

Supplement Materials

Dietary sodium to potassium ratio as a risk factor for stroke, cardiovascular diseases and all-cause mortality in Japan: The NIPPON DATA80 Cohort Study

Akira Okayama, MD, PhD, Nagako Okuda, MD, PhD, Katsuyuki Miura, MD, PhD, Tomonori Okamura, MD, PhD, Takehito Hayakawa, PhD, Hiroshi Akasaka, MD, PhD, Hirofumi Ohnishi, MD, PhD, Shigeyuki Saitoh, MD, PhD, Yusuke Arai, PhD, Yutaka Kiyohara, MD, PhD, Miho Nozue, PhD, Naoyuki Takashima, MD, PhD, Katsushi Yoshita, PhD, Akira Fujiyoshi, MD, PhD, Maryam Zaid, PhD, Takayoshi Ohkubo, MD, PhD, and Hirotsugu Ueshima, MD, PhD, on behalf of the NIPPON DATA80 Research Group

Corresponding author:

Akira Okayama, MD, PhD

Research Institute of Strategy for Prevention

Shinkawa 1-3-9 4F, Chuohku, Tokyo 104-0033, Japan

Email address: aokayama@jrisp.com

TEL: +81-3-4560-1955 FAX: +81-3-4560-1960

List of online materials

Online Supplement Table 1.

Definition of underlying causes of death using International Classification of Disease (ICD) during follow-up period (1980-2004).

Online Supplement Table 2.

Age-adjusted relative risks and 95 percent confidence interval for deaths from all causes, cardiovascular and stroke subtypes according to the quintiles of dietary sodium-to-potassium ratio by Mantel-Haenszel method for 24-year follow-up NIPPON DATA80.

Online Supplement Table 3.

Quadratic nonlinear multivariate-adjusted hazard ratio (HR) and 95% confidence interval (95% CI) for deaths from all causes, cardiovascular diseases (CVD), stroke, and stroke subtypes for the highest quintile vs. the lowest quintile of dietary sodium-to-potassium ratio in men and women.

Online Supplement Table 4.

Person-years, mortality numbers (No.) and age-adjusted mortality rate (per 100,000 person-years) according to quintiles of dietary sodium-to-potassium ratio for deaths from all causes, cardiovascular diseases (CVD), stroke and stroke subtypes by 24-year follow-up of the

participants of National Survey on Cardiovascular Disease in 1980 (NIPPON DATA80) using density value.

Online Supplement Table 5.

Age-adjusted relative hazard and 95 percent confidence interval for deaths from all causes, cardiovascular diseases (CVD), stroke and stroke subtypes according to dietary sodium-to-potassium ratio quintiles using density value by Mantel-Haenszel method for 24-year follow-up among participants without antihypertensive drugs in NIPPON DATA80.

Online Supplement Table 6.

Quadratic multivariate-adjusted hazard ratio (HR) and 95% confidence interval (95% CI) for deaths from all causes, cardiovascular diseases (CVD), stroke, and stroke subtypes for the highest quintile vs. the lowest quintile dietary sodium-to-potassium ratio from density value in total participants.

Online Supplement Figure.

Participants Flow Chart

Online Supplement Table 1. Definition of underlying causes of death using International Classification of Disease (ICD) during follow-up period (1980-2004).

	ICD-9 (1980-1994)	ICD-10 (1995-2004)
Total stroke	430-438	I60-I69
Ischemic stroke	433, 434, 437.7a, 7b	I63, I69.3
Hemorrhagic stroke	431-432	I61, I69.1
Cardiovascular diseases	390-459	I00-I99

Online Supplement Table 2. Age-adjusted relative risks and 95 percent confidence interval for deaths from all causes, cardiovascular and stroke subtypes according to the quintiles of dietary sodium-to-potassium ratio by Mantel-Haenszel method for 24-year follow-up NIPPON DATA80.

	Q1	Q2	Q3	Q4	Q5	P *	P **
Men							
All causes	1	0.95 (0.78- 1.16)	1.10 (0.91- 1.33)	1.16 (0.96- 1.40)	1.26 (1.04- 1.51)	0.003	<0.001
CVD	1	1.10 (0.77- 1.59)	1.03 (0.71- 1.49)	1.18 (0.82- 1.70)	1.56 (1.11- 2.20)	0.020	<0.001
Stroke	1	1.08 (0.63- 1.87)	1.42 (0.85- 2.37)	1.44 (0.86- 2.41)	1.63 (0.97- 2.72)	0.061	0.032
Ischemic stroke	1	0.93 (0.48- 1.81)	1.10 (0.58- 2.08)	1.32 (0.65- 2.70)	1.05 (0.57- 1.93)	0.534	0.073
Hemorrhagic stroke	1	6.81 (1.20- 38.79)	10.48 (2.10- 52.30)	8.87 (1.75- 45.05)	11.10 (2.24- 54.69)	0.010	0.041
Women							
All causes	1	1.13 (0.91- 1.39)	0.93 (0.75- 1.15)	1.04 (0.84- 1.29)	1.16 (0.94- 1.42)	0.356	0.119
CVD	1	1.20 (0.82- 1.75)	0.94 (0.64- 1.40)	1.11 (0.76- 1.63)	1.23 (0.86- 1.77)	0.465	0.096
Stroke	1	1.19 (0.64- 2.22)	1.22 (0.67- 2.24)	1.17 (0.63- 2.17)	1.81 (1.05- 3.13)	0.052	0.003
Ischemic stroke	1	1.34 (0.57- 3.12)	1.29 (0.56- 2.99)	1.27 (0.54- 2.98)	1.66 (0.76- 3.60)	0.231	0.277
Hemorrhagic stroke	1	0.76 (0.25- 2.34)	0.44 (0.12- 1.60)	0.61 (0.19- 1.99)	1.27 (0.48- 3.35)	0.855	0.139

* P values of the test for linear trends were calculated using Cox proportional hazards model. ** P values of the test for quadratic nonlinear trends were calculated using Cox proportional hazards model.

Online Supplement Table 3. Quadratic nonlinear multivariate-adjusted hazard ratio (HR) and 95% confidence interval (95% CI) for deaths from all causes, cardiovascular diseases (CVD), stroke, and stroke subtypes for the highest quintile vs. the lowest quintile of dietary sodium-to-potassium ratio in men and

	Men		Women	
	H.R.	(95% CI)	H.R.	(95% CI)
Model I				
All causes	1.23	(1.09- 1.38)	1.11	(0.97- 1.28)
CVD	1.51	(1.24- 1.83)	1.21	(0.97- 1.52)
Stroke	1.37	(1.02- 1.85)	1.47	(1.13- 1.92)
Ischemic stroke	1.49	(1.01- 2.20)	1.39	(0.90- 2.14)
Hemorrhagic stroke	1.65	(0.97- 2.80)	1.47	(0.79- 2.75)
Model II				
All causes	1.21	(1.07- 1.37)	1.09	(0.95- 1.26)
CVD	1.54	(1.27- 1.88)	1.22	(0.97- 1.53)
Stroke	1.40	(1.03- 1.88)	1.48	(1.13- 1.94)
Ischemic stroke	1.53	(1.04- 2.25)	1.38	(0.88- 2.16)
Hemorrhagic stroke	1.65	(0.97- 2.81)	1.49	(0.79- 2.79)
Model III				
All causes	1.19	(1.05- 1.35)	1.09	(0.95- 1.26)
CVD	1.50	(1.23- 1.83)	1.22	(0.98- 1.53)
Stroke	1.35	(0.99- 1.84)	1.49	(1.14- 1.94)
Ischemic stroke	1.50	(1.01- 2.22)	1.39	(0.89- 2.17)
Hemorrhagic stroke	1.59	(0.92- 2.75)	1.53	(0.82- 2.87)

Model I was adjusted for age, sex (for total participants), BMI, smoking and drinking habits.

Model II was adjusted for variables in model I plus diabetes and serum total cholesterol.

Model III was adjusted for variables in model II plus percent energy intake from protein and total fat

Online Supplement Table 4. Person-years, mortality numbers (No.) and age-adjusted mortality rate (per 100,000 person-years) according to quintiles of dietary sodium-to-potassium ratio for deaths from all causes, cardiovascular diseases (CVD), stroke and stroke subtypes by 24-year follow-up of the participants of National Survey on Cardiovascular Disease in 1980 (NIPPON DATA80) using density value.

	Total	Q1		Q2		Q3		Q4		Q5	
		No.	(rate)	No.	(rate)	No.	(rate)	No.	(rate)	No.	(rate)
Men											
<i>Person years</i>	76399	15052		15288		15953		15604		14502	
All Causes		186	(824)	192	(882)	201	(856)	243	(1013)	264	(1082)
CVD		52	(227)	56	(259)	52	(219)	65	(276)	84	(342)
Stroke		24	(106)	28	(133)	28	(118)	35	(150)	40	(157)
Ischemic Stroke		18	(78)	17	(79)	14	(61)	19	(79)	22	(80)
Hemorrhagic Stroke		1	(4)	8	(41)	8	(32)	9	(38)	13	(49)
Women											
<i>Person years</i>	100546	20129		20177		20404		20499		19337	
All Causes		159	(471)	158	(499)	155	(457)	161	(437)	219	(554)
CVD		46	(137)	54	(173)	49	(141)	45	(115)	75	(177)
Stroke		14	(45)	19	(67)	24	(64)	17	(44)	41	(98)
Ischemic Stroke		8	(22)	9	(27)	15	(39)	10	(26)	18	(42)
Hemorrhagic Stroke		4	(16)	7	(22)	3	(9)	3	(8)	11	(26)
Men and women combined											
<i>Person years</i>	176944	35181		35464		36358		36103		33838	
All Causes		1938	345 (615)	350 (656)		356 (622)		404 (674)		483 (771)	
CVD		579	98 (173)	110 (208)		101 (172)		110 (181)		160 (243)	

Stroke	270	38	(69)	47	(93)	52	(86)	52	(86)	81	(122)
Ischemic Stroke	150	26	(45)	26	(47)	29	(48)	29	(46)	40	(56)
Hemorrhagic Stroke	67	5	(11)	15	(30)	11	(19)	12	(19)	24	(35)

Online Supplement Table 5. Age-adjusted relative hazard and 95 percent confidence interval for deaths from all causes, cardiovascular diseases (CVD), stroke and stroke subtypes according to dietary sodium-to-potassium ratio quintiles using density value by Mantel-Haenszel method for 24-year follow-up among participants without antihypertensive drugs in NIPPON DATA80.

	Q1	Q2	Q3	Q4	Q5	P*	P**
Men							
All Causes	1	1.07 (0.87- 1.34)	1.03 (0.85- 1.26)	1.22 (1.01- 1.52)	1.26 (1.04- 1.52)	0.014	-
CVD	1	1.07 (0.77- 1.68)	0.95 (0.66- 1.43)	1.17 (0.81- 1.90)	1.43 (1.01- 2.03)	0.075	-
Stroke	1	1.18 (0.71- 2.29)	1.24 (0.66- 1.97)	1.38 (0.82- 2.86)	1.46 (0.88- 2.45)	0.180	-
Ischemic Stroke	1	0.91 (0.52- 2.07)	0.75 (0.38- 1.53)	0.99 (0.52- 2.20)	1.03 (0.55- 1.95)	0.980	-
Hemorrhagic Stroke	1	5.99 (1.45- 38.89)	7.46 (1.23- 45.23)	8.69 (1.53- 42.58)	12.19 (2.36- 71.43)	0.014	-
Women							
All Causes	1	1.06 (0.85- 1.19)	0.96 (0.77- 1.19)	0.95 (0.76- 1.18)	1.15 (0.94- 1.42)	0.509	-
CVD	1	1.27 (0.86- 1.87)	1.05 (0.70- 1.56)	1.91 (0.61- 1.38)	1.37 (0.95- 1.97)	0.481	-
Stroke	1	1.44 (0.73- 2.86)	1.68 (0.88- 3.22)	1.13 (0.56- 2.30)	2.44 (1.35- 4.43)	0.016	-
Ischemic Stroke	1	1.25 (0.49- 3.19)	1.84 (0.79- 4.26)	1.16 (0.46- 1.16)	1.79 (0.80- 4.03)	0.189	-
Hemorrhagic Stroke	1	1.78 (0.53- 5.93)	0.73 (0.16- 3.29)	0.73 (0.16- 3.25)	2.41 (0.73- 7.89)	0.505	-
Men and women combined							
All Causes	1	1.06 (0.92- 1.32)	1.00 (0.86- 1.16)	1.10 (0.95- 1.27)	1.20 (1.05- 1.38)	0.018	0.001
CVD	1	1.19 (0.91- 1.56)	1.01 (0.76- 1.33)	1.05 (0.80- 1.38)	1.39 (1.08- 1.79)	0.086	0.005
Stroke	1	1.31 (0.86- 2.86)	1.68 (0.88- 3.22)	1.13 (0.56- 2.30)	2.44 (1.35- 1.23)	0.011	0.002
Ischemic Stroke	1	1.08 (0.63- 1.86)	1.10 (0.65- 1.86)	1.04 (0.61- 1.76)	1.25 (0.77- 2.05)	0.438	0.024
Hemorrhagic Stroke	1	3.03 (1.17- 7.88)	2.1 (0.74- 5.96)	2.3 (0.83- 6.42)	4.33 (1.69- 11.08)	0.023	0.099

* P values of the test for linear trends were calculated using Cox proportional hazards model.

** P value of the test for quadratic nonlinear trends were calculated using Cox proportional hazards model.

Online Supplement Table 6. Quadratic multivariate-adjusted hazard ratio (HR) and 95% confidence interval (95% CI) for deaths from all causes, cardiovascular diseases (CVD), stroke, and stroke subtypes for the highest quintile vs. the lowest quintile dietary sodium-to-potassium ratio from density value in total participants.

	H.R.	(95% CI)
Model I (adjusted for age, sex, BMI, smoking and drinking habits)		
All Causes	1.14	(1.05- 1.24)
CVD	1.29	(1.13- 1.47)
Stroke	1.37	(1.14- 1.64)
Ischemic Stroke	1.36	(1.05- 1.74)
Hemorrhagic Stroke	1.48	(1.04- 2.11)
Model II (Model I + diabetes and serum cholesterol levels)		
All Causes	1.13	(1.03- 1.23)
CVD	1.31	(1.15- 1.49)
Stroke	1.38	(1.15- 1.65)
Ischemic Stroke	1.37	(1.07- 1.77)
Hemorrhagic Stroke	1.49	(1.04- 2.13)
Model III (Model II + protein and total fat intake)		
All Causes	1.13	(1.03- 1.24)
CVD	1.34	(1.16- 1.54)
Stroke	1.39	(1.14- 1.69)
Ischemic Stroke	1.37	(1.04- 1.80)
Hemorrhagic Stroke	1.53	(1.04- 2.25)

Model I was adjusted for age, sex, BMI, smoking and drinking habits.

Model II was adjusted for variables in model I plus diabetes and serum total cholesterol.

Model III was adjusted for variables in model II plus percent energy intake from protein and total fat

Participants Flow Chart

