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Dietary and Urinary Metabonomic Factors Possibly Accounting for Higher Blood Pressure of African-Americans Compared to White Americans – – The INTERMAP Study RR

Jeremiah Stamler, MD[1], **Ian J. Brown, PhD**[2], **Ivan K.S. Yap, PhD**[3,4], **Queenie Chan, PhD**[2,6], **Anisha Wijeyesekera, PhD**[3,6], **Isabel Garcia-Perez, PhD**[3,6], **Marc Chadeau-Hyam, PhD**[2,6], **Timothy M.D. Ebbels, PhD**[3,6], **Maria De Iorio, PhD**[2,5], **Joram Posma, MSc**[3,6], **Martha L. Daviglus, MD PhD**[1], **Mercedes Carnethon, PhD**[1], **Elaine Holmes, PhD**[3,6], **Jeremy K. Nicholson, PhD**[3,6], **Paul Elliott, MB PhD**[2,6], and **the INTERMAP Research Group**

[1]Department of Preventive Medicine, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA

[2]Department of Epidemiology and Biostatistics, School of Public Health, Faculty of Medicine, Imperial College London, UK

[3]Section of Computational and Systems Medicine, Department of Surgery and Cancer, Faculty of Medicine, Imperial College London, UK

[4] Department of Life Sciences, School of Pharmacy and Health Sciences, International Medical University, Kuala Lumpur, Malaysia

[5] Department of Statistical Science, University College, London, UK

[6] MRC-HPA Centre for Environment and Health, Imperial College London, UK

Abstract

African-Americans compared to non-Hispanic-White-Americans have higher systolic, diastolic blood pressure and rates of prehypertension/hypertension. Reasons for these adverse findings remain obscure. Analyses here focused on relations of foods/nutrients/urinary metabolites to higher African-American blood pressure for 369 African-Americans compared to 1,190 non-Hispanic-White-Americans ages 40-59 from 8 population samples. Standardized data were from four 24-hour dietary recalls/person, two 24-h urine collections, 8 blood pressure measurements; multiple linear regression quantitating role of foods, nutrients, metabolites in higher African-American blood pressure. Compared to non-Hispanic-White-Americans, African-Americans average systolic/diastolic pressure was higher by 4.7/3.4 mm Hg (men) and 9.0/4.8 mm Hg (women). Control for higher body mass index of African-American women reduced excess African-American systolic/diastolic pressure to 6.8/3.8 mm Hg. African American intake of multiple foods, nutrients related to blood pressure was less favorable - - less vegetables, fruits, grains, vegetable protein, glutamic acid, starch, fiber, minerals, potassium; more processed meats, pork, eggs, sugar-sweetened beverages, cholesterol, higher sodium to potassium ratio. Control for 11 nutrient and 10 non-nutrient correlates reduced higher African-American systolic/diastolic pressure to 2.3/2.3 mm Hg (52% and 33% reduction) (men) and to 5.3/2.8 mm Hg (21% and 27% reduction) (women). Control also for foods/urinary metabolites had little further influence on

Corresponding Author: Dr. Jeremiah Stamler, Department of Preventive Medicine, Feinberg School of Medicine, Northwestern University, 680 N.Lake Shore Drive, Suite-1400, Chicago, IL 60611, USA. Tel: 312-303-4037; Fax: 312-908-9588; j-stamler@northwestern.edu.

DISCLOSURES
None.

higher African-American blood pressure. Multiple nutrients with less favorable intakes by African-Americans than non-Hispanic-White-Americans account at least in part for higher African-American blood pressure. Improved dietary patterns can contribute to prevention/control of more adverse African-American blood pressure levels.

Keywords

African-American; blood pressure; nutrient; food intake; urinary metabolites

INTRODUCTION

Adverse blood pressure (BP) is an established major risk factor for cardiovascular diseases (CVD). Repeated U.S. population surveys, including the International Collaborative Study on Macro-/Micronutrients and Blood Pressure (INTERMAP), document that BP is higher in African-Americans (AA) than non-Hispanic-White- Americans (NHWA).[1-3] Etiopathogenesis of this BP difference remains unexplained, i.e., it continues to be - - theoretically and practically - - a major unsolved challenge for CVD research. Here we hypothesize that multiple AA-NHWA differences in food/nutrient intake and urinary metabolites account for higher AA BP; we use INTERMAP data to test this hypothesis.[3-6]

METHODS

Population Samples, Field Methods (1996-1999)

Participants are 369 AA and 1,190 NHWA women and men ages 40-59 years recruited as eight stratified random U.S. population samples (Online Table S1). Participants attended four times - - two visits on consecutive days, two further visits on consecutive days.[3] Demographic data were obtained by interviewer-administered questionnaire. Height and weight were measured at two visits. Each participant provided two timed 24-hour urine collections, aliquots were air-freighted frozen to the Central Laboratory (Leuven, Belgium) for urinary biochemistry, and to Imperial College London for proton nuclear magnetic resonance (^{1}H NMR) spectroscopy.[6] Dietary data were collected and computerized by a certified interviewer using the multi-pass 24-hour recall method.[3,7] Institutional ethics committee approval was obtained for each site; all participants gave written informed consent.

Blood Pressure Measurements

Systolic and diastolic BP (first and fifth Korotkoff sounds) were measured twice/visit by a certified technician using a random-zero sphygmomanometer - -participant seated for at least five minutes in a quiet room, bladder empty, arm at heart level.[3]

Statistical Methods

Measurements/person were averaged for BP and nutrients across the four visits; for 24-hour urinary excretions, across the two collections.[3,7] Inter-ethnic differences were assessed for statistical significance by Student's t-test or χ^2 test. Approximate reliability - - observed univariate regression coefficient as percent of theoretical 'true' coefficient - - was estimated for relevant variables.[8,9]

Based on AA-NHWA differences in dietary and urinary variables, multiple linear regression was used to examine relations of these traits to inter-ethnic differences in BP.[5,6,10] Model A included age, gender, sample, and an indicator for African-American; Model B added other nondietary factors; model C added body mass index (BMI). Then each dietary/urinary factor was added to model C separately; percentage reduction from the model C AA-NHWA BP difference was calculated to assess influence of the added variable on higher BP of AA. Finally, dietary/urinary variables were included in combinations to assess joint impact on higher AA BP.

RESULTS

Descriptive Statistics

African-Americans had higher average BP than NHWA and higher prevalence rates of hypertension (Online Table S2). AA women had higher average BMI and rates of overweight/obesity than NHWA women. AA and NHWA of both genders differed in intake of multiple foods/nutrients (Online Tables S2 and S3).

African-American intake lower, foods/nutrients with possible favorable relation to BP—African-Americans had lower intakes of total and raw vegetables, fresh fruits, pasta/rice, total grains; vegetable protein, glutamic acid, starch, fiber, calcium (Ca), magnesium (Mg), phosphorus (P), potassium (K), iron (Fe), non-heme Fe.

African-American intake higher, foods/nutrients with possible adverse relation to BP—African-Americans had higher intakes of processed meats, pork, eggs, sugar-sweetened beverages; dietary cholesterol, total sugars, fructose/glucose/sucrose, glycine, sodium (Na)/K ratio.

African-American intakes were relatively favorable for only a few foods/nutrients

African-American intake higher, foods/nutrients with possible favorable relation to BP: Fish/fish roe/shellfish, poultry; polyunsaturated fatty acids (PFA), PFA/saturated fatty acid ratio, oleic acid.

African-American intake lower, foods/nutrients with possible adverse relation to BP: Cream, cheese, dairy product recipes, alcoholic beverages; no nutrients.

Urinary metabolites: The median urinary 600 MHz ^{1}H NMR spectra for AA and NHWA subsamples are shown in Figure 1. Urinary metabolites significantly[12] higher in AA than NHWA included creatinine, 3-hydroxyisovalerate, *N*-acetyls of glycoprotein fragments, dimethylglycine, lysine, *N*-acetyl neuraminic acid, leucine, dimethylamine (DMA), taurine, and 2-hydroxyisobutyrate; metabolites significantly higher in NHWA, trimethylamine, *N*-methyl nicotinic acid (NMNA), hippurate, succinate (Table 1). Hippurate and NMNA quantified 24-h excretions are in Online Table S4.

Partial correlations: Partial correlation coefficients >0.5 (adjusted for age, gender, sample) were recorded for many pairs of foods/nutrients (Online Table S5).

Reliability data: For foods, 29 of 68 reliability estimates were >50%, without apparent pattern across gender/ethnic strata (Online Table S6). Nutrient reliability estimates were generally higher than or foods; 75 of 108 were >50%, somewhat lower for AA than for NHWA. Reliability estimates were high for hippurate, NMNA, systolic BP (SBP), diastolic BP (DBP).

Relation of Foods, Nutrients, Urinary Metabolites to Higher AA BP

With control for possible non-dietary confounders, SBP/DBP was significantly higher for AA than NHWA by 4.7/3.4 mm Hg (men) and 9.0/4.8 mm Hg (women) (Online Table S6, row B). With BMI in the model (Online Table S7, row C), these differences remained about the same for men; for women, they were reduced to 6.8/3.8 mm Hg.

Foods considered singly—Of 17 foods with significantly different intakes by AA and NHWA, most had only a small influence on the higher BP of AA (Online Table S7).

Nutrients and urinary metabolites considered singly—Addition to the regression model of individual nutrients generally led to greater influences on SBP and DBP (Online Table S7) than addition of individual foods: 24-h urinary K excretion (inversely related to BP and lower in AA than NHWA) produced the largest effect in men, reduction of higher AA SBP by 1.2 mm Hg (26%), DBP by 0.8 mm Hg (24%), but without effect in women. Dietary glycine (% total protein) (directly related to BP and higher in AA) had a similar SBP effect in men and the largest effect in women. Inclusion of Ca, Mg, P singly (inversely related to BP and lower in AA than NHWA) produced 0.5 to 0.6 mm Hg (>10%) reductions in higher SBP of AA men, and qualitatively similar effects for AA women.

With inclusion of urinary hippurate, lower in AA men (Online Table S4) and inversely related to BP, higher SBP and DBP of AA men and women were reduced by only 0.1 mm Hg (Online Table S7). With addition to the model of NMNA, lower in AA than NHWA men and women (reportedly not related to BP), higher SBP and DBP of AA men and women were increased, not decreased.

Foods, nutrients, urinary metabolites in combination—With 10 foods considered together (all with significantly less favorable intakes for AA than NHWA), effects on higher AA SBP/DBP were modest (Table 2, row D). With 13 nutrients combined (most with significantly less favorable intakes for AA than NHWA), effects on higher AA BP were larger, particularly for men - - e.g., male SBP/DBP difference reduced to 2.3/2.3 mm Hg (Z-scores 1.72 and 2.41), a decrease of 2.2/1.1 mm Hg (−52% and −33%) (Table 2, row E1). Female AA SBP/DBP differences remained substantial, with nutrient related smaller effect of 1.5/1.0 mm Hg (−21% and −27%). No significant gender interaction was found (data not tabulated).

Combinations of nutrients and foods yielded little or no additional reduction in higher AA BP (Table 2, row F2). With the two quantified urinary metabolites in the model together (without and with nutrients), higher AA SBP/DBP was not reduced (Table 2, rows H, J).

DISCUSSION

Main findings here on higher SBP/DBP of AA than NHWA are: multiple nutrients, possibly related to BP, with less favorable intakes by AA than NHWA, account in part for higher AA SBP/DBP. These include vegetable protein, its main amino acid glutamic acid, starch, fiber, K, Ca and/or Mg and/or P, non-heme Fe; also, dietary cholesterol and glycine.[11-25]

To the best of our knowledge, these INTERMAP findings are unique. The ARIC population study, involving over 8,000 nonhypertensive women and men ages 45-64, reported that Whites consuming three or more daily servings of low-fat milk, compared to those consuming less than one, had a 2.7 mm Hg smaller SBP increase with 9 year follow-up; an association not prevailing for AA.[26] No data were given on relations of dietary variables to BP differences between AAs and Whites. The CARDIA young adult population study reported that with 10 year follow-up, intake of low-fat dairy products was associated with lower incidence of high BP in AA and Whites.[27] The study did not assess whether these or other foods/nutrients related to higher AA BP. The Third U.S. National Health and Nutrition Survey (NHANES III) (1988-1994) reported lower serum 25-hydroxyvitamin D (25(OH)D) of AA than NHWA, and an inverse relation of 25(OH)D to BP.[28] These differences were estimated to "explain" about half the greater AA high BP prevalence. No dietary data were given.

The INTERMAP findings here are reproducible, supporting the inference that they are etiologically significant, they have important implications, especially need for greater efforts to improve AA nutrition. Adoption of dietary recommendations for prevention/control of adverse BP, e.g., per Dietary Approaches to Stop Hypertension (DASH)-low Na or Optimal Macronutrient Intake Trial for Heart Health (OMNIHEART) plus low Na,[15,16] results in such improved nutrition. To extend their use among AA, specific factors influencing AA diet need to be considered, e.g., ethnic traditions; lower average income; reduced accessibility to modern supermarkets.[29] For AA women there is a particular need to reduce their higher BMI, known to relate importantly to higher BP.

Metabolome-wide association analysis revealed 12 urinary metabolites that differed significantly between AA and NHWA. Hippurate (higher in NHWA) is a gut-microbial co-metabolite produced by bacterial metabolism of plant phenols;[30,31] hippurate related inversely to BP of INTERMAP participants.[6] Observed differences in DMA and dimethylglycine (both higher in AA) also likely relate to inter-ethnic microbiotal differences.[33,33] Creatinine and guanidinoacetate (involved in creatinine metabolism) were higher in AA than NHWA. Creatinine excretion is related to muscle turnover;[34] these metabolite differences could reflect greater AA physical activity and muscle mass. Lower AA excretion of *N*-methyl nicotinic acid, a product of nicotinic acid/nicotinamide metabolism, could reflect lower AA dietary intakes of niacin and tryptophan (observed; data not tabulated). Trimethylamine (lower in AA) is linked to dietary choline-induced atherosclerosis;[35] this difference could reflect lower AA dietary intakes of the B-complex vitamins.

Multiple nutrients accounted only in part for higher AA BP. This may reflect regression dilution bias and other limitations in the nutrient data, despite their quality.[5,9] In this regard, two prior INTERMAP investigations - - on higher BP of less educated Americans, and higher BP of northern than southern Chinese - - showed that multiple nutrients accounted ***completely*** for the higher BP.[13,25] Thus, the fact that here multiple foods/nutrients/metabolites apparently account only in part for higher AA BP suggests that other traits may operate, e.g., in utero influences, early life dietary patterns, psychosocial factors, genetic factors.[36-40]

Study strengths

Findings here are solidly based, with participants from 8 diverse U.S. random samples, and dietary/metabolite/BP data collected by standardized, quality-controlled repetitive methods.

Study limitations

Data are cross-sectional, subject to random regression dilution bias despite multiple measurements, and - - in regard to the dietary data - - non-random biases inherent in the methodology.[9]

PERSPECTIVES

Delineation of factors responsible for the more adverse BP patterns of AA compared to other Americans is a long-term major unresolved research challenge. Its importance relates not only to the need to overcome this inequality in health of African-Americans. It also stems from the likelihood that resolving this problem will clarify understanding on the etiopathogenesis of epidemic prehypertension/hypertension in all strata of the population.

The INTERMAP data reported here show that about a quarter (SBP, women) to a half (SBP, men) of the higher BP of AA is attributable to less favorable AA intake of multiple nutrients, and that greater obesity among AA women also is a significant factor. Improved AA eating patterns can help prevent/control adverse AA BP patterns.

Acknowledgments

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NOVELTY AND SIGNIFICANCE

Novelty: To the best of our knowledge, the data here are the first reported on multiple food/nutrient intakes/urinary metabolites that apparently account - - at least in part - - for the more adverse BP patterns of AA compared to NHWA.

Relevance: These data point the way to specific dietary enhancements for the prevention/control of adverse BP patterns in AA.

Summary: Data here from the population-based US samples of the INTERMAP Study support the conclusion that the inordinately high rates of prehypertension/hypertension -- common among AA - - can be ameliorated by improved nutrition.

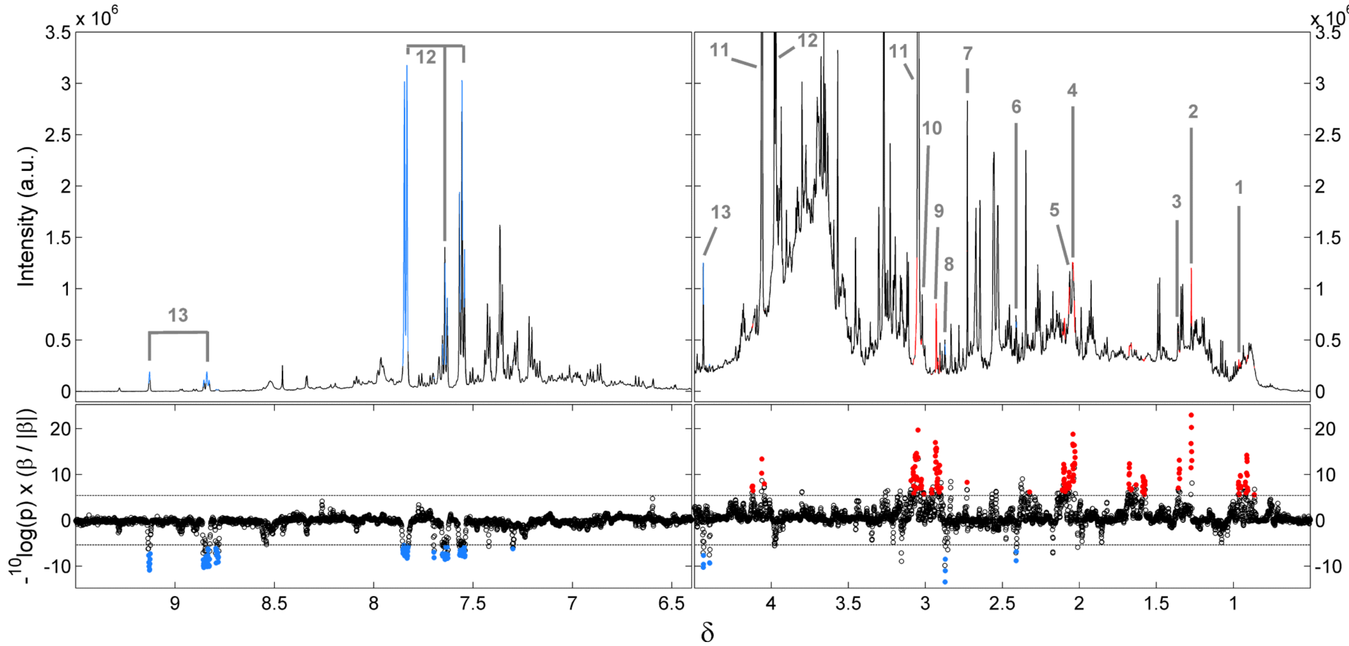

Figure 1.

Top: median urinary ^{1}H NMR spectrum of INTERMAP U.S. AA and NHWA participants, based on the first urine collection (N=1,455). Bottom: Manhattan plot indicating the significant spectral variables. Metabolites higher in AA individuals compared to NHWA are shown in red; in blue for metabolites higher in NHWA individuals compared to AA. Key: 1, Leucine; 2, 3-hydroxyisovalerate; 3, 2-hydroxyisobutyrate; 4, *N*-acetyls of glycoprotein fragments; 5, *N*-acetyl neuraminic acid; 6, Succinate; 7, Dimethylamine; 8, Trimethylamine; 9, Dimethylglycine; 10, Lysine; 11, Creatinine; 12, Hippurate; 13, *N*-methyl nicotinic acid.

Table 1

^{1}H NMR-derived urinary metabolites differing significantly[*] between African-Americans (AA) and non-Hispanic-White Americans (NHWA) participants, all and by gender

Metabolites	Chemical Shifts, ppm (multiplicity)	Minimum P-value[†]					
		All		Men		Women	
		1st collection	2nd collection	1st collection	2nd collection	1st collection	2nd collection
Higher in AA (154 men and 184 women)							
Creatinine	3.05 (s); 4.05 (s)	*3.8x10^{-25}*	*1.8×10^{-20}*	*4.4×10^{-13}*	*1.1×10^{-11}*	*5.8×10^{-14}*	*9.3×10^{-10}*
3-hydroxyisovalerate	1.27 (s); 2.37 (s)	*1.0×10^{-23}*	*4.6×10^{-24}*	*4.1×10^{-13}*	*3.6×10^{-17}*	*1.8×10^{-11}*	*4.3×10^{-9}*
N-acetyls of glycoprotein fragments	2.02 -2.04 (s)	*1.6×10^{-22}*	*1.5×10^{-19}*	*3.9×10^{-12}*	*1.5×10^{-9}*	*1.4×10^{-12}*	*3.1×10^{-12}*
Dimethylglycine	2.93 (s); 3.72 (s)	*5.2×10^{-18}*	*9.7×10^{-18}*			*4.1×10^{-15}*	*2.2×10^{-11}*
Lysine	3.02 (t)	*1.3×10^{-9}*	*4.2×10^{-15}*				
N-acetyl neuraminic acid	2.06 (s)	*2.9×10^{-14}*	*3.0×10^{-11}*	*4.3×10^{-10}*	*2.7×10^{-9}*		
Leucine	0.96 (d)	*1.7×10^{-10}*	*3.9×10^{-11}*				
Dimethylamine	2.73 (s)	*3.3×10^{-10}*	*4.7 ×10^{-9}*	*4.1×10^{-10}*	*1.7×10^{-11}*		
2-hydroxyisobutyrate	1.36 (s)	*5.3×10^{-10}*	*8.6×10^{-8}*				
Hiaher in NHWA (594 men and 523 women)							
Trimethylamine	2.87 (s)	*2.6×10^{-15}*	*9.5×10-12*	*9.8×10^{-8}*	*4.0×10^{-9}*		
A/-methyl nicotinic acid	4.44 (s); 8.84 (t); 9.13 (s)	*3.1×10^{-13}*	*1.2×10^{-10}*	*4.1×10^{-8}*	*2.2×10^{-7}*		
Hippurate	3.98 (d); 7.55 (t); 7.64 (t); 7.84 (d)	*5.9×10^{-10}*	*3.1×10^{-9}*				
Succinate	2.41 (s)	*1.5×10^{-9}*	*4.0×10^{-10}*			*3.9×10^{-9}*	*3.4×10^{-8}*

Abbreviations: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet.

[*] Mean population differences in peak intensity for spectral variables were assessed for statistical significance using Family Wise Error Rate <0.01 ($P < 4\times10^{-6}$ for group mean population differences by Student's t) for the two urine collections considered separately.

[†] Minimum *P*-values for mean population differences in peak intensity assigned to a particular metabolite, obtained separately for first and second urine collections, give a ranking of the discriminatory strength of the metabolites.

Table 2

Relation of combinations of foods/nutrients/urinary metabolites, significantly different in AA and NHWA, to higher BP of AA than NHWA, by gender

Model	Systolic BP, mm Hg			Diastolic BP, mm Hg		
	BP difference	(Z-score)	% change from C*	BP difference	(Z-score)	% change from C*
Men (N=165 AA, 620 NHWA)						
A: age, sample	5.41	(4.40)		3.46	(3.94)	
B: A+ medical history of CVD/diabetes, family history of hypertension, physical activity, special diet, supplement use	4.68	(3.80)		3.38	(3.84)	
C: B+ BMI	4.76	(4.04)		3.43	(4.05)	
Combination of foods						
D: C+ raw vegetables, fresh fruit, pasta/rice, total grains, eggs, sugar-sweetened beverages, cream/cheese/ice cream/milk & cheese recipes, pork, processed meats, alcoholic beverages	3.64	(3.00)	−23.5	2.88	(3.28)	−16.1
Combinations of nutrients						
E1: C+ vegetable protein, glutamic acid %kcal, starch, fiber, Ca, non-heme Fe, riboflavin, urinary K, Σ long chain PFA, dietary cholesterol, glycine %protein, 14-day alcohol, urinary Na	2.28	(1.72)	−52.1	2.31	(2.41)	−32.7
E2: as E1 except removing 14-day alcohol & urinary Na	2.51	(1.89)	−47.3	2.43	(2.53)	−29.2
E3: as E1 except glutamic acid as %protein (instead of %kcal)	2.77	(2.12)	−41.9	2.61	(2.75)	−24.1
E4: as E1 except Mg instead of Ca	2.41	(1.82)	−49.4	2.44	(2.55)	−28.9
E5: as E1 except P instead of Ca	2.39	(1.81)	−49.9	2.41	(2.52)	−29.8
E6: as E1 except urinary Na/K ratio instead of urinary K & Na	2.47	(1.88)	−48.1	2.51	(2.63)	−27.0
E7: E1+ Mg, P	2.29	(1.72)	−52.0	2.33	(2.42)	−32.2
Combinations of foods/nutrients						
F1: including variables with largest SBP differences for men, D+E1	2.17	(1.62)	−54.3	2.17	(2.04)	−36.7
F2: as F1, excluding variables correlated partial r >0.5†	2.25	(1.69)	−52.7	2.14	(2.21)	−37.8
Men with Quantitated Urinary Metabolites (N=146 AA, 578 NHWA)						
Combinations of nutrients and urinary metabolite variables						
G: as C except based on above N	3.81	(3.15)		3.12	(3.57)	
H: G+ hippurate, A/-methylnicotinic acid	4.10	(3.29)	7.6	3.09	(3.44)	−0.8
I: as E1 except based on above N	2.05	(1.51)	−46.2	2.46	(2.50)	−21.1
J: I+ hippurate, A/-methyl nicotinic acid	2.44	(1.78)	−36.0	2.55	(2.56)	−18.2
Women (N=204 AA, 570 NHWA)						
A: age, sample	9.66	(8.02)		5.03	(6.52)	

Model	Systolic BP, mm Hg			Diastolic BP, mm Hg		
	BP difference	(Z-score)	% change from C*	BP difference	(Z-score)	% change from C*
B: A+ medical history of CVD/diabetes, family history of hypertension, physical activity, special diet, supplement use	9.00	(7.42)		4.83	(6.20)	
C: B+ BMI	6.76	(5.76)		3.77	(4.87)	
Combination of foods						
D: C+ raw vegetables, fresh fruit, pasta/rice, total grains, eggs, sugar-sweetened beverages, cream/cheese/ice cream/milk & cheese recipes, pork, processed meats, alcoholic beverages	6.18	(4.74)	−8.5	3.58	(4.14)	−5.2
Combinations of nutrients						
E1: C+ vegetable protein, glutamic acid %kcal, starch, fiber, Ca, non-heme Fe, riboflavin, urinary K, Σ long chain PFA, dietary cholesterol, glycine %protein, 14-day alcohol, urinary Na	5.31	(3.82)	−21.4	2.76	(3.01)	−26.8
E2: as E1 except removing 14-day alcohol & urinary Na	5.22	(3.78)	−22.8	2.61	(2.86)	−30.9
E3: as E1 except glutamic acid as %protein (instead of %kcal)	5.42	(3.90)	−19.8	2.78	(3.02)	−26.2
E4: as E1 except Mg instead of Ca	5.46	(3.94)	−19.2	2.80	(3.05)	−25.8
E5: as E1 except P instead of Ca	5.39	(3.89)	−20.2	2.73	(2.98)	−27.6
E6: as E1 except urinary Na/K ratio instead of urinary K & Na	5.13	(3.69)	−24.1	2.65	(2.88)	−29.7
E7: E1+ Mg, P	5.40	(3.87)	−20.2	2.84	(3.09)	−24.6
Combinations of foods/nutrients						
F1: including variables with largest SBP differences for women, D + E6	5.38	(3.79)	−20.4	3.04	(3.23)	−19.4
F2: As F1, excluding variables correlated partial r >0.5‡	5.14	(3.68)	−24.0	2.83	(3.06)	−25.0
Women with Quantitated Urinary Metabolites (N=188 AA, 514 NHWA)						
Combinations of nutrients and urinary metabolite variables						
G: as C except based on above N	6.80	(5.48)		3.78	(4.60)	
H: G+ hippurate, A/-methyl nicotinic acid	6.92	(5.52)	1.6	4.01	(4.83)	6.0
I: as E1 except based on above N	5.37	(3.63)	−21.1	2.77	(2.82)	−26.8
J: I+ hippurate, A/-methyl nicotinic acid	5.33	(3.60)	−21.7	2.80	(2.86)	−26.0

Abbreviations: Σ, sum of; Ca, calcium; Fe, iron; K, potassium; Mg, magnesium; Na, sodium; SFA, saturated fatty acids; P, phosphorus; PFA, polyunsaturated fatty acids.

Units for nutrients are %kcal, g/1,000kcal, or mg/1,000kcal; for glutamic acid and glycine, also % total protein; for urinary hippurate and *N*-methyl nicotinic acid, mmol/24-hours.

Z-score = regression coefficient/standard error. $|Z| \geq 1.96$, uncorrected $P \leq 0.05$; $|Z| \geq 2.58$, uncorrected $P \leq 0.01$; $|Z| \geq 3.29$, uncorrected $P \leq 0.001$.

*For rows H, I and J, % change from row G.

†Model F2 (men) includes: raw vegetables, fresh fruit, pasta/rice, eggs, sugar-sweetened beverages, cream/cheese/ice cream/milk & cheese recipes, pork, processed meats, vegetable protein, glutamic acid %kcal, riboflavin, urinary K, Σ long chain PFA, glycine %protein, 14-day alcohol, urinary Na.

‡Model F2 (women) includes: raw vegetables, fresh fruit, pasta/rice, total grains, sugar- sweetened beverages, cream/cheese/ice cream/milk & cheese recipes, pork, processed meats, alcoholic beverages, glutamic acid %kcal, cholesterol, riboflavin, glycine %protein, urinary Na/K ratio.