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SUGAR-SWEETENED BEVERAGE, SUGAR INTAKE OF INDIVIDUALS AND THEIR BLOOD PRESSURE: INTERMAP STUDY

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Abstract

The obesity epidemic has focused attention on relationships of sugars and sugar-sweetened beverages (SSB) to cardiovascular risk factors. Here we report cross-sectional associations of SSB, diet beverages, sugars with blood pressure (BP) for UK and USA participants of the International Study of Macro/Micro-nutrients and Blood Pressure (INTERMAP). Data collected includes four 24-h dietary recalls, two 24-h urine collections, eight BP readings, questionnaire data for 2,696 people ages 40-59 from 10 USA/UK population samples. Associations of SSB, diet beverages, and sugars (fructose, glucose, sucrose) with BP were assessed by multiple linear regression. Sugar-sweetened beverage intake related directly to BP, *P*-values 0.005 to <0.001 (systolic BP), 0.14 to <0.001 (diastolic BP). Sugar-sweetened beverage intake higher by 1 serving/day (355 ml/24-h) was associated with systolic/diastolic BP differences of +1.6/+0.8 mm Hg (both *P* <0.001); +1.1/+0.4 mm Hg (*P* <0.001/<0.05) with adjustment for weight, height. Diet beverage intake was inversely associated with BP, *P* 0.41 to 0.003. Fructose- and glucose-BP associations were direct, with significant sugar-sodium interactions: for individuals with above-median 24-h urinary sodium excretion, fructose intake higher by 2 SD (5.6 %kcal) was associated with systolic/

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DISCLOSURES

None.

diastolic BP differences of +3.4/+2.2 mm Hg (both P <0.001); 2.5/1.7 mm Hg (both P 0.002) with adjustment for weight, height. Observed independent, direct associations of SSB intake and BP are consistent with recent trial data. These findings, plus adverse nutrient intakes among SSB consumers, and greater sugar-BP differences for persons with higher sodium excretion, lend support to recommendations that intake of SSB, sugars, and salt be substantially reduced.

Keywords

Sugar-sweetened beverages; sodium; nutrition; blood pressure; epidemiology; population study

INTRODUCTION

Adverse blood pressure (BP) – prevalent worldwide – is an independent major risk factor for cardiovascular diseases (CVD).[1] Public health measures are needed to address this problem, with an emphasis on primary and primordial prevention.[2] Established modifiable risk factors for elevated BP are high sodium intake, inadequate potassium intake, high body mass index (BMI), and excessive alcohol intake.[3,4] Other dietary factors possibly related to adverse BP levels include lower intakes of calcium, magnesium, phosphorus[5], iron[6], vegetable protein[7], glutamic acid[8], polyunsaturated fatty acids (PFA)[9,10], starch[11]; and higher intakes of cholesterol[12], animal protein, red meat.[6,7]

The western obesity epidemic has focused attention on the relationships to cardiovascular disease risk factors of diets rich in added sugars –particularly glucose, sucrose, and fructose, e.g., as high-fructose corn syrup, abundant in sugar-sweetened beverages (SSBs).[13-15] Animal data indicate direct pressor effects of glucose, fructose, and sucrose on BP.[16-20] Limited short-term human trial data are mostly compatible with animal findings[21-23]; observational and long-term trial data are inconsistent.[24-29] The most compelling evidence to date comes from the PREMIER Study, a behavioral intervention trial of 810 pre-hypertensive and hypertensive individuals, where reduced intake of SSBs or sugar over 18 months was associated with reduced BP.[30]

Here we report cross-sectional associations with BP of SSBs, diet (non-caloric-sweetened) beverages, and sugars (fructose, glucose, sucrose) for 2,696 participants of the International Study of Macro/Micro-nutrients and Blood Pressure (INTERMAP) from ten population samples in the United States of America (USA) and the United Kingdom (UK).

METHODS

Population Samples, Field Methods (1996-1999)

INTERMAP surveyed 4,680 men and women ages 40-59 from Japan (4 samples), People's Republic of China (3), UK (2), and USA (8). We focus here on the 2,696 USA and UK participants, as SSB and diet beverage intake was negligible in the Japanese and Chinese samples. Participants were randomly recruited from general and occupational populations. [31] Each participant attended four times, the first two visits on consecutive days, the second two visits on consecutive days on average three weeks later. For BP measurement, each participant – having emptied his/her bladder – was seated for five minutes, feet flat on the floor, in a quiet room, with no physical activity, and no eating, drinking, or smoking in the preceding half hour. Blood pressure was measured twice at each visit with a random-zero sphygmomanometer; Korotkoff sounds I and V were criteria for systolic BP and diastolic BP. Measurements of height and weight, and questionnaire data on daily alcohol consumption over the previous seven days were obtained at two visits. Dietary data were collected at each visit by a trained interviewer with use of the in-depth multi-pass 24-hour

recall method.[32] Questionnaire data were obtained on possible confounders. Each participant provided two 24-hour urine collections, start and end timed at the research center; measurements included urinary volume, sodium, potassium, calcium, magnesium, urea, creatinine.[31] Urinary sodium, potassium, and urea excretion were used to validate dietary intake of sodium, potassium and protein; correlations ranged from r =0.42 to r =0.55. [32] The study received institutional ethics committee approval for each site; all participants gave written consent; study procedures were in accordance with institutional guidelines.

Statistical Methods

Sugar-sweetened and diet beverage intakes were estimated from food records. Sugar-sweetened beverages included uncarbonated and carbonated soft drinks (e.g., soda), fruit drinks (excluding 100% fruit juices), lemonade, but excluded diet beverages. Diet beverages included uncarbonated and carbonated drinks sweetened with artificial (non-caloric) sweeteners. Dietary data were converted to nutrient intakes (83 nutrients) with use of enhanced country-specific food tables, standardized across countries by the Nutrition Coordinating Center, University of Minnesota.[32,33] Measurements/person were averaged across the four visits for beverage, nutrient and BP variables; across the two collections for 24-hour urinary variables.

Reliability as a measure of possible regression dilution bias [34] for beverage, nutrient and BP variables – expressed as the observed univariate regression coefficient as a percent of the theoretical 'true' coefficient – was estimated by the formula $1/[1+(\text{ratio}/2)]\times 100$. The ratio is intra-individual variance divided by inter-individual variance, calculated from mean intakes/BP levels of the first and second two visits, to account for higher correlation between intakes/BP levels on consecutive days.[35]

Associations among dietary variables were explored by partial Pearson correlation, adjusted for age, gender, and sample, pooled by country. Multiple regression analyses assessed relations to systolic and diastolic BP of each person's intake of SSB and diet beverages (ml/24-h, models adjusted for energy intake), fructose, glucose, and sucrose (% kcal). Four models were used, each controlled successively for a larger number of possible non-dietary and dietary confounders, with and without adjustment for weight and height; followed by a further series of sensitivity analyses that included censored normal regression to adjust for potential antihypertensive treatment bias.[36] USA and UK regression coefficients were pooled (weighted by inverse of their variance). A test for heterogeneity was done to examine differences between USA and UK regression coefficients. Age, gender, BMI, and sodium interactions were assessed by interaction terms in regression models. Departure from linearity was tested with squared terms.

Analyses were done with SAS 9.1 (SAS Institute, Cary, NC, USA) by I.J.B. Statistical tests were two-sided. Main findings are presented as BP differences associated with beverage intake higher by 1 serving (355ml/24-h), or with sugar intake higher by 2 SD; statistical significance is expressed as Z-scores (regression coefficient/standard error): $Z \geq 1.96$, $P \leq 0.05$; $Z \geq 2.58$, $P < 0.01$; $Z \geq 3.29$, $P < 0.001$, uncorrected for regression dilution bias or multiple testing.

RESULTS

Descriptive Statistics

Mean systolic/diastolic BP was 118.6/73.4 mm Hg in the USA, 120.4/77.3 mm Hg in the UK (please see http://hyper.ahajournals.org, Table S1). Mean SSB and diet beverage intakes were higher in USA than UK: mean SSB intake 0.9 servings/day (306 ml/24-h) in the USA, 0.2 servings/day (66 ml/24-h) in the UK. Expressed as ml/1,000 kcal, SSB intake was higher

in men, diet beverage intake higher in women. Fructose, glucose, and sucrose intakes (% kcal) were higher in USA than UK; similar in men and women.

Nutrient Intakes and Other Variables by Category of Beverage Intake

Compared to participants who consumed no SSBs, adjusted mean energy intake was higher by 120 kcal/24-h for those who consumed 1 or less servings/day (≤355 ml/24-h); higher by 397 kcal/24-h for those who consumed >1 serving/day (Table 1). Mean intakes of starch, fiber, protein (animal, vegetable), polyunsaturated and monounsaturated fatty acids, alcohol, minerals, caffeine (variables expressed as percentage of kilocalories or amount per 1000 kcal), and urinary potassium excretion were lowest in those consuming >1 serving/day. Fructose, glucose, sucrose intake, and urinary sodium/potassium ratio were highest in those consuming >1 serving/day. Mean BMI was lowest for non-consumers (28.5 kg/m^2), highest for those consuming >1 serving/day (30.0 kg/m^2). Mean participant age and years of education completed were lowest in the highest category of SSB consumption; physical activity, BMI, and BP (systolic, diastolic) highest in the same category. Findings were consistent for men and women analyzed separately (data not tabulated).

Nutrient intakes among diet beverage consumers were mostly higher than non-consumers (please see http://hyper.ahajournals.org, Table S2); exceptions were sugars and vitamin C (lowest in those consuming >1 serving/day); energy, fiber, omega-3 polyunsaturated fatty acids, cholesterol, alcohol, urinary sodium/potassium ratio (no difference). Diet beverage consumers had higher mean BMI than non-consumers, lower physical activity. No differences in participant age, education, or BP were observed.

Reliability

Reliability estimates for SSBs were 80% (USA), 58% (UK); for diet beverages 91% (USA), 85% (UK) (please see http://hyper.ahajournals.org, Table S3). Reliability estimates for fructose, glucose, and sucrose ranged from 68% (sucrose, USA) to 81% (sucrose, UK). Blood pressure reliability estimates were uniformly high (>90%).

Partial Correlation

Intakes of SSBs, fructose, glucose (amount/24-h, adjusted for sample, age, gender) were positively correlated: SSBs with fructose or glucose, r=0.72; fructose and glucose r=0.94 (please see http://hyper.ahajournals.org, Table S4); correlations with sucrose were positive, smaller than the foregoing. Expressed as a proportion of energy intake, SSB intake was similarly correlated with sugars, inversely correlated with starch, fiber, vegetable protein, minerals, and urinary potassium (r= −0.25 to −0.37) (please see http://hyper.ahajournals.org, Table S5). No correlations |r|>0.2 were observed for diet beverage intake (please see http://hyper.ahajournals.org, Table S5). Expressed as %kcal, fructose and glucose intake were positively correlated with vitamin C (r=0.40 and 0.43 respectively) (please see http://hyper.ahajournals.org, Table S5). Fructose, glucose, and sucrose were inversely correlated with starch, animal protein, fatty acids, alcohol, minerals, urinary electrolytes (r= −0.02 to −0.37).

Multiple Regression

Sugar-sweetened beverages—Associations with systolic BP were consistently direct, Z-scores 2.82 to 4.98 (*P*-values 0.005 to <0.001), in models adjusted separately for potential confounders including vegetable protein, minerals, and caffeine (Table 2). In Model 3 – adjusted for energy, urinary sodium, potassium, dietary alcohol, cholesterol, polyunsaturated, and saturated fatty acids – SSB intake higher by 1 serving/day (355 ml/24-h) was associated with a systolic BP difference of +1.6 mm Hg (Z 4.98, *P* <0.001), +1.1 mm

Hg (Z 3.40, *P* <0.001) with control for weight and height. Associations with diastolic BP were direct, Z-scores 1.47 to 3.42 (*P* 0.14 to <0.001). BP differences/Z-scores were larger in censored normal regressions and subgroup analyses excluding individuals with high day-to-day variability in nutrient intakes or BP; smaller in subgroup analyses of nonhypertensive participants (please see http://hyper.ahajournals.org, Table S6); similar in models adjusted for fructose, glucose, or sucrose intake (data not tabulated). Sugar-sweetened beverage-BMI interactions *P* <0.05 were observed for 7/8 systolic BP models; in stratified analyses, direct SSB-BP associations were stronger for individuals with lower BMI (please see http://hyper.ahajournals.org, Table S7). Sugar-sweetened beverage-sodium interactions were non-significant; in stratified analyses, direct SSB-BP associations were stronger for individuals with higher 24-h urinary sodium excretion (please see http://hyper.ahajournals.org, Table S8).

Diet beverages—Associations with systolic and diastolic BP were consistently inverse, Z-scores −0.83 to −2.94 (*P* 0.41 to 0.003). In Model 3, diet beverage intake higher by 1 serving/day was associated with a systolic BP difference of −0.35 mm Hg (Z −1.34, *P* 0.18), −0.58 mm Hg (Z −2.32, *P* 0.02) with control for weight and height (Table 2). Blood pressure differences/Z-scores were larger when diet beverage intake was expressed as a proportion of energy intake, and for censored normal regressions; smaller in subgroup analyses of nonhypertensive participants (please see http://hyper.ahajournals.org, Table S9). Diet beverage-BMI interactions *P* <0.05 were detected for 3/8 diastolic BP models. In stratified analyses, inverse diet beverage-BP associations were stronger for individuals with higher BMI (please see http://hyper.ahajournals.org, Table S7).

Individual sugars—Associations of fructose and glucose with BP were direct, BP differences and Z-scores smaller than those observed for SSB (Z-scores 0.23 to 3.14, *P* 0.82 to 0.002) (please see http://hyper.ahajournals.org, Table S10). Sucrose-BP associations were bidirectional, BP differences and Z-scores small (please see http://hyper.ahajournals.org, Table S10). Fructose- and glucose-sodium interactions *P* <0.05 were observed for all models. In stratified analyses, fructose- and glucose-related BP differences were observed only for individuals with higher urinary sodium excretion. Blood pressure differences and Z scores were large: in Model 3, fructose intake higher by 2 SD (5.6 %kcal) was associated with a systolic BP difference of +3.4 mm Hg (Z 4.01, *P* <0.001), +2.5 mm Hg (Z 3.10, *P* 0.002) with control for weight and height (Table 3). Glucose-BP associations were of a similar magnitude (Table 3).

DISCUSSION

Main findings here are a direct association of SSB consumption with BP, and direct associations of fructose and glucose intake with BP, stronger among individuals with higher urinary sodium excretion.

Observed direct associations of SSB with BP are compatible with the findings of the PREMIER intervention trial, where reduction in SSB consumption by 355 ml/day was associated with systolic/diastolic BP lower by 1.8/1.1 mm Hg, 0.7/0.4 mm Hg with adjustment for change in body weight[30] For diet beverages, findings similar to INTERMAP, i.e., inverse, non-significant in multivariate models; and caffeine, no association. In INTERMAP, SSB-BP associations were independent of caffeine, and caffeine intake was inversely associated with SSB consumption. While some SSBs, e.g., cola, are important sources of caffeine, it is likely that SSB consumption displaced coffee and tea consumption (main dietary sources of caffeine) for many individuals. In analyses of women from the Nurses Health Studies (NHS) I and II, sugared and diet cola consumption, but not caffeine consumption, were associated with risk of incident hypertension.[37]

Among adolescents of the National Health and Nutrition Examination Survey (NHANES) 1999-2004, sugar-sweetened beverage intake was associated with systolic BP and serum uric acid concentration (see below).[28]

To our knowledge, no observational studies have reported associations of glucose intake with BP. Forman et al.[27] found no link between fructose intake (assessed by food frequency questionnaire) and incident hypertension among >200,000 women and men of the Nurses' Health Study I and II, and the Health Professionals Follow-up Study; Jalal et al. [29] reported a direct association between fructose intake and odds of elevated BP in cross-sectional analysis of 4,528 adults from NHANES 2003-2006.

The direct associations reported here for SSB/fructose intake and BP are consistent with the hypothesized effect on the uric acid pathway. Fructose consumption may lead to increased serum uric acid via phosphorylation of fructose by hepatocytes and generation of adenosine diphosphate, which is metabolized to uric acid [38]; raised serum uric acid may influence BP by reducing levels of nitric oxide, a potent vasodilator.[39] Sugar consumption has also been linked to enhanced sympathetic nervous system activity and sodium retention.[21,40] Detection of significant interaction with sodium excretion, i.e., direct fructose- and glucose-BP associations stronger for individuals with higher urinary sodium excretion, is compatible with the findings of several animal studies.[41-44] He et al. [45] reported that SSB consumption was directly associated with salt intake (assessed by 7 day dietary record) in UK children and adolescents. Here, sodium excretion was not associated with SSB consumption in US and UK adults; however urinary sodium/potassium ratio was directly associated with SSB. Significant interaction with BMI, i.e., direct SSB-BP associations weaker for individuals with higher BMI, could be due to greater misclassification of SSB intake in this subgroup due to differential under-reporting of SSB intake. [46]

Limitations of the INTERMAP findings include: their cross-sectional nature; underestimation of effect size, attributable to limited reliability in the measurement of nutrients (i.e., regression dilution bias, despite repeated measures – although observed BP differences were of similar magnitude to the PREMIER intervention trial); possible systematic bias (likely minimized by observer training, standardization, multi-pass methods, open non-leading questioning, and extensive ongoing quality control); and possible residual confounding. There was little evidence from multiple sensitivity analyses to indicate substantial bias. SSB-, glucose- and fructose-BP associations were reduced with control for weight and height. Interpretation of this finding is problematic: If intakes of SSB/sugars act on BP through positive energy balance and increased body mass, then body mass is in the causal pathway, and statistical control for weight (standardized for height) is over-adjustment [34]. Findings adjusted for BMI (not presented here) were quantitatively similar to those adjusted for weight and height. We are presently unable to quantify high-fructose corn syrup (HFCS), however SSB intake may be a good proxy, as HFCS is the most common caloric sweetener used by the US beverage industry.[14] Fructose intake was higher, urinary potassium and fiber intake lower for participants consuming >1 serving/day SSB, compared to those consuming ≤1 serving/day, indicating that higher fructose intake in SSB consumers likely reflects HFCS consumption rather than fruit intake. Since INTERMAP was designed primarily as a study of individual-level diet-BP associations the samples were not intended to be nationally representative, but – given the heterogeneity of the 8 USA samples particularly, and the similarity of USA and UK SSB-BP associations – it is reasonable to infer that findings may be applicable to middle-aged USA and UK men and women.

Perspectives

Higher intake of SSB was associated with more adverse overall nutritional quality, and there were independent direct associations of SSB, fructose, glucose with BP; sugar-BP associations were stronger among higher sodium consumers. These findings are consistent with recent trial data [30] and lend support to recommendations for reducing intake of SSB/added sugars/salt, for the improvement cardiovascular health.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Adjusted* Mean or Prevalence, Nutrients Intakes and Other Variables, by Category of Sugar-Sweetened Beverage Intake, INTERMAP USA and UK Participants (N=2,696)

	Sugar-Sweetened Beverage Intake				
	Zero (N=808)	≤1 serving/day† (N=1,153)	>1 serving/day† (N=735)		
Variable	**Mean (95% CI)**	**Mean (95% CI)**	**Mean (95% CI)**	**F-score**	***P-value***
Sugar-sweetened beverages, ml/1,000 kcal	0.0 (0.0, 0.0)	69.1 (62.2, 76.0)	288.2 (279.7, 296.6)	---	---
Diet beverages, ml/1,000 kcal	151.8 (136.9, 166.7)	69.1 (54.3, 84.0)	2.0 (0, 20.2)	129.87	*<0.001*
Energy, kcal/24-h	2043 (1994, 2092)	2163 (2114, 2212)	2440 (2380, 2499)	86.59	*<0.001*
Fructose, % kcal	3.1 (2.9, 3.3)	4.1 (3.9, 4.3)	7.4 (7.2, 7.7)	635.65	*<0.001*
Glucose, % kcal	3.4 (3.2, 3.6)	4.3 (4.1, 4.5)	7.3 (7.1, 7.5)	643.62	*<0.001*
Sucrose, % kcal	9.2 (8.7, 9.6)	10.1 (9.6, 10.5)	11.5 (11.0, 12.1)	40.74	*<0.001*
Starch, % kcal	25.5 (25.1, 26.0)	24.3 (23.8, 24.8)	20.9 (20.4, 21.5)	132.91	*<0.001*
Fiber, g/1,000 kcal	11.8 (11.6, 12.1)	10.8 (10.5, 11.1)	9.1 (8.7, 9.4)	124.25	*<0.001*
Animal protein, % kcal	10.5 (10.2, 10.8)	10.2 (9.9, 10.4)	9.6 (9.3, 10.0)	12.76	*<0.001*
Vegetable protein, % kcal	6.2 (6.0, 6.3)	5.7 (5.6, 5.9)	4.9 (4.7, 5.0)	145.91	*<0.001*
Total SFA, % kcal	11.2 (10.9, 11.5)	11.2 (11.0, 11.5)	10.9 (10.6, 11.3)	2.33	*0.10*
Total MFA, % kcal	11.5 (11.3, 11.8)	11.6 (11.4, 11.9)	11.3 (11.0, 11.6)	3.02	*0.049*
Total PFA, % kcal	6.6 (6.4, 6.8)	6.7 (6.5, 6.9)	6.4 (6.2, 6.6)	4.75	*0.009*
Omega-3 PFA, % kcal	0.75 (0.72, 0.77)	0.75 (0.73, 0.78)	0.69 (0.66, 0.72)	10.49	*<0.001*
Omega-6 PFA, % kcal	5.9 (5.8, 6.1)	6.0 (5.9, 6.2)	5.7 (5.5, 6.0)	4.65	*0.01*
Trans-fatty acids, % kcal	1.6 (1.5, 1.7)	1.6 (1.5, 1.7)	1.6 (1.5, 1.6)	1.32	*0.27*
Dietary cholesterol, mg/1,000 kcal	126.9 (121.9, 131.9)	127.4 (122.4, 132.4)	131.2 (125.1, 137.3)	1.16	*0.31*
Keys dietary lipid score‡	37.7 (36.9, 38.6)	37.8 (36.9, 38.6)	37.7 (36.6, 38.7)	0.02	*0.98*
Phosphorus, mg/1,000 kcal	679.5 (669.4, 689.6)	635.9 (625.9, 646.0)	567.2 (554.9, 579.5)	158.19	*<0.001*
Magnesium, mg/1,000 kcal	166.8 (163.8, 169.8)	153.5 (150.5, 156.5)	126.5 (122.8, 130.2)	232.14	*<0.001*
Calcium, mg/1,000 kcal	444.1 (432.6, 455.6)	412.3 (400.8, 423.8)	350.2 (336.2, 364.3)	86.22	*<0.001*
Iron, mg/1,000 kcal	7.8 (7.6, 8.0)	7.2 (7.0, 7.4)	5.8 (5.6, 6.1)	118.01	*<0.001*
Vitamin C, mg/1,000 kcal	48.8 (45.8, 51.7)	50.5 (47.6, 53.5)	47.7 (44.1, 51.3)	1.59	*0.20*
Caffeine, mg/1,000 kcal	151.1 (140.4, 161.9)	120.4 (109.7, 131.1)	91.4 (78.2, 104.5)	39.15	*<0.001*

	Sugar-Sweetened Beverage Intake				
	Zero (N=808)	**≤1 serving/day† (N=1,153)**	**>1 serving/day† (N=735)**		
Variable	**Mean (95% CI)**	**Mean (95% CI)**	**Mean (95% CI)**	**F-score**	***P-value***
14-day alcohol, g/24-h	10.8 (9.5, 12.1)	10.1 (8.9, 11.4)	8.6 (7.1, 10.2)	3.93	*0.02*
Urinary sodium, mmol/24-h	156.0 (151.3, 160.8)	154.7 (149.9, 159.4)	153.1 (147.3, 158.9)	0.47	*0.63*
Urinary potassium, mmol/24-h	66.2 (64.5, 67.8)	62.5 (60.9, 64.2)	56.0 (53.9, 58.0)	47.96	*<0.001*
Urinary sodium/potassium ratio	2.5 (2.4, 2.6)	2.7 (2.6, 2.8)	3.1 (3.0, 3.2)	40.47	*<0.001*
Age, years	50.4 (49.9, 50.8)	49.9 (49.5, 50.4)	48.6 (48.0, 49.2)	19.09	*<0.001*
Education, years completed	13.8 (13.6, 14.1)	13.6 (13.3, 13.8)	12.9 (12.6, 13.2)	19.27	*<0.001*
Moderate and heavy physical activity, hours/24-h	2.3 (2.1, 2.6)	2.5 (2.2, 2.7)	3.4 (3.0, 3.7)	23.99	*<0.001*
Body mass index, kg/m^2	28.4 (27.9, 28.9)	28.6 (28.1, 29.1)	30.2 (29.6, 30.8)	22.35	*<0.001*
Systolic blood pressure, mm Hg	118.8 (117.6, 120.0)	119.5 (118.3, 120.6)	122.5 (121.1, 123.9)	14.54	*<0.001*
Diastolic blood pressure, mm Hg	73.5 (72.7, 74.3)	74.0 (73.2, 74.9)	75.5 (74.5, 76.5)	8.13	*<0.001*
	% (95% CI)	% (95% CI)	% (95% CI)	F-score	*P*
Obese§	31.4 (27.4, 35.5)	32.5 (28.5, 36.5)	44.8 (39.9, 49.8)	17.87	*<0.001*
Hypertensive‖	28.7 (25.0, 32.4)	29.5 (25.8, 33.2)	34.5 (30.0, 39.0)	3.82	*0.02*

SFA=saturated fatty acids; MFA=monounsaturated fatty acids; PFA=polyunsaturated fatty acids.

*Estimated by analysis of variance and least squares means. Adjusted for country, sex, (age), special diet, supplement use, CVD or diabetes diagnosis, (physical activity), family history of high BP.

†1 serving = 355 ml/24-h.

‡Keys dietary lipid score = 1.35×(2×SFA [%kcal]–PFA [%kcal])+1. 5×√cholesterol [mg/1,000kcal].

§Body mass index ≥30 kg/m^2.

‖SBP ≥140 mm Hg, or DBP ≥90 mm Hg, or taking antihypertensive medication for high blood pressure.

Table 2

Estimated Mean Difference in Blood Pressure (mm Hg), Sugar-Sweetened Beverage or Diet Beverage Intake Higher by 1 Serving/day (355 ml/24-h), Regressed Separately in Sequential Models, INTERMAP USA and UK Participants (N=2,696)

	Systolic Blood Pressure						Diastolic Blood Pressure					
	Not adjusted for Weight, Height			Adjusted for Weight, Height			Not adjusted for Weight, Height			Adjusted for Weight, Height		
Beverage	**Difference**			**Difference**			**Difference**			**Difference**		
Model	**mm Hg**	**(95% CI)**	**Z**	**mm Hg**	**(95% CI)**	**Z**	**mm Hg**	**(95% CI)**	**Z**	**mm Hg**	**(95% CI)**	**Z**
Sugar-sweetened beverages												
1	1.26	(0.68, 1.84)	4.28	1.05	(0.50, 1.60)	3.74	0.61	(0.21, 1.01)	3.02	0.49	(0.11, 0.87)	2.51
2	1.35	(0.75, 1.95)	4.38	0.94	(0.36, 1.52)	3.20	0.61	(0.20, 1.02)	2.90	0.37	(−0.03, 0.77)	1.81
3	1.60	(0.97, 2.23)	4.98	1.05	(0.44, 1.66)	3.40	0.76	(0.32, 1.20)	3.42	0.43	(0.004, 0.86)	1.98
4a (Veg protein)	1.36	(0.67, 2.05)	3.87	0.99	(0.33, 1.65)	2.95	0.58	(0.11, 1.05)	2.42	0.36	(−0.10, 0.82)	1.54
4b (Calcium)	1.42	(0.78, 2.06)	4.36	0.91	(0.29, 1.53)	2.90	0.66	(0.22, 1.10)	2.95	0.35	(−0.08, 0.78)	1.61
4c (Magnesium)	1.25	(0.57, 1.93)	3.59	0.96	(0.30, 1.62)	2.86	0.60	(0.13, 1.07)	2.52	0.43	(−0.03, 0.89)	1.83
4d (Phosphorus)	1.41	(0.76, 2.06)	4.25	0.90	(0.27, 1.53)	2.82	0.63	(0.18, 1.08)	2.77	0.33	(−0.11, 0.77)	1.47
4e (Caffeine)	1.61	(0.98, 2.24)	4.98	1.08	(0.47, 1.69)	3.49	0.74	(0.31, 1.17)	3.36	0.43	(0.01, 0.85)	2.00
Diet beverages												
1	−0.27	(−0.78, 0.24)	−1.03	−0.68	(−1.16, −0.20)	−2.75	−0.26	(−0.60, 0.08)	−1.49	−0.50	(−0.83, −0.17)	−2.94
2	−0.32	(−0.82, 0.18)	−1.25	−0.58	(−1.07, −0.09)	−2.34	−0.28	(−0.63, 0.07)	−1.59	−0.43	(−0.76, −0.10)	−2.52
3	−0.35	(−0.86, 0.16)	−1.34	−0.58	(−1.07, −0.09)	−2.32	−0.30	(−0.65, 0.05)	−1.70	−0.44	(−0.78, −0.10)	−2.52
4a (Veg protein)	−0.28	(−0.80, 0.24)	−1.06	−0.54	(−1.03, −0.05)	−2.17	−0.26	(−0.61, 0.09)	−1.46	−0.42	(−0.76, −0.08)	−2.40
4b (Calcium)	−0.31	(−0.83, 0.21)	−1.17	−0.54	(−1.03, −0.05)	−2.15	−0.28	(−0.63, 0.07)	−1.57	−0.42	(−0.76, −0.08)	−2.40
4c (Magnesium)	−0.28	(−0.79, 0.23)	−1.08	−0.55	(−1.04, −0.06)	−2.18	−0.27	(−0.62, 0.08)	−1.53	−0.43	(−0.77, −0.09)	−2.48
4d (Phosphorus)	−0.22	(−0.74, 0.30)	−0.83	−0.48	(−0.97, 0.01)	−1.91	−0.22	(−0.57, 0.13)	−1.23	−0.38	(−0.72, −0.04)	−2.16
4e (Caffeine)	−0.36	(−0.87, 0.15)	−1.38	−0.60	(−1.09, −0.11)	−2.41	−0.30	(−0.65, 0.05)	−1.68	−0.44	(−0.78, −0.10)	−2.55

Model 1: adjusted for age, gender, sample, special diet, supplement use, history of CVD/diabetes, physical activity, family history of high BP, energy intake. **Model 2**: adjusted for Model 1 variables + urinary Na, urinary K, 14-day alcohol. **Model 3**: adjusted for Model 2 variables + dietary cholesterol, polyunsaturated fatty acids, saturated fatty acids. **Model 4a–4e**: adjusted for Model 3 variables + (**a**) vegetable protein, (**b**) calcium, (**c**) magnesium, (**d**) phosphorus, (**e**) caffeine.

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

No significant USA-UK difference detected, $P < 0.05$.

Table 3

Estimated Mean Difference in Blood Pressure (mm Hg), Fructose or Glucose Intake Higher by 2 SD, Regression Models 3 and 4c, INTERMAP USA and UK Participants Dichotomized by Median 24-h Urinary Sodium Excretion*

	Systolic Blood Pressure						Diastolic Blood Pressure					
Sugar (2 SD)	**Not adjusted for Weight, Height**			**Adjusted for Weight, Height**			**Not adjusted for Weight, Height**			**Adjusted for Weight, Height**		
Subcohort	**Difference**			**Difference**			**Difference**			**Difference**		
Model	**mm Hg**	**(95% CI)**	**Z**	**mm Hg**	**(95% CI)**	**Z**	**mm Hg**	**(95% CI)**	**Z**	**mm Hg**	**(95% CI)**	**Z**
Fructose (5.6 %kcal)												
Lower Sodium (N=1,349)												
3	0.36	(−1.17, 1.89)	0.46	−0.09	(−1.56, 1.38)	−0.12	0.00	(--- , ---)	0.00	−0.32	(−1.33, 0.69)	−0.62
4c (Mg)	−0.13	(−1.72, 1.46)	−0.16	−0.33	(−1.87, 1.21)	−0.42	−0.26	(−1.37, 0.85)	−0.46	−0.42	(−1.49, 0.65)	−0.77
Higher Sodium (N=1,347)												
3	3.40	(1.74, 5.06)	4.01	2.50	(0.92, 4.08)	3.10	2.20	(1.07, 3.33)	3.81	1.71	(0.61, 2.81)	3.05
4c (Mg)	2.70	(0.97, 4.43)	3.06	2.27	(0.63, 3.91)	2.71	1.97	(0.79, 3.15)	3.28	1.74	(0.60, 2.88)	2.98
Glucose (5.1 %kcal)												
Lower Sodium (N=1,349)												
3	0.42	(−1.10, 1.94)	0.54	−0.15	(−1.70, 1.40)	−0.19	0.13	(1.15, −0.89)	−0.25	−0.27	(−1.29, 0.75)	−0.52
4c (Mg)	−0.15	(−1.78, 1.48)	−0.18	−0.45	(−2.03, 1.13)	−0.56	−0.16	(−1.28, 0.96)	−0.28	−0.38	(−1.44, 0.68)	−0.70
Higher Sodium (N=1,347)												
3	3.68	(2.03, 5.33)	4.36	2.69	(1.11, 4.27)	3.34	2.14	(1.02, 3.26)	3.73	1.61	(0.51, 2.71)	2.88
4c (Mg)	2.94	(1.20, 4.68)	3.31	2.47	(0.81, 4.13)	2.92	1.91	(0.72, 3.10)	3.15	1.66	(0.51, 2.81)	2.82

Model 3: adjusted for age, gender, sample, special diet, supplement use, history of CVD/diabetes, physical activity, family history of high BP, urinary Na, urinary K, 14-day alcohol, dietary cholesterol, polyunsaturated fatty acids, saturated fatty acids. **Model 4c:** adjusted for Model 3 variables + magnesium.

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

*Urinary sodium excretion dichotomized by country-gender-specific medians: UK men, 155 mmol/24-h; UK women, 125 mmol/24-h; USA men, 174 mmol/24-h; USA women, 137 mmol/24-h.