P for linearity	P for non-linearity	P for linearity	P for non-linearity	P for linearity
3 knots @ 5, 50, 95%	0.11	<0.001	0.04	0.004	0.21	0.12	0.21	<0.001
4 knots @ 5, 35, 65, 95%	0.23	<0.001	0.12	0.004	0.29	0.12	0.29	<0.001
5 knots @ 5, 27.5, 50, 72.5, 95%	0.22	<0.001	0.12	0.004	0.42	0.12	0.46	<0.001
3 knots @ 5%, 3,800 mg/day, 95%	0.11	<0.001	0.04	0.004	0.22	0.12	0.22	<0.001
3 knots @ 5%, 4,000 mg/day, 95%	0.11	<0.001	0.04	0.004	0.22	0.12	0.22	<0.001

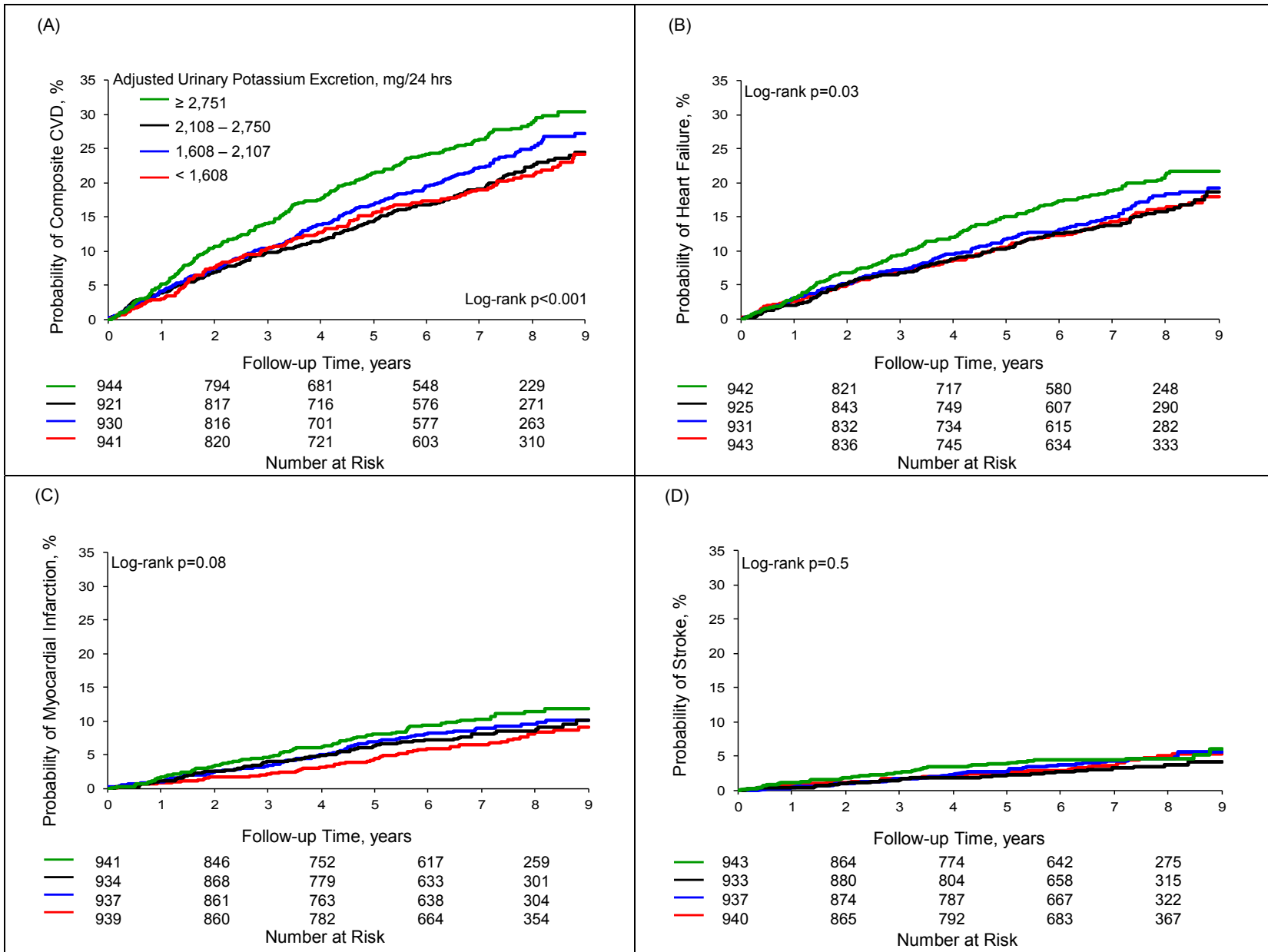
CVD=cardiovascular disease; CHF=congestive heart failure; MI=myocardial infarction

**eFigure 1. Multiple-adjusted Hazard Ratios and 95% Confidence Intervals of Cardiovascular Disease Associated with 24-hour Urinary Sodium Excretion**



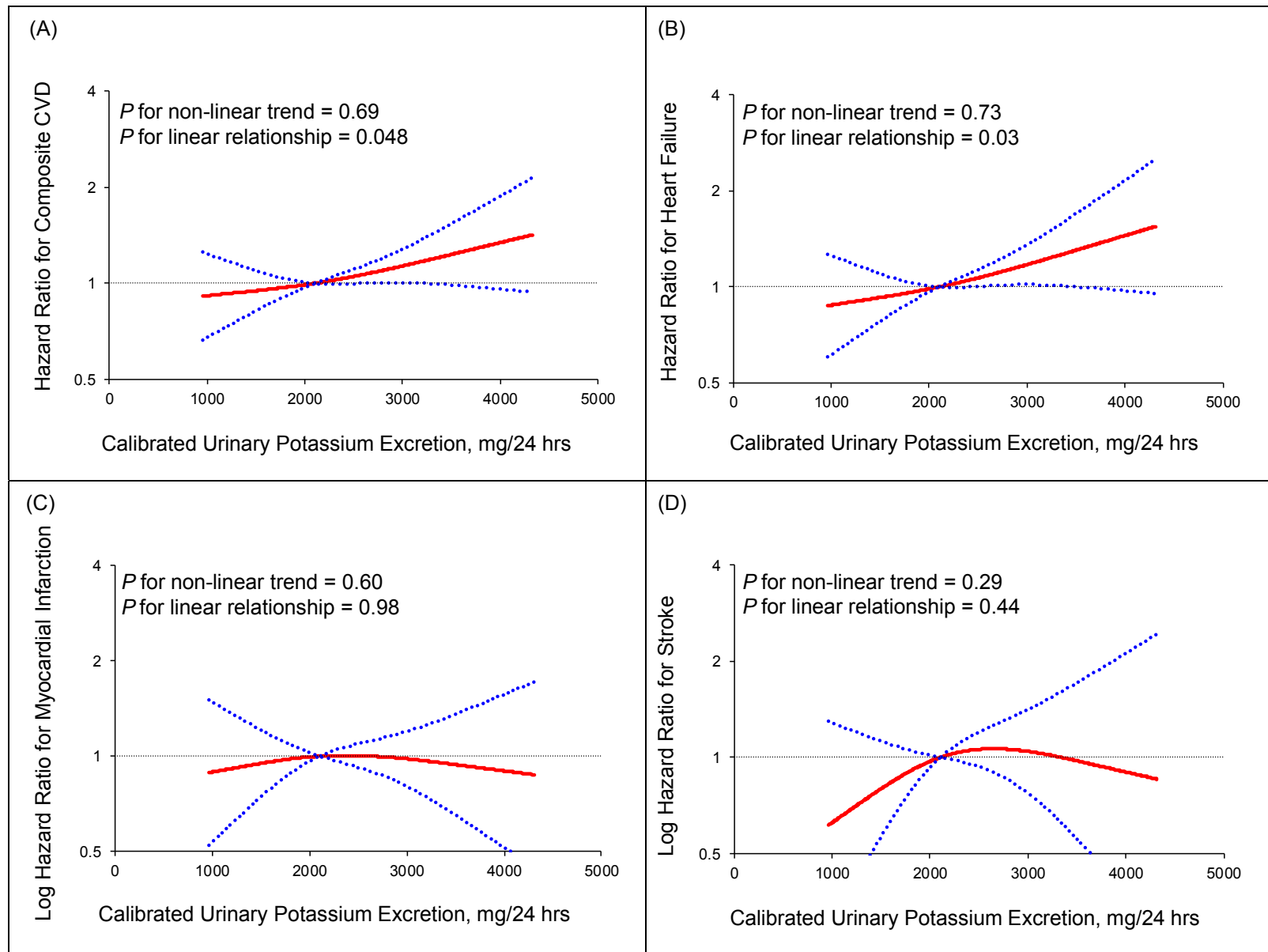
(A) Composite Cardiovascular Disease, (B) Congestive Heart Failure, (C) Myocardial Infarction, and (D) Stroke. Adjusted for age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, glucose, LDL-cholesterol, history of CVD, use of antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, and baseline eGFR.

**eFigure 2. Cumulative Kaplan Meier Estimates of Cardiovascular Diseases According to Quartile of Calibrated 24-Hour Urinary Potassium Excretion**



(A) Composite Cardiovascular Disease, (B) Congestive Heart Failure, (C) Myocardial Infarction, and (D) Stroke

**eFigure 3. Multiple-adjusted Hazard Ratios and 95% Confidence Intervals of Cardiovascular Disease Associated with Calibrated 24-hour Urinary Potassium Excretion**



(A) Composite Cardiovascular Disease, (B) Congestive Heart Failure, (C) Myocardial Infarction, and (D) Stroke. Adjusted for age, sex, race, clinic site, education, waist circumference, lean body mass index, body mass index, cigarette smoking, alcohol drinking, physical activity, glucose, LDL-cholesterol, history of CVD, use of antidiabetic medications, lipid-lowering medications, diuretics, renin-angiotensin system blocking agents, and other antihypertensive medications, urinary creatinine excretion, and baseline eGFR.