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. Characteristics of Women in the *Outcome Cohort*[a] by Tertiles of the 24-Hour Urinary Sodium Excretion at Baseline

	24-Hour Urinary Sodium Excretion Tertiles		
	Low (n=645)	**Medium (n=658)**	**High (n=638)**
Participant characteristics, No (%)			
Diabetes mellitus	21 (3.3)	19 (2.9)	31 (4.9)
Antihypertensive treatment	96 (14.9)	82 (12.5)	106 (16.6)[M]
Smokers	167 (25.9)	146 (22.2)	141 (22.1)
Alcohol intake ≥5 g/day	69 (10.7)	68 (10.3)	89 (14.0)[M]
Educational attainment, No. (%)			
≤ Elementary school	281 (43.6)	241 (36.6)	188 (29.5)
Secondary school	289 (44.8)	318 (48.3)	327 (51.3)
Higher education	75 (11.6)	99 (15.1)[L]	123 (19.3)[LM]
Characteristic, mean (SD)			
Age, y	42.5 (17.6)	41.0 (16.0)	39.2 (14.7)[LM]
Blood pressure, mm Hg[b]			
Systolic	123.3 (19.4)	121.0 (16.8)[L]	121.7 (15.8)
Diastolic	74.7 (11.0)	74.6 (9.7)	75.4 (10.2)
Weight, kg	63.4 (12.9)	65.4 (12.3)[L]	68.7 (13.9)[LM]
BMI, kg/m^2	24.6 (5.1)	24.9 (4.6)	25.9 (5.3)[LM]
Total cholesterol, mg/dL	213 (51)	209 (47)	204 (45)[L]
24-hour urinary measurements, mean (SD)			
Duration, h:m	23:54 (00:50)	23:47 (00:56)	23:55 (00:53)
Volume, L	1.37 (0.64)	1.51 (0.62)[L]	1.67 (0.65)[LM]
Sodium, mmol	95.1 (22.0)	150.2 (15.0)[L]	231.7 (50.9)[LM]
Potassium, mmol	51.6 (17.8)	61.0 (20.5)[L]	69.1 (24.0)[LM]
Sodium-to-potassium ratio	2.02 (0.84)	2.76 (1.19)[L]	3.75 (1.73)[LM]
Creatinine, mmol	8.4 (2.2)	9.5 (2.0)[L]	10.6 (2.5)[LM]

Abbreviation: BMl, body mass index, which is calculated as weight in kilograms divided by height in meters squared.

Sl conversion factors: To convert millimoles of sodium to grams, multiply by 0.02299; to convert millimoles of potassium to grams, multiply by 0.039098; to convert millimoles of creatinine to grams, multiply by 0.11312; cholesterol from mg/dl to mmol/L, multiply by 0.0259.

[a]This analysis includes the *Outcome Cohort* (*n*=3681; see Figure 1 and Table 1).

[b]For the blood pressure determination and diabetes mellitus diagnosis, see the "Methods" section.

P<.05 *vs* low (L) or middle (M) tertile of 24-hour urinary sodium excretion.

eTable 2. Characteristics of Men in the *Outcome Cohort*[a] by Tertiles of the 24-Hour Urinary Sodium Excretion at Baseline

	24-Hour Urinary Sodium Excretion Tertiles		
	Low **(n=575)**	**Medium** **(n=592)**	**High** **(n=573)**
Participant characteristics, No (%)			
Diabetes mellitus	29 (5.0)	26 (4.4)	26 (4.5)
Antihypertensive treatment	64 (11.1)	44 (7.4)[L]	51 (8.9)
Smokers	202 (35.1)	221 (37.3)	167 (29.1)[LM]
Alcohol intake ≥5 g/day	197 (34.3)	211 (35.6)	252 (44.0)
Educational attainment, No. (%)			
≤ Elementary school	199 (34.6)	188 (31.8)	113 (19.7)
Secondary school	288 (50.1)	327 (55.2)	347 (60.6)
Higher education	88 (15.3)	77 (13.0)	113 (19.7)
Characteristic, mean (SD)			
Age, y	41.8 (18.1)	41.3 (16.4)	39.5 (14.4)[LM]
Blood pressure, mm Hg[b]			
Systolic	128.7 (17.9)	126.6 (14.9)[L]	128.1 (15.3)
Diastolic	77.8 (11.0)	76.6 (10.4)	79.0 (10.9)[M]
Weight, kg	74.1 (13.0)	76.9 (12.4)[L]	81.2 (14.1)[LM]
BMI	24.7 (3.8)	25.2 (3.8)[L]	26.1 (4.3)[LM]
Total cholesterol, mg/dL	205 (48)	206 (47)	205 (48)
24-hour urinary measurements, mean (SD)			
Duration, h:m	23:51 (01:04)	23:50 (01:07)	23:54 (01:01)
Volume, L	1.32 (0.59)	1.48 (0.57)[L]	1.78 (0.63)[LM]
Sodium, mmol	120.1 (28.4)	188.8 (17.6)[L]	290.5 (56.2)[LM]
Potassium, mmol	61.6 (26.3)	71.6 (27.1)[L]	84.5 (29.2)[LM]
Sodium-to-potassium ratio	2.21 (0.93)	2.99 (1.58)[L]	3.89 (1.79)[LM]
Creatinine, mmol	12.1 (3.2)	13.9 (3.4)[L]	16.1 (3.8)[LM]

Abbreviation: BMl, body mass index, which is calculated as weight in kilograms divided by height in meters squared.

Sl conversion factors: To convert millimoles of sodium to grams, multiply by 0.02299; to convert millimoles of potassium to grams, multiply by 0.039098; to convert millimoles of creatinine to grams, multiply by 0.11312; cholesterol from mg/dl to mmol/L, multiply by 0.0259.

[a]This analysis includes the *Outcome Cohort* (*n*=3681; see Figure 1 and Table 1).

[b]For the blood pressure determination and diabetes mellitus diagnosis, see the "Methods" section.

P<.05 *vs* low (L) or middle (M) tertile of 24-hour urinary sodium excretion.

eTable 3. Characteristics of Women in the *Hypertension Cohort*[a] by Tertiles of the 24-Hour Urinary Sodium Excretion at Baseline

	24-Hour Urinary Sodium Excretion Tertiles		
	Low (n=375)	**Medium (n=385)**	**High (n=373)**
Participant characteristics, No (%)			
Diabetes mellitus	7 (1.9)	6 (1.6)	7 (1.9)
Smokers	121 (32.3)	91 (23.6)	89 (23.9)
Alcohol intake 5 g/day	33 (8.8)	38 (9.9)	48 (12.9)
Educational attainment, No. (%)			
Elementary school	149 (39.7)	151 (39.2)	116 (31.1)
Secondary school	186 (49.6)	179 (46.5)	194 (52.0)
Higher education	40 (10.7)	55 (14.3)	63 (16.9)[L]
Characteristic, mean (SD)			
Age, y	38.9 (15.3)	38.7 (14.1)	36.7 (13.1)[LM]
Blood pressure, mm Hg[b]			
Systolic	115.6 (11.2)	115.6 (10.7)	116.8 (10.0)
Diastolic	71.3 (8.0)	72.1 (7.6)	73.0 (8.0)[L]
Weight, kg	61.6 (11.2)	63.7 (11.2)[L]	66.4 (12.4)[LM]
BMI, kg/m^2	23.6 (4.2)	24.1 (4.1)	25.0 (4.6)[LM]
Total cholesterol, mg/dL	208 (49)	208 (47)	200 (44)[LM]
24-hour urinary measurements, mean (SD)			
Duration, h:m	23:51 (00:58)	23:49 (00:55)	23:55 (00:56)
Volume, L	1.36 (0.67)	1.52 (0.64)[L]	1.68 (0.67)[LM]
Sodium, mmol	94.4 (21.5)	147.4 (14.3)[L]	222.1 (47.2)[LM]
Potassium, mmol	51.2 (17.2)	62.9 (21.1)[L]	69.4 (23.4)[LM]
Sodium-to-potassium ratio	2.00 (0.76)	2.63 (1.21)[L]	3.56 (1.66)[LM]
Creatinine, mmol	8.6 (2.2)	9.6 (2.0)[L]	10.8 (2.5)[LM]

Abbreviation: BMl, body mass index, which is calculated as weight in kilograms divided by height in meters squared.

Sl conversion factors: To convert millimoles of sodium to grams, multiply by 0.02299; to convert millimoles of potassium to grams, multiply by 0.039098; to convert millimoles of creatinine to grams, multiply by 0.11312; cholesterol from mg/dl to mmol/L, multiply by 0.0259.

[a]This analysis includes the *Hypertension Cohort* (*n*=2096; see Figure 1 and Table 1).

[b]For the blood pressure determination and diabetes mellitus diagnosis, see the "Methods" section.

P<.05 *vs* low (L) or middle (M) tertile of 24-hour urinary sodium excretion.

eTable 4. Characteristics of Men in the *Hypertension Cohort*[a] by Tertiles of the 24-Hour Urinary Sodium Excretion at Baseline

	24-Hour Urinary Sodium Excretion Tertiles		
	Low (n=318)	**Medium (n=328)**	**High (n=317)**
Participant characteristics, No (%)			
Diabetes mellitus	6 (1.9)	8 (2.4)	6 (1.9)
Smokers	120 (37.7)	128 (39.0)	104 (32.8)
Alcohol intake ≥5 g/day	112 (35.2)	108 (32.9)	126 (39.8)
Educational attainment, No. (%)			
≤ Elementary school	101 (31.8)	105 (32.0)	57 (18.0)
Secondary school	173 (54.4)	182 (55.5)	204 (64.3)
Higher education	44 (13.8)	41 (12.5)	56 (17.7)[LM]
Characteristic, mean (SD)			
Age, y	39.3 (16.0)	40.1 (15.4)	38.2 (13.4)
Blood pressure, mm Hg[b]			
Systolic	121.8 (9.7)	121.8 (8.7)	122.0 (9.3)
Diastolic	74.8 (8.2)	74.0 (7.9)	75.5 (7.7)[M]
Weight, kg	74.0 (12.1)	76.1 (11.1)[L]	78.6 (11.8)[LM]
BMI, kg/m^2	24.6 (3.4)	24.9 (3.3)	25.2 (3.6)[L]
Total cholesterol, mg/dL	206 (47)	206 (47)	205 (48)
24-hour urinary measurements, mean (SD)			
Duration, h:m	23:51 (01:11)	23:49 (01:11)	23:51 (01:06)
Volume, L	1.34 (0.61)	1.49 (0.57)[L]	1.75 (0.61)[LM]
Sodium, mmol	121.3 (27.9)	185.3 (16.1)[L]	282.2 (56.4)[LM]
Potassium, mmol	62.5 (26.3)	73.5 (23.4)[L]	84.1 (28.8)[LM]
Sodium-to-potassium ratio	2.19 (0.87)	2.78 (0.97)[L]	3.74 (1.49)[LM]
Creatinine, mmol	12.2 (3.1)	14.1 (3.2)[L]	16.1 (3.4)[LM]

Abbreviation: BMl, body mass index, which is calculated as weight in kilograms divided by height in meters squared.

Sl conversion factors: To convert millimoles of sodium to grams, multiply by 0.02299; to convert millimoles of potassium to grams, multiply by 0.039098; to convert millimoles of creatinine to grams, multiply by 0.11312; cholesterol from mg/dl to mmol/L, multiply by 0.0259.

[a]This analysis includes the *Hypertension Cohort* (*n*=2096; see Figure 1 and Table 1).

[b]For the blood pressure determination and diabetes mellitus diagnosis, see the "Methods" section.

P<.05 *vs* low (L) or middle (M) tertile of 24-hour urinary sodium excretion.

eTable 5. Characteristics of the Participants in the *Blood Pressure Cohort*[a] at Baseline and at Follow-up by Country						
Characteristic		**FLEMENGHO Belgium (n=1109)**	**Pilsen Czech Republic (n=69)**	**Padova Italy (n=148)**	**Kraków Poland (n=107)**	**Novosibirsk Russian Federation (n=66)**
Median follow-up, y (IQR)		5.59 (4.87–9.02)	5.74 (5.50–5.87)[B]	6.99 (6.60–7.23)	6.59 (6.34–6.84)[B]	7.69 (6.94–8.17)[C]
Participant characteristics, No. (%)						
Women		568 (51.2)	42 (60.9)	79 (53.4)	55 (51.4)	42 (63.6)[B]
Smokers	BL	359 (32.4)	18 (26.1)	39 (26.4)	24 (22.4)[B]	15 (22.7)
	FU	307 (27.7)	14 (20.3)	32 (21.6)	25 (23.4)	16 (24.2)
Alcohol intake ≥5 g/day	BL	216 (19.5)	28 (40.6)[B]	55 (37.2)[B]	20 (18.7)[CI]	26 (39.4)[BP]
	FU	345 (31.1)	32 (46.8)[B]	66 (44.6)[B]	30 (28.0)[CI]	20 (30.3)[I]
Contraceptive pill	BL	120 (10.8)	12 (17.4)	15 (10.1)	2 (1.9)[BI]	4 (6.1)[C]
	FU	98 (8.8)	9 (13.0)	0[BC]	5 (4.7)[CI]	1 (1.5)[BC]
NSAIDs	BL	146 (13.2)	1 (1.5)[B]	11 (7.4) [B]	10 (9.4)[C]	17 (25.8)[BCIP]
	FU	105 (9.5)	8 (11.6)	14 (9.5)	9 (8.4)	4 (6.1)
Characteristic, mean (SD)						
Age, y	BL	47.3 (15.2)	38.4 (12.7)[B]	44.3 (13.2)[C]	38.6 (13.0)[BI]	42.2 (13.2)[B]
BMI, kg/m^2	BL	24.7 (4.0)	24.6 (4.0)	24.3 (3.6)	24.3 (4.3)	23.7 (4.0)
	FU	25.6 (4.2)‡	25.4 (4.9)†	25.5 (3.9)‡	25.2 (4.5)	25.4 (4.6)‡
	Change, y	0.12 (0.34)	0.14 (0.35)	0.17 (0.29)	0.14 (0.30)	0.23 (0.36)
Blood pressure, mm Hg[b]						
Systolic	BL	121.6 (13.0)	116.7 (10.1)[B]	119.9 (12.6)	120.2 (12.3)	115.8 (10.7)[B]
	FU	124.4 (15.1)‡	116.7 (10.9)[B]	126.0 (15.3)[C]‡	130.0 (14.9)[BC]	119.3 (14.8)[IP]*
	Change, y	0.22 (2.04)	–0.01 (1.56)	0.87 (1.61)[C]	1.51 (1.80)[BC]	0.40 (1.59)[IP]
Diastolic	BL	74.3 (9.0)	74.3 (8.4)	77.2 (8.5)[B]	75.2 (8.7)	73.4 (8.0)[I]
	FU	77.7 (9.4)‡	77.7 (7.6)†	83.5 (9.2)[BC]‡	79.0 (9.6)[I]	77.1 (10.8)[I]†
	Change, y	0.40 (1.55)	0.60 (1.45)	0.91 (1.15)[B]	0.60 (1.38)	0.46 (1.32)
24-hour urinary measurements, mean (SD)						
Duration, h:m	BL	23:58 (00:50)	24:00	22:12	24:06 (00:43)[I]	23:57

				(00:29)[B]	(02:01)[BC]		(00:31)[CI]
	FU	23:58 (00:52)	23:40 (00:45)	25:19 (01:52)[BC]	24:01 (00:08)[I]	23:36 (01:02)[I]
Volume, L	BL	1.58 (0.67)	1.87 (0.67)[B]	1.27 (0.41)[BC]	1.43 (0.57)[C]	1.31 (0.52)[BC]
	FU	1.65 (0.73)†	2.09 (0.63)[B]*	1.72 (0.55)[C]‡	1.41 (0.37)[BCI]	1.39 (0.48)[BCI]
Sodium, mmol	BL	165.2 (58.5)	180.8 (55.9)	172.8 (57.2)	230.2 (72.6)[BCI]	197.5 (72.9)[BIP]
	FU	166.4 (61.4)	188.0 (69.1)[B]	169.3 (60.8)	188.9 (68.6)[B]‡	186.8 (66.9)
	Change, y	0.057 (11.41)	1.26 (11.10)	−0.43 (9.86)	−6.27 (10.75)[BCI]	−1.37 (9.43)[C]
Potassium, mmol	BL	69.6 (26.5)	58.5 (20.0)[B]	60.4 (22.5)[B]	63.2 (22.2)	59.6 (17.2)[B]
	FU	71.3 (25.8)	65.3 (22.3)‡	68.0 (20.7)‡	53.3 (16.9)[BCI]‡	59.4 (24.7)[B]
	Change, y	0.40 (4.91)	1.26 (4.47)	1.07 (3.32)	−1.39 (3.68)[BCI]	−0.020 (3.48)
Creatinine, mmol	BL	12.0 (3.8)	13.0 (3.5)	10.7 (3.0)[BC]	11.9 (3.6)	10.6 (2.8)[BC]
	FU	11.8 (4.0)	11.7 (3.8)‡	12.5 (3.6)‡	12.0 (3.9)	10.6 (3.9)[I]
	Change, y	−0.040 (0.61)	−0.24 (0.49)[B]	0.26 (0.41)[BC]	0.0048 (0.51)[CI]	0.0039 (0.45)[I]

Abbreviations: BMl, body mass index, which is calculated as weight in kilograms divided by height in meters squared; FLEMENGHO, the Flemish Study on Environment, Genes, and Health Outcomes; IQR, interquartile range; NSAID, nonsteroidal anti-inflammatory drug. BL and FU refer to measurements obtained at baseline and follow-up. In Belgium, BL and FU observations were collected from 1985 until 2004 and from 1990 until 2009; in the other countries, these intervals ranged from 1999 until 2001 and from 2006 until 2008, respectively.

Sl conversion factors: To convert millimoles of sodium to grams, multiply by 0.02299; to convert millimoles of potassium to grams, multiply by 0.039098; to convert millimoles of creatinine to grams, multiply by 0.11312.

[a]This analysis includes the *Blood Pressure Cohort* (*n*=1499; see Figure 1 and Table 1).

[b]For the blood pressure determination, see the "Methods" section.

Significance of the paired differences between BL and FU: *$P<.05$, †$P<.01$, ‡$P<.001$. *P*-values for between-countries differences were adjusted for multiple comparisons (Tukey test): $P<.05$ *vs* Belgium (B), the Czech Republic (C), Italy (I), Poland (P).

eTable 6. Causes of Cardiovascular Mortality and Morbidity in the *Outcome Cohort*.

		Number of events		
		All (n=3681)	FLEMENGHO (n=2674)	EPOGH (n=1007)
Stroke	Fatal	20	18	2
	Nonfatal	13	13	…
Myocardial infarction	Fatal	19	18	1
	Nonfatal	27	19	8
Acute coronary syndrome	Nonfatal	4	4	…
Ischemic heart disease	Fatal	6	6	…
	Nonfatal	3	3	…
Sudden death	Non-resuscitated	6	6	…
Coronary revascularization	Surgical	20	13	7
	Percutaneous	13	13	…
Heart failure	Fatal	29	29	…
	Nonfatal	43	37	6
Arterial embolism	Fatal	1	1	…
Pulmonary embolism	Fatal	2	2	…
	Nonfatal	9	9	…
Aortic aneurysm	Fatal	1	1	…
	Nonfatal	2	2	…
Pulmonary heart disease	Nonfatal	14	14	…

Abbreviations: EPOGH, the European Project on Genes in Hypertension; FLEMENGHO, the Flemish Study on Environment, Genes, and Health Outcomes.
This analysis includes the *Outcome Cohort* (*n*=3681; see Figure 1 and Table 1).

eTable 7. Multivariable-Adjusted Hazard Ratios for Mortality and Cardiovascular Events by Tertiles of the 24-Hour Urinary Sodium Excretion at Baseline in 3194 Participants Younger Than 60 Years.

		24-Hour Urinary Sodium Excretion Tertiles			
		Low (n=1059)	Medium (n=1082)	High (n=1053)	
No. of women		556	573	555	
Range, mmol		50–129	130–180	181–400	
Mean (SD), mmol		97.3 (22.7)	153.3 (15.1)	235.1 (51.3)	
No. of men		503	509	498	
Range, mmol		50–162	163–227	228–400	
Mean (SD), mmol		122.3 (28.7)	193.2 (17.6)	296.4 (55.2)	

	Total No. of Events	No. of Events	Adjusted HR (95% CI)[a]	No. of Events	Adjusted HR (95% CI)[a]	No. of Events	Adjusted HR (95% CI)[a]	P Value
Mortality								
All causes	77	30	0.98 (0.68 to 1.41)	28	1.05 (0.76 to 1.46)	19	0.95 (0.69 to 1.31)	.71
Cardiovascular	16	8	1.41 (0.70 to 2.83)	7	1.32 (0.67 to 2.58)	3	0.76 (0.39 to 1.49)	.61
Noncardiovascular	59	22	0.91 (0.59 to 1.38)	21	1.01 (0.69 to 1.46)	16	0.99 (0.68 to 1.44)	.56
Fatal and nonfatal events								
All cardiovascular	134	53	1.12 (0.86 to 1.46)	45	1.09 (0.84 to 1.41)	36	0.92 (0.71 to 1.19)	.57
Coronary	60	27	1.35 (0.88 to 2.07)	20	1.09 (0.76 to 1.56)	13	0.92 (0.64 to 1.32)	.14
Stroke	11	3	0.64 (0.24 to 1.70)	4	1.23 (0.46 to 3.32)	4	0.81 (0.30 to 2.18)	.18

Abbreviations: Cl, confidence interval; HR, hazard ratio.

This analysis includes the 3194 participants from the *Outcome Cohort* (see Figure 1 and Table 1), who were younger than 60 years.

[a]HRs were computed by deviation from mean coding and express the risk in each tertile of the distribution of 24-hour urinary sodium excretion at baseline compared with the overall risk in the whole group. We applied Cox proportional hazard regression to derive HRs, while adjusting for covariables and accounting for family clusters. All HRs were adjusted for study population, sex and baseline variables: age, body mass index, systolic blood pressure, 24-hour urinary potassium excretion, antihypertensive drug treatment, smoking and drinking alcohol, diabetes, total cholesterol, and educational attainment. Adjustment for diastolic blood pressure or mean arterial pressure instead of systolic blood pressure did not materially alter the findings.

P-values are for linear trend across the tertiles of 24-hour sodium excretion.

eTable 8. Multivariable-Adjusted Hazard Ratios for Mortality and Cardiovascular Events by Tertiles of the 24-Hour Urinary Sodium Excretion at Baseline in 487 Participants 60 Years or Older.

			24-Hour Urinary Sodium Excretion Tertiles					
			Low (n=1059)		Medium (n=1082)		High (n=1053)	
No. of women			85		88		84	
Range, mmol			50–109		110–155		156–345	
Mean (SD), mmol			82.9 (16.9)		129.5 (11.5)		203.7 (45.9)	
No. of men			76		79		75	
Range, mmol			50–138		139–192		193–400	
Mean (SD), mmol			105.2 (26.8)		164.7 (15.0)		244.0 (51.3)	
	Total No. of Events	No. of Events	Adjusted HR (95% CI)[a]	No. of Events	Adjusted HR (95% CI)[a]	No. of Events	Adjusted HR (95% CI)[a]	*P* Value
Mortality								
All causes	142	64	1.26 (0.90 to 1.75)	49	1.05 (0.80 to 1.37)	29	0.96 (0.73 to 1.25)	.14
Cardiovascular	66	31	1.52 (0.94 to 2.47)	22	1.06 (0.73 to 1.56)	13	0.94 (0.64 to 1.37)	.056
Noncardiovascular	76	33	1.12 (0.73 to 1.71)	27	1.06 (0.75 to 1.49)	16	0.95 (0.67 to 1.34)	.68
Fatal and nonfatal events								
All cardiovascular	98	39	1.09 (0.77 to 1.56)	32	0.90 (0.67 to 1.21)	27	1.11 (0.83 to 1.50)	.28
Coronary	38	16	1.05 (0.57 to 1.93)	11	0.75 (0.46 to 1.24)	11	1.33 (0.80 to 2.20)	.40
Stroke	22	9	0.85 (0.42 to 1.75)	6	0.73 (0.41 to 1.32)	7	1.36 (0.76 to 2.45)	.90

Abbreviations: CI, confidence interval; HR, hazard ratio.
This analysis includes the 487 participants from the *Outcome Cohort* (see Figure 1 and Table 1), who were 60 years or older.
[a]HRs were computed by deviation from mean coding and express the risk in each tertile of the distribution of 24-hour urinary sodium excretion at baseline compared with the overall risk in the whole group. We applied Cox proportional hazard regression to derive HRs, while adjusting for covariables and accounting for family clusters. All HRs were adjusted for study population, sex and baseline variables: age, body mass index, systolic blood pressure, 24-hour urinary potassium excretion, antihypertensive drug treatment, smoking and drinking alcohol, diabetes, total cholesterol, and educational attainment. Adjustment for diastolic blood pressure or mean arterial pressure instead of systolic blood pressure did not materially alter the findings.
P-values are for linear trend across the tertiles of 24-hour sodium excretion.

eTable 9.   Multivariable-Adjusted Hazard Ratios for Mortality and Cardiovascular Events by Tertiles of the 24-Hour Urinary Sodium Excretion at Baseline Excluding Any Adjustment for Blood Pressure

		24-Hour Urinary Sodium Excretion Tertiles						
		Low (n=1220)		**Medium (n=1250)**		**High (n=1211)**		
No. of women		645		658		638		
Range, mmol		50–126		127–177		178–400		
Mean (SD), mmol		95.1 (22.0)		150.2 (15.0)		231.7 (50.9)		
No. of men		575		592		573		
Range, mmol		50–158		159–221		222–400		
Mean (SD), mmol		120.1 (28.4)		188.8 (17.6)		290.5 (56.2)		
	Total No. of Events	**No. of Events**	**Adjusted HR (95% CI)[a]**	**No. of Events**	**Adjusted HR (95% CI)[a]**	**No. of Events**	**Adjusted HR (95% CI)[a]**	**P Value**
Mortality								
All causes	219	118	1.12 (0.86 to 1.45)	64	0.93 (0.74 to 1.16)	37	1.08 (0.87 to 1.35)	.10
Cardiovascular	84	50	1.41 (0.94 to 2.12)	24	0.98 (0.69 to 1.40)	10	1.02 (0.71 to 1.45)	.034
Noncardiovascular	135	68	0.99 (0.71 to 1.36)	40	0.91 (0.68 to 1.20)	27	1.10 (0.83 to 1.47)	.64
Fatal and nonfatal events								
All cardiovascular	232	100	1.12 (0.90 to 1.41)	79	1.09 (0.89 to 1.34)	53	0.92 (0.74 to 1.13)	.54
Coronary	98	45	1.41 (0.99 to 2.01)	34	1.15 (0.87 to 1.52)	19	0.87 (0.66 to 1.15)	.093
Stroke	33	13	1.05 (0.56 to 1.96)	13	1.28 (0.75 to 2.17)	7	0.78 (0.46 to 1.33)	.61

Abbreviations: Cl, confidence interval; HR, hazard ratio.
This analysis includes the *Outcome Cohort* (*n*=3681; see Figure 1 and Table 1).
[a]HRs were computed by deviation from mean coding and express the risk in each tertile of the distribution of 24-hour urinary sodium excretion at baseline compared with the overall risk in the whole group. We applied Cox proportional hazard regression to derive HRs, while adjusting for covariables and accounting for family clusters. All HRs were adjusted for study population, sex and baseline variables: age, body mass index, 24-hour urinary potassium excretion, antihypertensive drug treatment, smoking and drinking alcohol, diabetes, total cholesterol, and educational attainment.
P-values are for linear trend across the tertiles of 24-hour sodium excretion.

eTable 10.—Multivariable-Adjusted Hazard Ratios for Mortality and Cardiovascular Events by Tertiles of the 24-Hour Urinary Sodium-to-Potassium Ratio at Baseline.

		24-Hour Urinary Sodium Excretion Tertiles			
		Low (n=1241)	**Medium (n=1232)**	**High (n=1208)**	
No. of women		653	649	639	
Range, mmol		0.8–2.1	2.2–3.1	3.2–6.0	
Mean (SD), mmol		1.64 (0.36)	2.59 (0.27)	4.15 (0.86)	
No. of men		588	583	569	
Range, mmol		0.8–2.3	2.4–3.3	3.4–6.0	
Mean (SD), mmol		1.75 (0.41)	2.80 (0.28)	4.37 (0.84)	

	Total No. of Events	No. of Events	Adjusted HR (95% CI)[a]	No. of Events	Adjusted HR (95% CI)[a]	No. of Events	Adjusted HR (95% CI)[a]	*P* Value
Mortality								
All causes	219	94	1.25 (1.00 to 1.57)	78	1.09 (0.90 to 1.33)	47	0.91 (0.75 to 1.12)	.063
Cardiovascular	84	41	1.61 (1.06 to 2.45)*	28	1.13 (0.79 to 1.61)	15	0.89 (0.62 to 1.27)	.0069
Noncardiovascular	135	53	1.10 (0.85 to 1.44)	50	1.10 (0.86 to 1.40)	32	0.91 (0.71 to 1.16)	.72
Fatal and nonfatal events								
All cardiovascular	232	93	1.26 (1.00 to 1.52)	89	1.09 (0.89 to 1.33)	50	0.92 (0.75 to 1.12)	.066
Coronary	98	42	1.31 (0.94 to 1.84)	33	0.97 (0.73 to 1.30)	23	1.03 (0.77 to 1.37)	.035
Stroke	33	15	1.32 (0.73 to 2.41)	12	0.99 (0.60 to 1.65)	6	1.01 (0.61 to 1.66)	.25

Abbreviations: CI, confidence interval; HR, hazard ratio.
This analysis includes the *Outcome Cohort* (*n*=3681; see Figure 1 and Table 1).

[a]HRs were computed by deviation from mean coding and express the risk in each tertile of the distribution of the 24-hour urinary sodium-to-potassium ratio at baseline compared with the overall risk in the whole group. We applied Cox proportional hazard regression to derive HRs, while adjusting for covariables and accounting for family clusters. All HRs were adjusted for study population, sex and baseline variables: age, body mass index, systolic blood pressure, antihypertensive drug treatment, smoking and drinking alcohol, diabetes, total cholesterol, and educational attainment. Adjustment for diastolic blood pressure or mean arterial pressure instead of systolic blood pressure did not materially alter the findings.
P-values are for linear trend across the tertiles of the 24-hour sodium-to-potassium ratio.
Significance of the HRs: *P=.025

eTable 11. Multivariable-Adjusted Hazard Ratios for Cardiovascular Mortality by Tertiles of the 24-Hour Urinary Sodium Excretion at Baseline with Censoring of Follow-up at 6, 9, 12, 15, 18 and 21 Years.

	24-Hour Urinary Sodium Excretion Tertiles						
	Low (n=1220)		Medium (n=1250)		High (n=1211)		
	No. of Events	Adjusted HR (95% CI)[a]	No. of Events	Adjusted HR (95% CI)[a]	No. of Events	Adjusted HR (95% CI)[a]	*P* Value
Model censored at							
6 years	16	1.65 (0.85 to 3.22)	9	1.91 (0.90 to 4.08)	4	0.52 (0.25 to 1.12)	.80
9 years	25	1.20 (0.54 to 2.63)	13	1.25 (0.57 to 2.76)	8	0.80 (0.36 to 1.76)	.98
12 years	29	1.61 (0.77 to 3.35)	18	1.56 (0.85 to 2.87)	8	0.64 (0.35 to 1.18)	.69
15 years	36	1.68 (0.88 to 3.20)	19	1.39 (0.84 to 2.32)	9	0.72 (0.43 to 1.19)	.33
18 years	42	1.66 (1.00 to 2.75)*	21	1.16 (0.77 to 1.74)	9	0.87 (0.58 to 1.30)	.049
21 years	50	1.56 (1.02 to 2.36)*	24	1.05 (0.72 to 1.53)	10	0.95 (0.66 to 1.38)	.020

Abbreviations: Cl, confidence interval; HR, hazard ratio.
This analysis includes the *Outcome Cohort* (*n*=3681; see Figure 1 and Table 1).
[a]Hazard ratios were computed by deviation from mean coding and express the risk in each tertile of the distribution of 24-hour urinary sodium excretion at baseline compared with the overall risk in the whole group. We applied Cox proportional hazard regression to derive HRs, while adjusting for covariables and accounting for family clusters. All HRs were adjusted for study population, sex and baseline variables: age, body mass index, systolic blood pressure, 24-hour urinary potassium excretion, antihypertensive drug treatment, smoking and drinking alcohol, diabetes, total cholesterol, and educational attainment. Adjustment for diastolic blood pressure or mean arterial pressure instead of systolic blood pressure did not materially alter the findings.
P-values are for linear trend across the tertiles of 24-hour sodium excretion.
Significance of the HRs: *P .048

eTable 12. Multivariable-Adjusted Hazard Ratios for Incidence of Hypertension by Tertiles of the 24-Hour Urinary Sodium Excretion at Baseline.

	24-Hour Urinary Sodium Excretion Tertiles			
	Low (n=693)	**Medium (n=713)**	**High (n=690)**	
No. of women	375	385	373	
Range, mmol	50–124	125–173	174–400	
Mean (SD), mmol	94.7 (21.5)	147.4 (14.3)	222.1 (47.2)	
No. of men	318	328	317	
Range, mmol	50–157	158–214	215–400	
Mean (SD), mmol	121.3 (27.9)	185.3 (16.1)	282.2 (56.4)	

	No. of Events	Adjusted HR (95% CI)[a]	No. of Events	Adjusted HR (95% CI)[a]	No. of Events	Adjusted HR (95% CI)[a]	*P* Value
Study population							
FLEMENGHO (434)	163	1.00 (0.84 to 1.19)	155	1.00 (0.86 to 1.16)	116	1.00 (0.86 to 1.16)	.97
EPOGH (118)	24	0.98 (0.76 to 1.27)	35	1.20 (0.89 to 1.62)	59	0.83 (0.62 to 1.12)	.55
All (552)	187	1.00 (0.87 to 1.16)	190	1.02 (0.89 to 1.16)	175	0.98 (0.86 to 1.12)	.93

Abbreviations: Cl, confidence interval; EPOGH, the European Project on Genes and Hypertension; FLEMENGHO, Flemish Study on Environment, Genes and Health Outcomes; HR, hazard ratio.

This analysis includes the *Hypertension Cohort* (*n*=2096; see Figure 1 and Table 1). At baseline, all subjects belonging to the *Hypertension Cohort* were untreated. Hypertension during follow-up was a blood pressure of 140 mm Hg systolic or 90 mm Hg diastolic or more or use of antihypertensive drugs.

[a]Hazard ratios were computed by deviation from mean coding and express the risk in each tertile of the distribution of 24-hour urinary sodium excretion at baseline compared with the overall risk in the whole group. We applied Cox proportional hazard regression to derive HRs, while adjusting for covariables and accounting for family clusters.   All HRs were adjusted for study population, sex and baseline variables: age, body mass index, systolic blood pressure, 24-hour urinary potassium excretion, drinking alcohol, and educational attainment.   HRs in all participants combined were additionally adjusted for study population.

P-values are for linear trend across the tertiles of 24-hour sodium excretion.

eTable 13. Multivariable-Adjusted Cross-Sectional Associations Between Blood Pressure and 24-Hour Urinary Sodium by Study Population and Study Phase[a]

Study Population		Baseline			Follow-Up	
		Estimates (95% CI)[b]	P		Estimates (95% CI)[b]	P
Systolic Pressure						
FLEMENGHO		0.525 (–0.793 to 1.843)	.43		2.002 (0.487 to 3.517)	.01
EPOGH		2.109 (0.282 to 3.937)	.02		−0.019 (−2.210 to 2.201)	.99
All		1.140 (0.055 to 2.224)	.04		1.459 (0.208 to 2.710)	.02
Diastolic Pressure						
FLEMENGHO		0.534 (–0.389 to 1.456)	.25		0.258 (–0.734 to 1.251)	.61
EPOGH		1.004 (–0.339 to 2.347)	.14		−0.324 (−1.865 to 1.217)	.68
All		0.739 (–0.025 to 1.500)	.16		0.090 (–0.724 to 0.942)	.80

Abbreviations: Cl, confidence interval; EPOGH, the European Project on Genes in Hypertension; FLEMENGHO is the Flemish Study on Environment, Genes, and Health Outcomes.

[a]Reasons for exclusion from analysis are explained in the "Methods" section.

[b]Estimates and 95% CIs express the difference in blood pressure associated with a 100 mmol increase in 24-hour urinary sodium excretion. All parameter estimates were adjusted for sex, age, body mass index, alcohol intake (0,1), 24-hour urinary potassium excretion, use of female sex hormones (0,1), and nonsteroidal anti-inflammatory drugs (0,1), and account for family clusters. Estimates in all participants combined were additionally adjusted for study population.

**eFigure 1.** Incidence of Mortality and All Cardiovasular Events
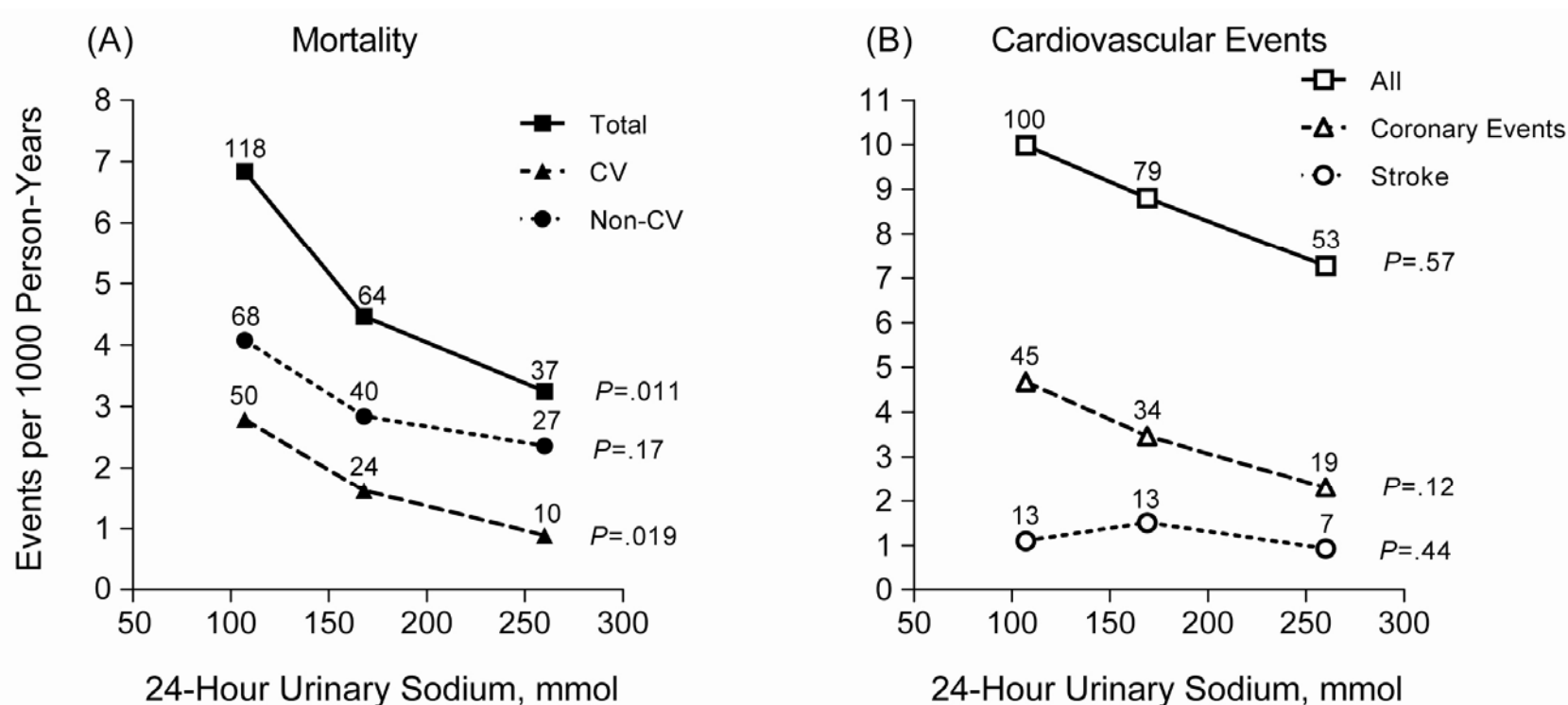
Incidence of mortality (A) and cardiovascular events (B) by tertiles of the distributions of the 24-hour urinary sodium excretion at baseline. This analysis includes the *Outcome Cohort* (n=3681; see Figure 1 and Table 1). Incidence rates were standardized for study population, sex, and age by the direct method. The number of events contributing to the rates is presented. CV and Non-CV indicate cardiovascular and noncardiovascular mortality, respectively. The data markers are centered to the means of the 24-hour urinary sodium excretion in each tertile of the distribution. For the mean and range of the 24-hour sodium excretion in each tertile, see Table 2. The *P*-values are for linear trend across the tertiles of the 24-hour sodium excretion and were computed using Cox proportional regression models with study population, sex and age at baseline as covariables.

eFigure 2. Kaplan-Meier Estimates for the Incidence of Hypertension by Tertiles of the 24-Hour Urinary Sodium Excretion at Baseline
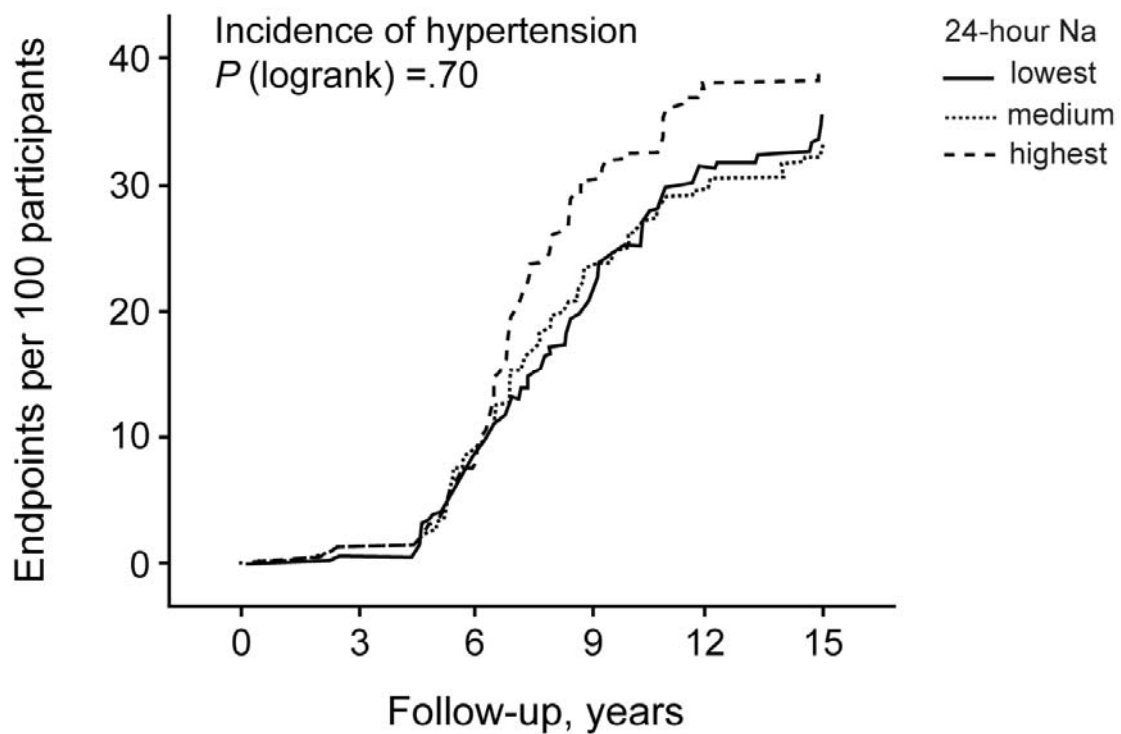

This analysis includes the *Hypertension Cohort* (n=2096; see Figure 1 and Table 1). Tertiles of the 24-hour urinary sodium excretion are sex-specific based on baseline measurements. For the mean and range of the 24-hour sodium excretion in each tertile, see eTable 12.

eFigure 3. Distribution of the Absolute (A, C, E) and Relative (B, D, F) Changes in Systolic Blood Pressure (A, B), Diastolic Blood Pressure (C, D), and 24-hour Urinary Sodium Excretion (E, F) in 1499 Participants of the *Blood Pressure Cohort* Followed Up for a Median of 6.1 Years
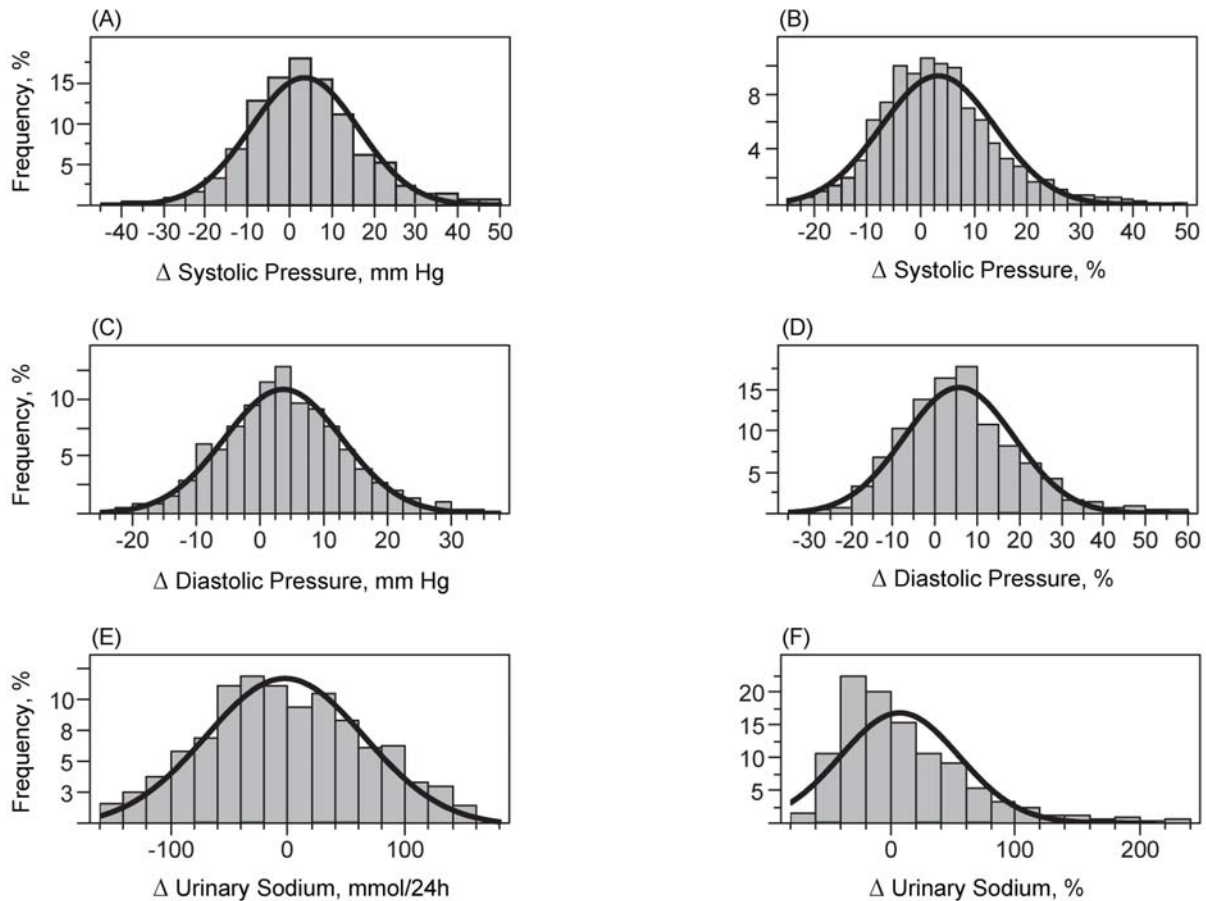

Distributions are represented by frequencies for given intervals and by a continuous line, which was fitted by means of the distribution density modeling software available in the SAS JMP add-on, version 8.0. All distributions were positively skewed (0.08) and departed from normality (Shapiro-Wilk statistic 0.92; *P*<.0001).

eFigure 4. Change in Systolic Blood Pressure During Follow-Up By Deciles of the Change in the 24-Hour Urinary Sodium Excretion in the *Blood Pressure Cohort* (n=1499)
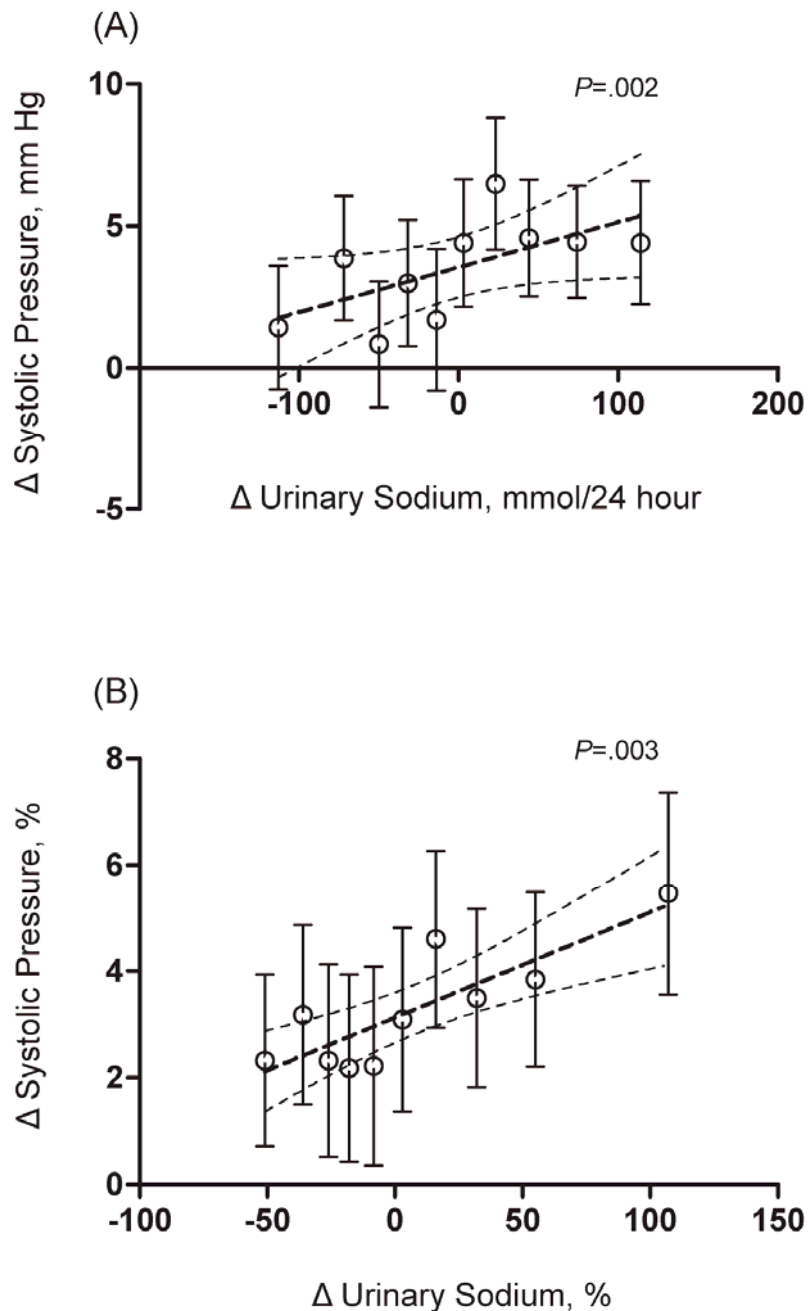
The data markers are centered on the means in each decile. The analyses were adjusted for study population, sex, baseline values of and changes in: age, body mass index, alcohol intake (stopping, no change and starting coded as –1, 0,1), 24-hour urinary potassium excretion, use of female sex hormones (–1, 0,1), and non-steroidal anti-inflammatory drugs (–1, 0,1), and account for family clusters. Changes are expressed in absolute units (A) or as percentage changes (B). The *P*-values are for linear trend. Dotted lines represent the regression line and the 95% confidence interval for the changes in systolic blood pressure across deciles. Mean values and limits of the changes in the 24 hour urinary sodium excretion from the bottom to top decile: Panel A: –113 (–159 to –90), –72 (–89 to –60), –50 (–59 to –42), –32 (–41 to –24), –14 (–23 to –5), +3 (–4 to +13), +23 (+14 to +33), +44 (+34 to +57), +74 (+58 to +90), +114 (+91 to +159); Panel B: –51(–72 to –43), –36 (–42 to –32), –26 (–31 to –23), –18 (–22 to –14), –8 (–13 to –4), +3 (–3 to +9), +16 (+9 to +22), +32 (+23 to +42), +55 (+43 to +73), +107 (+74 to +230).

eFigure 5. Change in Diastolic Blood Pressure During Follow-Up by Deciles of the Change in 24-Hour Urinary Sodium Excretion in the *Blood Pressure Cohort* (n=1499).
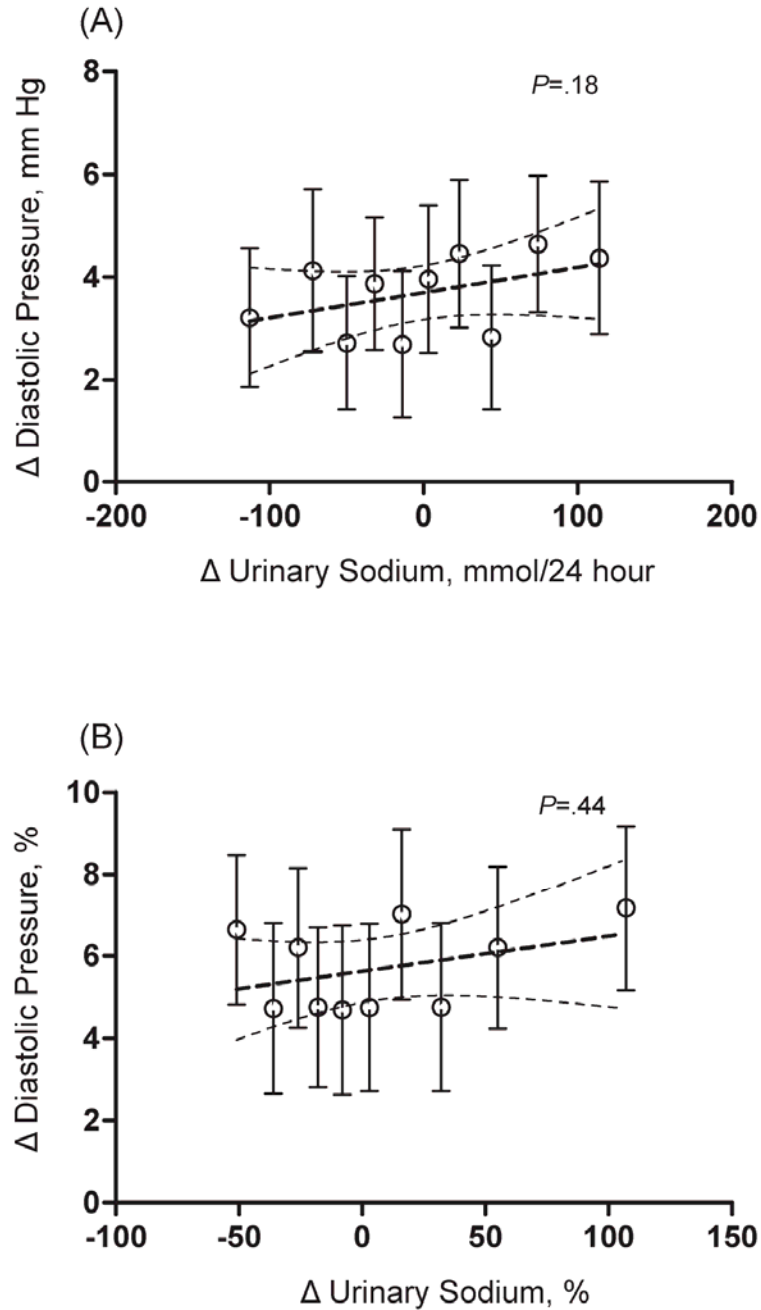
The data markers are centered to the means in each decile. Changes are expressed in absolute units (A) or as percentage changes (B).
The *P*-values are for linear trend. Dotted lines represent the regression line and 95% confidence interval for the changes in diastolic blood pressure across deciles. For adjustments and range of deciles, see eFigure 4.

FLEMENGHO and EPOGH Investigators

Belgium (Leuven) – R. Fagard, L. Thijs, Y. Jin, T. Kuznetsova, Y. Liu, T. Richart, L. Thijs, and J.A. Staessen; *Czech Republic (Pilsen and Prague)* – O. Beran, M. Dolejsová, J. Filipovský, L. Golán, T. Grus, G. Grusová, M. Jachymová, J. Seidlerová, Z. Marecková, J. Peleška, and V. Svobodova; *Germany (Münster)* – E. Brand and S.M. Brand; *Italy (Padova)* – E. Casiglia and V. Tikhonoff; *Poland (Kraków)* – M. Cwynar, J. Gąsowski, T. Grodzicki, K. Kawecka-Jaszcz, M. Kloch-Badełek, M. Loster, A. Olszanecka, A. Sałakowski, K. Stolarz-Skrzypek, B. Wizner, and W. Wojciechowska; *Poland (Gdańsk)* – K. Kunicka, K. Narkiewicz, W. Sakiewicz, E. Świerblewska, and M. Wójtowicz; *Romania (Bucharest)* – S. Babeanu, D. Jianu, C. Sandu, D. State, and M. Udrea; *Russian Federation (Novosibirsk)* – T. Kuznetsova, S. Malyutina, Y. Nikitin, E. Pello, A. Ryabikov, and M. Voevoda.

Project Coordinator – **J.A. Staessen;** *Scientific Coordinator* – **K. Kawecka-Jaszcz;** *Steering Committee* – **E. Casiglia, J. Filipovský , K. Kawecka-Jaszcz, Y. Nikitin, and J.A. Staessen;** *Data Management Committee* – **T. Kuznetsova, L. Thijs, J.A. Staessen, K. Stolarz-Skrzypek, and V. Tikhonoff;** *Advisory Committee on Molecular Biology* – **G. Bianchi (Universitá Vita Salute, Milano, Italy), E. Brand, S.M. Brand, and H.A. Struijker-Boudier (Cardiovascular Research Institute Maastricht, Maastricht University, The Netherlands).**