Published in final edited form as:

J Hypertens. 2009 January ; 27(1): 48–54.

Gender Difference in Blood Pressure Responses to Dietary Sodium Intervention in the GenSalt Study

Jiang He, Dongfeng Gu, Jing Chen, Cashell E. Jaquish, Dabeeru C. Rao, James E. Hixson, Ji-chun Chen, Xiufang Duan, Jian-feng Huang, Chung-Shiuan Chen, Tanika N. Kelly, Lydia A. Bazzano, and Paul K. Whelton for the GenSalt Collaborative Research Group*

Department of Epidemiology, Tulane University School of Public Health and Tropical Medicine (JH, JC, CC, TNK, LAB), and Department of Medicine, Tulane University School of Medicine (JH, JC, LAB), New Orleans, LA; Cardiovascular Institute and Fu Wai Hospital, Chinese Academy of Medical Sciences (DG, J-CC, XD, J-FH), Beijing, China; National Heart, Lung, and Blood Institute, National Institute of Health (CEJ), Bethesda, MD; Washington University in St. Louis School of Medicine (DCR), St. Louis, MO; University of Texas School of Public Health (JEH), Houston, TX; and Loyola University Medical Center (PKW), Maywood, IL.

Abstract

Objective—To examine factors related to blood pressure (BP) responses to dietary sodium and potassium interventions.

Methods—We conducted a dietary feeding study that included a 7-day low-salt intervention (51.3 mmol/day), a 7-day high-salt intervention (307.8 mmol/day), and a 7-day high-salt plus potassium supplementation (60 mmol/day) intervention among 1,906 study participants in rural China. BP was measured 9 times during the 3-day baseline observation and during the last 3 days of each intervention phase using a random-zero sphygmomanometer.

Results—BP responses to low-sodium intervention were significantly greater in women compared to men: -8.1 (95% confidence interval $(-8.6$ to $-7.6)$ versus -7.0 (-7.5 to -6.6) mmHg for systolic and -4.5 (-4.9 to -4.1) versus -3.4 (-3.8 to -3.0) mmHg for diastolic. Likewise, BP responses to high-sodium interventions were significantly greater in women compared to men: 6.4 (5.9 to 6.8) versus 5.2 (4.8 to 5.7) mmHg for systolic and 3.1 (2.7 to 3.5) versus 1.7 (1.4 to 2.1) mmHg for diastolic (all $p < 0.001$). In addition, systolic BP responses to the sodium interventions increased with age and both systolic and diastolic BP responses to the sodium interventions increased with baseline BP levels. BP responses to potassium supplementation also increased with baseline BP levels.

Conclusions—These results suggest that female gender, older age, and hypertension increase sensitivity to dietary sodium intervention. Furthermore, low dietary sodium intake may be more effective in reducing BP among these subgroups.

Introduction

Hypertension is a global public health challenge because of its high prevalence and the concomitant increase in risk of vascular disease (1). Epidemiologic studies and clinical trials have documented that a diet low in sodium or high in potassium reduces blood pressure (BP) in both hypertensive and normotensive persons (2). BP reduction in response to a low dietary

Correspondence and request for reprints to: Jiang He, MD, PhD Department of Epidemiology Tulane University School of Public Health and Tropical Medicine 1440 Canal Street, Suite 2000 New Orleans, Louisiana, USA Telephone: 504-988-5165 Fax: 504-988-1568 jhe@tulane.edu.

*A full list of all investigators and staff participating in this study is given in the appendix.

sodium or high potassium intake, however, might vary considerably among individuals (3-6). In the DASH-Sodium Study, a randomized controlled feeding study conducted among 412 persons with pre-hypertension or stage-1 hypertension, reduction in BP associated with lowering sodium intake was significantly greater among hypertensives, African-Americans, and those who were older (4,5). The gender difference in BP responses to dietary sodium intake has not been well examined. In addition, the determinants of BP responses to dietary potassium intake have not been reported.

We examined BP responses to dietary sodium and potassium interventions by gender, age, and baseline BP sub-groups among 1,906 Chinese men and women aged 16 years or older who participated in the Genetic Epidemiology Network of Salt Sensitivity (GenSalt) study. Identifying subgroups that are more sensitive to dietary sodium or potassium intake will allow us to develop targeted dietary interventions for the treatment and prevention of hypertension.

Methods

The details of study population and methods for the GenSalt study have been published elsewhere (7). In brief, the GenSalt study was conducted in rural areas in north China from October 2003 to July 2005. A community-based BP screening was conducted among persons aged 18-60 years in the study villages to identify potential probands and their families for the study. Those with mean systolic BP between 130-160 mmHg and/or diastolic BP between 85-100 mmHg and no use of antihypertensive medications and their siblings and offspring were recruited for the dietary intervention study. Individuals who had stage-2 hypertension, secondary hypertension, a history of clinical cardiovascular disease or diabetes, were using antihypertensive medications, pregnant, heavy alcohol users, or currently on a low-sodium diet were excluded from the dietary intervention.

A standard questionnaire was administered by trained staff at the baseline examination to collect information on demographic characteristics, personal and family medical history, and lifestyle risk factors. Three BP measurements were obtained at each clinical visit by trained and certified observers using a random-zero sphygmomanometer according to a common protocol (8). BP was measured with the participant in the sitting position after 5 minutes of rest. In addition, participants were advised to avoid alcohol, cigarette smoking, coffee/tea, and exercise for at least 30 minutes prior to their BP measurement. BP was measured in the morning of the 3 day baseline observation, and the last 3 days of each intervention phase by the same BP technician using the same sphygmomanometer to avoid observation variation. All BP observers were blinded to the dietary intervention.

The study participants received a low-salt diet (3 grams of salt or 51.3 mmol of sodium per day) for 7 days. Then, they received a high-salt diet (18 grams of salt or 307.8 mmol of sodium per day) for 7 days. During the first 2 intervention phases, potassium intake remained unchanged. In the final week, the participants maintained a high-salt diet and took a 60 mmol potassium (potassium chloride) supplement daily. Although dietary salt intake was the same for all study participants, dietary total energy intake was varied according to their baseline energy intake. All foods were cooked without salt, and pre-packaged salt was added to the individual study participant's meal, as specified in the protocol, when it was served by the study staff. To ensure study participants' compliance to the intervention program, they were required to have their breakfast, lunch and dinner at the study kitchen under supervision of the study staff during the entire study period. Food consumption of study participants was carefully recorded at each meal by study staff members. The study participants were instructed to avoid consuming any foods that were not provided by the study. In addition, three timed urinary specimens (one 24-hour and two overnight) were collected at baseline and in each phase of intervention to monitor participants' compliance to dietary sodium and potassium intake. The

overnight urinary excretions of sodium and potassium were converted to 24-hour values based on formulas developed from a random subsample of 238 participants who had collected overnight and 24-hour measures on the same days at baseline and in each phase of intervention.

BP levels at baseline and during intervention were calculated as the mean of 9 measurements from 3 clinical visits during the 3-day baseline observation or on days 5, 6 and 7 of each intervention phase. Responses were defined as follows: BP response to low-sodium = BP on low-sodium diet – BP at baseline; BP response to high-sodium = BP on high-sodium diet – BP on low-sodium diet; and BP response to potassium supplement = BP on high-sodium diet with potassium supplementation – BP on high-sodium diet.

The means and percentages of baseline characteristics were presented by gender and the statistical significance of differences were examined by t-test for continuous variables or χ^2 test for categorical variables. The differences in urinary excretion of sodium and potassium and BP levels by gender and dietary salt and potassium interventions as well as their interactions were examined using 2-way analysis of variance. Multiple linear regression analyses were used to examine the association between BP responses to low-salt, high-salt and potassium-supplementation interventions and gender, age, and baseline BP levels.

The Institutional Review Board at all participating institutes approved the GenSalt study. Written informed consents for the baseline observation and for the intervention were obtained from each participant prior to data collection or intervention, respectively.

Results

A total of 1,906 GenSalt study participants took part in the dietary sodium and potassium interventions. Of them, 1,879 (98.6%) completed the entire 21-day dietary interventions. The baseline characteristics of study participants are presented in Table 1. On average, female participants were a little younger, less likely to have graduated from secondary school, smoke, or drink alcohol, and engaged in less physical activity than their male counterparts. BMI was slightly higher while waist circumference, systolic and diastolic BP levels were lower in female compared to male participants.

The average 24-hour urinary excretion of sodium decreased more than 5-fold from baseline during the low-salt intervention and increased more than 5-fold from the low-salt intervention during the high-salt intervention (Table 2). During the same periods, the average 24-hour urinary excretion of potassium decreased slightly during the low-salt intervention and returned to baseline level during the high-salt interventions. Mean decrease in urinary sodium excretion was greater in men during the low-salt intervention and mean increase in urinary sodium excretion was greater in women during the high-salt intervention. During potassium supplementation, the average 24-hour urinary excretion of potassium was more than doubled while urinary sodium excretion was slightly increased. The average 24-hour urinary excretion of creatinine was lower in women than in men.

Mean systolic and diastolic BP levels at baseline and during low-salt, high-salt and potassium-supplementation interventions are presented in Table 3. Both systolic and diastolic BP levels were reduced during low-salt intervention compared to baseline and increased during high-salt intervention compared to low-salt intervention. Both systolic and diastolic BP levels were reduced during the high-salt plus potassium supplementation phase compared to the high-salt only intervention. The BP changes during dietary salt interventions were greater in women compared to men.

The distributions of systolic and diastolic BP responses to low-salt, high-salt, and potassium-supplementation interventions are shown in Figure 1. Both systolic and diastolic BP levels

decreased during low-salt intervention and during potassium-supplementation but increased during high-salt intervention among the majority of study participants. For example, systolic BP reduced by 4, 6, and 8 mmHg among 62.4%, 45.9%, and 33.1% of study participants during the low-salt intervention; systolic BP increased by 4, 6, and 8 mmHg among 60.7%, 46.6%, and 32.9% of study participants during high-salt intervention; and systolic BP decreased by 4, 6, and 8 mmHg among 46.7%, 31.5%, and 21.6% of study participants during potassium-supplementation intervention, respectively. On the other hand, systolic BP did not decrease (≥ 0 mmHg) among 23.2% and 30.6% of study participants during the low-salt and potassium-supplementation interventions, respectively and systolic BP did not increase (≤ 0 mmHg) among 26.1% of study participants during the high-salt intervention.

Both systolic and diastolic BP responses to low-salt and high-salt interventions were greater in females compared to their male counterparts while diastolic BP responses to potassium-supplementation intervention were also greater in female compared to male participants (Table 4). There was a dose-response relationship between age and systolic BP responses to low-salt, high-salt, and potassium-supplementation interventions. In addition, there was a dose-response relationship between baseline BP categories and both systolic and diastolic BP responses to low-salt, high-salt, and potassium-supplementation interventions.

Discussion

This study contributes to our understanding of salt-sensitivity in several ways. First, this large, well-controlled feeding study indicated that BP responses to dietary sodium intake were normally distributed in populations and there was no evidence for a bimodal distribution. Therefore, using a cut-point to categorize subjects into salt-sensitive and salt-resistant is arbitrary. Second, salt-sensitivity appears to be a common biological phenomenon in human populations. In our study, only approximately 25% of participants did not experience a decrease in BP during the low-salt intervention or did not experience an increase during the high-salt intervention (“salt-resistance”). Furthermore, BP responses to dietary sodium intake were greater in women, those aged 45 years or older, and those with a higher baseline BP level. Finally, our study indicated that BP responses to potassium-supplementation also varied among individuals and the responses were normally distributed. More than 30% of participants did not experience a decrease in BP during potassium-supplementation.

Our investigation is the largest feeding-study to examine salt-sensitivity and potassium-sensitivity in a free-living population. The compliance to dietary sodium and potassium interventions was excellent as measured by multiple 24-hour urinary excretions in our study. In addition, the 24-hour urinary excretions of sodium and potassium were similar in participants whose BP changed and among those whose BP did not during each dietary intervention. A minimum of 9 BP readings were obtained from multiple clinical visits using a random-zero sphygmomanometer by trained observers during each phase of the study which should minimize measurement bias. Furthermore, our study is the first to report the variation in BP responses to potassium-supplementation. The limitations of our study include the short duration of dietary sodium and potassium interventions. A large change in sodium intake over a short period of time conceivably stimulated the renin-angiotensin axis and the sympathetic nervous system; these reactions might reduce the size of the BP responses and generate a number of salt-resistant cases that would probably not be apparent over a long-period with more gradual changes in sodium intake (9,10). A recent study among 36 Olivetti Heart Study participants indicates that individuals with greater BP change during a short-term dietary sodium intervention have a higher incidence of hypertension during 15-year follow-up (11).

Kawasaki et al and later on Weinberger et al were among the first to recognize the heterogeneity of BP response to sodium and to develop the concept of salt-sensitivity in humans (12,13). In

their initial study, Kawasaki et al defined salt-sensitivity arbitrarily as an increase in mean arterial pressure (MAP) $\geq 10\%$ with a high-sodium diet (250 mmol/day) compared with a low-sodium diet (10 mmol/day) over a 7-day period (12). Subsequently, a variety of experimental protocols have been used to test for salt-sensitivity of BP in humans (13,14). The definition of salt-sensitivity has varied between studies, mostly being defined as a proportional change (i.e., $\geq 5\%$ to $\geq 10\%$) or an absolute change (i.e., ≥ 5 mmHg to ≥ 10 mmHg) in MAP. In our study, if an absolute change of MAP ≥ 5 mmHg was used to define salt-sensitivity, 33.9% of participants during low-salt intervention and 32.4% of participants during high-salt intervention would have met the criteria. If a proportional change of MAP $\geq 5\%$ was used to define salt-sensitivity, 38.7% of participants during low-salt intervention and 39.2% of participants during high-salt intervention would have met the criteria.

Previous studies have documented that salt-sensitivity is more common among individuals who are older, hypertensive, or of African-American descent (14-16). Our study indicated that BP responses to dietary sodium intervention were increased with aging and higher baseline BP levels, especially for systolic BP. Our findings were consistent with those from other dietary intervention studies with a longer duration (4,5). For example, in the DASH-Sodium Trial, systolic BP reduction associated with lower (50 mmol/day) versus higher sodium (150 mmol/day) intakes was -8.3 (95% CI -10.0 to -6.6) mmHg in hypertensives and -5.6 (-7.0 to -4.1) mmHg in normotensives ($p < 0.05$ for difference) among persons eating a typical American diet (5). The corresponding systolic BP reduction was -7.5 (-8.9 to -6.1) mmHg in those > 45 years and -5.3 (-7.0 to -3.5) mmHg in those ≤ 45 years ($p < 0.05$ for difference).

Our study showed that BP responses to dietary sodium intervention were more pronounced in women than in men. Wilson and colleagues compared BP responses to a low (50 mmol/day) and a high (150 mmol/day) sodium diet intervention among 135 black adolescents (17). BP decreased more in girls during low sodium intervention but increased more in boys during high sodium intervention. In the DASH-Sodium Trial, systolic BP reduction associated with lower versus higher sodium intakes was -4.0 (95% CI -5.4 to -2.5) in females and -1.7 (-3.4 to 0.0) in males ($p < 0.01$ for difference) among persons eating the DASH diet (5). Physiological studies have suggested that female hormones (estrogen and progesterone) might be associated with increased renal sodium reabsorption and water retention (18,19). These findings warrant future research into the gender difference in BP responses to dietary sodium intakes.

The variation of BP responses to potassium supplementation among individuals has not been reported in the literature. Our study documented that BP responses to potassium-supplementation were normally distributed among a population with high dietary sodium intakes. In addition, BP responses to potassium-supplementation were associated with baseline BP levels. In a previous meta-regression analysis of 33 randomized controlled trials of potassium-supplementation, we reported that average baseline BP levels and dietary sodium intake were statistically significantly associated with mean BP reduction among trials (6). Future studies are needed to investigate factors associated with potassium-sensitivity of BP.

In conclusion, the current study suggests that female gender, older age, and elevated baseline BP levels increase BP responses to dietary sodium intervention. In addition, elevated baseline BP levels increase BP responses to dietary potassium intervention. Therefore, a diet low in sodium and high in potassium should be especially effective in reducing BP among persons with hypertension or prehypertension while a diet low in sodium may be more effective in reducing BP among women and elderly.

Acknowledgments

The Genetic Epidemiology Network of Salt Sensitivity (GenSalt) is supported by a cooperative agreement project grant (U01HL072507) from the National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda,

Maryland. The GenSalt investigators acknowledge Upsher-Smith Laboratories, Inc. for providing potassium chloride tablets (Klor-Con®M20).

APPENDIX

The GenSalt Study Steering Committee: Dongfeng Gu, Jiang He (Chair), James E Hixson, Cashell E Jaquish, Depei Liu, DC Rao, Paul K Whelton, and Zhijian Yao.

GenSalt Collaborative Research Group

Tulane University Health Sciences Center, New Orleans, USA: Jiang He (PI), Lydia A Bazzano, Chung-Shiuan Chen, Jing Chen, Mei Hao, Lee Hamm, Tanika Kelly, Paul Muntner, Kristi Reynolds, Paul K Whelton, Wenjie Yang, and Qi Zhao.

Washington University School of Medicine, St Louis, USA: DC Rao (PI), Matthew Brown, Charles Gu, Hongyan Huang, Treva Rice, Karen Schwander, and Shiping Wang.

University of Texas Health Sciences Center at Houston: James E Hixson (PI) and Lawrence C Shimmin.

National Heart, Lung, and Blood Institute: Cashell E Jaquish

Chinese Academy of Medical Sciences, Beijing, China: Dongfeng Gu (PI), Jie Cao, Jichun Chen, Jingping Chen, Zhenhan Du, Jianfeng Huang, Hongwen Jiang, Jianxin Li, Xiaohua Liang, Depei Liu, Xiangfeng Lu, Donghua Liu, Qunxia Mao, Dongling Sun, Hongwei Wang, Qianqian Wang, Xigui Wu, Ying Yang, and Dahai Yu.

Shandong Academy of Medical Sciences, Shandong, China: Fanghong Lu (PI), Zhendong Liu, Shikuan Jin, Yingxin Zhao, Shangwen Sun, Shujian Wang, Qengjie Meng, Baojin Liu, Zhaodong Yang, and Chuanrui Wei.

Shandong Center for Diseases Control and Prevention, Shandong, China: Jixiang Ma (PI), Jiyu Zhang, and Junli Tang.

Zhengzhou University: Dongsheng Hu, Hongwei Wen, Chongjian Wang, Minghui Shen, Jingjing Pan, and Liming Yang.

Xinle Traditional Chinese Medicine Hospital, Hebei, China: Xu Ji (PI), Rongyan Li, Haijun Zu, and Junwei Song.

Ganyu Center for Disease Control and Prevention: Delin Wu (PI), Xushan Wang, and Xiaofeng Zhang.

Xi'an Jiaotong University, Shanxi, China: Jianjun Mu (PI), Enrang Chen, Fuqiang Liu, and Guanji Wu.

Chinese National Human Genome Center at Beijing: Zhi-Jian Yao (PI), Shufeng Chen, Dongfeng Gu, Hongfan Li, Laiyuan Wang, and Penghua Zhang.

References

1. Kearney PM, Whelton M, Reynolds K, Muntner P, Whelton PK, He J. Global burden of hypertension: analysis of worldwide data. *Lancet* 2005;365:217–23. [PubMed: 15652604]
2. Whelton PK, He J, Appel LJ, Cutler JA, Havas S, Kotchen TA, et al. Primary Prevention of Hypertension. Clinical and Public Health Advisory from the National High Blood Pressure Education Program. *JAMA* 2002;288:1882–1888. [PubMed: 12377087]

3. Weinberger MH. Salt sensitivity of blood pressure in humans. *Hypertension* 1996;27:481–490. [PubMed: 8613190]
4. Obarzanek E, Proschan MA, Vollmer WM, Moore TJ, Sacks FM, Appel LJ, Svetkey LP, Most-Windhauser MM, Cutler JA. Individual blood pressure responses to changes in salt intake: Results from the DASH-sodium trial. *Hypertension* 2003;42:459–467. [PubMed: 12953018]
5. Vollmer WM, Sacks FM, Ard J, Appel LJ, Bray GA, Simons-Morton DG, Conlin PR, Svetkey LP, Erlinger TP, Moore TJ, Karanja N, for the DASH-Sodium Trial Collaborative Research Group. Effects of diet and sodium intake on blood pressure: subgroup analysis of the DASH-Sodium trial. *Ann Intern Med* 2001;135:1019–1028. [PubMed: 11747380]
6. Whelton PK, He J, Cutler JA, Brancati FL, Appel LJ, Follmann D, Klag MJ. Effects of oral potassium on blood pressure. Meta-analysis of randomized controlled clinical trials. *JAMA* 1997;277:1624–1632. [PubMed: 9168293]
7. GenSalt Collaborative Research Group. GenSalt: rationale, design, methods and baseline characteristics of study participants. *J Hum Hypertens* 2007;21:639–46. [PubMed: 17443206]
8. Perloff D, Grim C, Flack J, Frohlich ED, Hill M, McDonald M, Morgenstern BZ. Human blood pressure determination by sphygmomanometer. *Circulation* 1993;88(5 Pt 1):2460–2470. [PubMed: 8222141]
9. He FJ, MacGregor GA. Salt, blood pressure and the renin-angiotensin system. *J Renin Angiotensin Aldosterone Syst* 2003;4:11–6. [PubMed: 12692748]
10. He FJ, Markandu ND, Sagnella GA, MacGregor GA. Importance of the renin system in determining blood pressure fall with salt restriction in black and white hypertensives. *Hypertension* 1998;32:820–4. [PubMed: 9822438]
11. Barba G, Galletti F, Cappuccio FP, Siani A, Venezia A, Versiero M, Della Valle E, Sorrentino P, Tarantino G, Farinaro E, Strazzullo P. Incidence of hypertension in individuals with different blood pressure salt-sensitivity: results of a 15-year follow-up study. *J Hypertens* 2007;25:1465–71. [PubMed: 17563570]
12. Kawasaki T, Delea CS, Bartter FC, Smith H. The effect of high-sodium and low-sodium intakes on blood pressure and other related variables in human subjects with idiopathic hypertension. *Am J Med* 1978;64:193–198. [PubMed: 629267]
13. Weinberger MH. Salt sensitivity of blood pressure in humans. *Hypertension* 1996;27:481–490. [PubMed: 8613190]
14. Luft FC, Weinberger MH. Heterogeneous responses to changes in dietary salt intake: the salt-sensitivity paradigm. *Am J Clin Nutr* 1997;65(suppl):612S–617S. [PubMed: 9022556]
15. Wright JT Jr, Rahman M, Scarpa A, Fatholahi M, Griffin V, Jean-Baptiste R, Islam M, Eissa M, White S, Douglas JG. Determinants of salt sensitivity in black and white normotensive and hypertensive women. *Hypertension* 2003;42:1087–92. [PubMed: 14610097]
16. Hurwitz S, Fisher ND, Ferri C, Hopkins PN, Williams GH, Hollenberg NK. Controlled analysis of blood pressure sensitivity to sodium intake: interactions with hypertension type. *J Hypertens* 2003;21:951–9. [PubMed: 12714870]
17. Wilson DK, Bayer L, Sica DA. Variability in salt sensitivity classifications in black male versus female adolescents. *Hypertension* 1996;28:250–5. [PubMed: 8707390]
18. Stachenfeld NS, Taylor HS. Effects of estrogen and progesterone administration on extracellular fluid. *J Appl Physiol* 2004;96:1011–1018. [PubMed: 14660504]
19. Stachenfeld NS, DiPietro L, Palter SF, Nadel ER. Estrogen influences osmotic secretion of AVP and body water balance in postmenopausal women. *Am J Physiol* 1998;274(1 Pt 2):R187–95. [PubMed: 9458917]

Figure 1.

Distribution of systolic (upper panels) and diastolic (lower panels) BP responses to low-salt intervention (left panels), high-salt intervention (middle panels), and potassium-supplementation (right panels). BP response to low-sodium = BP on low-sodium diet – BP at baseline; BP response to high-sodium = BP on high-sodium diet – BP on low-sodium diet; and BP response to potassium supplement = BP on high-sodium diet with potassium-supplementation – BP on high-sodium diet.

Table 1

Baseline characteristics of 1,906 dietary sodium and potassium intervention participants

	Men (N=1,010)	Women (N=896)	p-value for difference
Age, years	39.3 ± 9.6	38.1 ± 9.4	0.008
≥ Secondary school, %	81.1	54.0	<0.0001
Married, %	91.1	92.6	0.22
Current alcohol drinkers, %	52.9	3.0	<0.0001
Current cigarette smoking, %	58.7	0.2	<0.0001
Physical activity, MET	68.2 ± 22.1	58.7 ± 18.6	<0.0001
BMI, kg/m ²	23.1 ± 3.1	23.5 ± 3.2	0.009
BMI ≥25 kg/m ²	26.9	28.4	0.48
Waist circumference, cm	81.9 ± 9.9	78.4 ± 9.5	<0.0001
Systolic BP, mm Hg	118.7 ± 12.8	114.9 ± 15.4	<0.0001
Diastolic BP, mm Hg	75.6 ± 9.9	71.7 ± 10.5	<0.0001
BP ≥140/90 mm Hg, %	10.8	8.1	0.05

Values are mean ± SD or percentage; MET: metabolic equivalent per week; BMI: body mass index; BP: blood pressure

Table 2
Mean 24-hour urinary excretion of sodium, potassium and creatinine at baseline and during dietary intervention

Variables	Men (N=1,010)	Women (N=896)	p-value for difference by gender	p-value for difference by intervention *	p-value for interaction by gender and intervention
Baseline					
Sodium, mmol/24-hour	251.1 ± 69.8	232.7 ± 61.6	<0.0001	--	--
Potassium, mmol/24-hour	37.2 ± 9.4	36.4 ± 9.9	0.07	--	--
Creatinine, μ mol/24-hour	9306.1 ± 2230.1	7831.6 ± 1681.4	<0.0001	--	--
Low-salt intervention					
Sodium, mmol/24-hour	45.2 ± 15.9	50.0 ± 15.8	0.0008	<0.0001	<0.0001
Potassium, mmol/24-hour	32.0 ± 8.0	30.8 ± 7.2	0.0001	<0.0001	0.27
Creatinine, μ mol/24-hour	8857.7 ± 1841.1	7477.1 ± 1329.5	<0.0001	<0.0001	0.34
High-salt intervention					
Sodium, mmol/24-hour	241.3 ± 37.3	247.7 ± 37.8	0.0004	<0.0001	0.19
Potassium, mmol/24-hour	36.0 ± 7.9	35.4 ± 7.0	0.09	<0.0001	0.10
Creatinine, μ mol/24-hour	8016.0 ± 1549.3	6787.3 ± 1128.4	<0.0001	<0.0001	0.19
High-salt/potassium supplementation					
Sodium, mmol/24-hour	249.9 ± 34.5	259.0 ± 37.1	<0.0001	<0.0001	0.29
Potassium, mmol/24-hour	77.5 ± 13.2	77.5 ± 12.4	0.99	<0.0001	0.38
Creatinine, μ mol/24-hour	8249.0 ± 1792.7	6977.4 ± 1230.7	<0.0001	<0.0001	0.72

Values are mean ± SD or percentage.

* p-values are for low-salt intervention compared to baseline, high-salt intervention compared to low-salt intervention, or potassium supplementation plus high-salt intervention compared to high-salt intervention.

Table 3

Mean systolic and diastolic blood pressure at baseline and during dietary intervention

Blood pressure, mm Hg	Men	Women	p-value for difference by gender	p-value for difference by intervention*	p-value for intervention
Baseline					
SBP	118.7 ± 12.8	114.9 ± 15.4	<0.0001	...	...
DBP	75.6 ± 9.9	71.7 ± 10.5	<0.0001	...	...
Low-salt intervention					
SBP	113.3 ± 11.1	109.3 ± 13.0	<0.0001	<0.0001	0.0002
DBP	73.1 ± 9.3	68.6 ± 9.5	<0.0001	<0.0001	0.0003
High-salt intervention					
SBP	117.8 ± 12.1	114.5 ± 15.0	<0.0001	<0.0001	<0.0001
DBP	74.5 ± 9.9	71.1 ± 10.3	<0.0001	<0.0001	0.001
High-salt/potassium supplementation					
SBP	114.2 ± 11.6	111.1 ± 14.3	<0.0001	<0.0001	<0.0001
DBP	73.4 ± 9.5	69.4 ± 9.9	<0.0001	<0.0001	0.001

Values are mean ± SD or percentage.

* p-values are for low-salt intervention compared to baseline, high-salt intervention compared to low-salt intervention, or potassium supplementation plus high-salt intervention compared to high-salt intervention.

Table 4

Multivariable-adjusted* mean changes (95% confidence interval) in systolic and diastolic blood pressure in response to low-salt, high-salt, and potassium-supplementation interventions by gender, age, and baseline blood pressure

	Low-sodium intervention		High-sodium intervention		Potassium supplement	
	ASBP	ΔDBP	ASBP	ΔDBP	ASBP	ΔDBP
Gender						
Men	-7.05 (-7.50, -6.59)	-3.39 (-3.77, -3.01)	5.25 (4.83, 5.66)	1.74 (1.36, 2.13)	-4.43 (-4.82, -4.04)	-1.52 (-1.85, -1.19)
Women	-8.07 (-8.57, -7.58)	-4.51 (-4.92, -4.09)	6.35 (5.90, 6.81)	3.08 (2.66, 3.50)	-4.45 (-4.88, -4.03)	-2.10 (-2.46, -1.74)
p-value for differences by gender	0.0004	<0.0001	<0.0001	<0.0001	0.93	0.007
Age, yrs						
<35	-6.04 (-6.64, -5.44)	-4.05 (-4.56, -3.55)	4.31 (3.75, 4.86)	2.00 (1.49, 2.51)	-3.88 (-4.40, -3.36)	-1.82 (-2.26, -1.38)
35-44	-7.59 (-8.08, -7.10)	-4.01 (-4.42, -3.59)	5.73 (5.28, 6.19)	2.57 (2.15, 2.99)	-4.01 (-4.43, -3.58)	-1.75 (-2.10, -1.39)
≥54	-9.05 (-9.62, -8.47)	-3.78 (-4.27, -3.29)	7.36 (6.83, 7.89)	2.66 (2.17, 3.16)	-5.44 (-5.94, -4.93)	-1.86 (-2.29, -1.44)
p-value for differences by age	<0.0001	0.66	<0.0001	0.08	<0.0001	0.90
Baseline BP, mm Hg						
<120/80	-3.28 (-3.66, -2.90)	-1.46 (-1.78, -1.14)	4.14 (3.79, 4.49)	1.44 (1.12, 1.77)	-2.89 (-3.22, -2.56)	-1.14 (-1.42, -0.86)
120-139/80-89	-7.57 (-8.06, -7.08)	-4.02 (-4.43, -3.61)	5.52 (5.07, 5.98)	2.40 (1.98, 2.82)	-4.04 (-4.47, -3.61)	-1.60 (-1.96, -1.23)
≥140/90	-11.8 (-12.8, -10.9)	-6.36 (-7.15, -5.57)	7.74 (6.88, 8.60)	3.38 (2.58, 4.18)	-6.40 (-7.21, -5.59)	-2.69 (-3.38, -2.00)
p-value for differences by baseline BP	<0.0001	<0.0001	<0.0001	<0.0001	<0.0001	0.0002

BP response (95% confidence interval), mm Hg[†]

* Adjusted for age, gender, baseline BP, body-mass index, education, alcohol consumption, current smoking, physical activity, and baseline 24-hour urinary excretion of sodium and potassium.

[†] BP response to low-sodium = BP on low-sodium diet - BP at baseline; BP response to high-sodium = BP on high-sodium diet - BP on low-sodium diet; and BP response to potassium supplement = BP on high-sodium diet with potassium supplementation - BP on high-sodium diet.