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### Higher blood pressure in middle-aged American adults with less education—role of multiple dietary factors: The INTERMAP Study

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#### Abstract

Extensive evidence exists that an inverse relation between education and blood pressure prevails in many adult populations, but little research has been carried out on reasons for this finding. A prior goal of the INTERMAP Study was to investigate this phenomenon further, and to assess the role of dietary factors in accounting for it. Of the 4680 men and women aged 40-59 years, from 17 diverse population samples in Japan, People's Republic of China, UK, and USA, a strong significant inverse education-BP relation was manifest particularly for the 2195 USA participants, independent of ethnicity. With participants stratified by years of education, and assessment of 100+ dietary variables from four 24-h dietary recalls and two 24-h urine collections/person, graded relationships were found between education and intake of many macro- and micronutrients, electrolytes, fibre, and body mass index (BMI). In multiple linear regression analyses with systolic BP (SBP) and diastolic BP (DBP) of individuals the dependent variables (controlled for ethnicity, other possible nondietary confounders), BMI markedly reduced size of education-BP relations, more so for women than for men. Several nutrients considered singly further decreased size of this association by 10%: urinary 24-h Na and K excretion, Keys dietary lipid score, vegetable protein, fibre, vitamins C and B<sub>6</sub>, thiamin, riboflavin, folate, calcium, magnesium, and iron. Combinations of these dietary variables and BMI attenuated the education–SBP inverse coefficient by 54–58%, and the education–DBP inverse coefficient by 59–67%, with over half these effects attributable to specific nutrients (independent of BMI). As a result, the inverse education-BP coefficients ceased to be statistically significant. Multiple specific dietary factors together with body mass largely account for the more adverse BP levels of less educated than more educated Americans. Special efforts to improve eating patterns of less educated strata can contribute importantly to overcoming this and related health disparities in the population.

#### Keywords

education; blood pressure; dietary factors; nutrition; population study

#### Introduction

An inverse relationship between education and blood pressure (BP) of individuals has been found repeatedly in cross-sectional surveys of US population samples of varied ethnicities and in many other population samples, particularly from economically developed countries. <sup>1–13</sup> Correspondingly, the CARDIA and Western Electric prospective studies found that people with less educational attainment at baseline experienced greater BP increase over the ensuing years.<sup>14,15</sup> Little information is available on factors accounting for these findings. In 1992, the INTERSALT Study, involving 52 population samples in 32 countries worldwide,

reported this inverse association in women for 38 samples and in men for 28 samples.<sup>16</sup> Five lifestyle traits—24-h urinary sodium and potassium excretion, alcohol intake, body mass index (BMI), and smoking—accounted for a large part of the inverse association in both men and women. Individuals with more education excreted less sodium and more potassium on average, drank less, smoked less, and had lower BMI.

A major prior objective of the INTERMAP Study was to elucidate further the role of dietary factors—particularly macronutrients, also micronutrients—in accounting for the education–BP inverse relationship.<sup>17</sup> Findings on this matter are presented here.

#### Methods

INTERMAP background, design, aims, and methods have been set down in detail.<sup>17,18</sup> In summary, INTERMAP is an international epidemiologic study involving 4680 men and women aged 40–59 years from 17 diverse population samples, four in Japan (north to south), three in the People's Republic of China (PRC) (north to south), two in the United Kingdom (UK), and eight across the USA.<sup>17</sup> Personnel from all participating centres were trained and certified in study standardized methods at national training sessions led by senior staff (national and international) based on detailed protocols set out in study.

#### Survey procedures

Each participant attended a research centre on four occasions: two visits were on consecutive days, then a further two visits on consecutive days about 3 weeks later. All participants gave written consent; institutional review boards or ethics committees gave prior approval for the work of all study facilities. *Blood pressure* of the seated participant was measured twice at each visit with a random zero sphygmomanometer, after at least 5 min rest.

Dietary data were collected on each occasion with the 24-h recall method.<sup>18</sup> All foods and drinks consumed in the previous 24 h, including dietary supplements, were recorded by a trained dietary interviewer. To facilitate accurate quantification of portion sizes, food and drink models, measuring devices, and other aids were used. Interviewers also employed neutral probing techniques to check completeness of each recall. Interviews were tape recorded (with participant permission); random samples of the tapes were independently reviewed for quality control and improvement (as needed). In the US, dietary information was directly entered into a computerized dietary data collection and nutrient analysis software system. In the other three countries, data were first entered onto standard forms, then coded and computerized; a random 10% of recalls were recoded and reentered, with staff blinded to original entries. Daily alcohol consumption over the previous seven daysand information on previous drinking-was obtained by interview twice, at the first and third visits. Alcohol consumption during the previous 24 h was also obtained during each of the four 24-h dietary interviews. Two timed 24-h urine collections were completed and analysed centrally for sodium, potassium, creatinine, urea, calcium, magnesium, microalbumin, amino acids, and metabolites. Urine was collected in standard 11 plastic jars containing boric acid (for preservation). After detailed participant instruction, timed collections were started at the research centre on the first and third visits, and completed at the centre the following day. Collections were rejected if duration fell outside the range 22–

26 h, if the participant responded that collection was incomplete, or that 'more than a few drops' of urine had been lost, or if total volume was less than 250 ml. When a urine collection was rejected, the participant was asked to repeat the collection.

*Height* and *weight* without shoes were measured at first and third visits. *Questionnaire data* were obtained by interview on demographic and other possibly relevant factors, including education, occupation, leisure-time and work physical activity, smoking, current special diet, previous medical history, medication use, and—for women—data on menopause, parity, and use of contraceptive or hormone replacement medication.

#### Exclusions and supplementary participants

Participants were excluded if they did not attend all four visits (110 people), diet data were considered unreliable by the dietary interviewer and the site nutritionist (seven people), energy intake from any 24 h dietary recall was below 500 kcal/day or greater than 5000 kcal/day for women and 8000 kcal for men (37 people), two acceptable urine collections were not completed (37 people), and data on BP and other key variables were incomplete, missing, or indicated violation of study protocol (24 people). When a participant was excluded, a supplementary participant was recruited from the same sample age and sex group.

#### Urine collection preparation and biochemical analyses

Height of urine in each jar was obtained with use of a specially designed measuring scale; height was later converted by computer into volume with an empiric formula based on repeated measurements of volume in like jars. All urine from a 24-h collection was then combined, mixed thoroughly by vigorous stirring, and several aliquots were taken and stored locally at  $-20^{\circ}$ C. Frozen aliquots were periodically sent by airplane to the *Central Laboratory* in Leuven, Belgium. Biochemical methods, quality control procedures, and technical error of analyses have been reported.<sup>17</sup>

#### Statistical methods

Dietary data were converted into nutrients with use of country-specific food tables enhanced and improved for comparability by the Nutrition Coordinating Center, University of Minnesota (NCC).<sup>18</sup> Total energy intake was estimated from conversion factorsFfat: 9 kcal/g; protein: 4 kcal/g; available carbohydrate: 4 kcal/g; alcohol: 7 kcal/g. Nutrient densities were calculated as follows: for nutrients supplying energy, as percent of total kilocalories, that is, (kcal from nutrient/total kcal) × 100; for other nutrients, per 1000 kcal, that is, (amount per day/total kcal) × 1000. Total protein was partitioned into animal and vegetable. Urinary variables (24 h values) were calculated as products of urinary concentrations and timed volumes standardized to 24 h. Urinary urea (g/24 h) was converted into urinary urea nitrogen (g/24 h) with the multiplier 0.4667 and then multiplied by (6.25 × 1.2787 = 7.99) to estimate dietary total protein.<sup>17,18</sup> BMI was calculated as weight (kg)/ height<sup>2</sup> (m<sup>2</sup>).

Based on questionnaire data from each participant, average years of education was much lower for PRC samples (all rural) than for Japanese, UK and USA samples—mean (standard

deviation) 5.4 (2.9) compared to 12.0 (2.1), 12.7 (3.1), and 15.0 (3.0) years. For analyses on education-BP relations for individuals, blood pressure of each person was the average of eight measurements from the four visits, nutrients were the average of four measurements from the four 24-h dietary recalls, and urinary variables were the average of two measurements from the two 24-h urine collections. Correlation, categorical, and linear regression analyses were used to assess first the country-specific relationships of years of education of individual participants to their systolic and diastolic blood pressure (SBP, DBP). These analyses were performed for all persons, men, and women, stratified initially by sample and then by country (Japan, PRC, UK, USA). They were controlled initially only for age and sample, and-for all persons-for gender (Model 1); heterogeneity of findings for the four countries was tested. For US INTERMAP participants of both genders, there were statistically significant strong inverse relations of education to SBP and DBP-regression coefficients (Z-scores) -0.5410 (-5.32) and -0.2473 (-3.58) for men and women combined. For participants from Japan and UK, education-BP coefficients were also inverse, but compared to US participants sizably smaller-for SBP -0.1267 and -0.1765 overall, and nonsignificant statistically; for DBP -0.0996 and -0.0343, and nonsignificant. For Chinese men and women, with low average educational attainment, the coefficients were nonsignificantly positive (not inverse). There was significant heterogeneity across the four countries in the relation of education to SBP (P < 0.01).

Based on the finding of significant inverse relationships of education to BP only for US INTERMAP participants, the sizably larger coefficients for this association for US participants than for Japanese and UK men and women with nonsignificant inverse education–BP associations, and the significant heterogeneity in the education–SBP relation across the four countries, this report focuses on the role of dietary factors in possibly accounting for the significant findings for Americans.

For all 2195 US INTERMAP participants, and for men and women separately, partial correlation coefficients, and categorical and regression analyses, all controlled for sample, were computed to assess relationships of multiple variables----nondietary and dietary-----to education, SBP, and DBP, respectively. Based on the findings showing significant relationships of several nondietary variables to education and/or to BP, Model 2 linear regression analyses were performed to assess relations of education to SBP, DBP with control also for these additional possible confounders: ethnicity (African-American-No, Yes); history of high BP, heart disease, myocardial infarction (MI), stroke, or diabetes; consumption of a special diet; also age and sample, and (for all persons) gender. Multiple linear regression analyses were then performed with addition to Model 2 of BMI (Model 3). Further such analyses were then performed with addition to Model 3 of other single dietary variables also significantly related to education, as shown by correlation and categorical analyses. Percentage reduction in size of the inverse education-BP coefficient was used for quantitative assessment of the effect of each dietary factor in attenuating strength of the education-BP inverse relationship. Finally, groups of nutrientsFover and above BMIFwere included in multiple linear regression models to assess their combined impact in attenuating the inverse relation of education to BP. Four groups of nutrients were evaluated, based on prior findings on their influence on the education-BP inverse association<sup>16</sup> or results of the univariate analyses: (1) 24 h urinary sodium and potassium, without and with alcohol intake

in the models; (2) macronutrients: vegetable protein and Keys dietary lipid score; (3) minerals: Mg, Ca, P, Fe; (4) vitamins: C, B<sub>6</sub>, folate, thiamin, riboflavin, plus fibre; and combinations of these four. When these models involved highly correlated variables (partial correlation coefficient 0.6, controlled for age, gender, sample), analyses were performed without and with both variables, to assess whether their inclusion together may have had aberrant influences.

#### Results

#### **Descriptive statistics, US INTERMAP participants**

Of the 2195 INTERMAP participants aged 40–59 years from the eight samples across the US, 1103 were men, 1092 were women; African-Americans numbered 369; Hispanic-Americans, 288; non-His-panic white Americans, 1190; other Americans (mainly of east Asian ethnicity), 348. For each food reported by these 2195 US INTERMAP participants in their 8780 24-h dietary recalls, data are available on content of 101 nutrients, including major macronutrients and their components (individual fatty acids, amino acids, sugars), also micronutrients (vitamins, minerals), and total fibre. Correlation, categorical, and regression analyses on associations between education and single nutrients considered separately (each expressed as caloric density), 24-h urinary electrolyte excretion, also nonnutrient variables (possible confounders) yielded multiple statistically significant relationships (Table 1). Most of these were monotonic and present for both genders (genderspecific data not shown), including direct continuous relationships between education and vegetable protein, total available carbohydrate, starch, galactose, lactose, maltose, fibre, pectin, PFA/SFA, Vitamin A, beta-carotene, Vitamin C, Vitamin E, thiamin, riboflavin, niacin, pantothenic acid, Vitamin B<sub>6</sub>, folate, calcium, phosphorus, magnesium, iron, copper, urinary potassium, current drinking, and inverse relationships between education and animal protein, sucrose, total fat, saturated and monounsaturated fatty acids, dietary cholesterol, trans fatty acids, Keys dietary lipid score, urinary Na, urinary Na/K ratio, BMI, and exdrinking. Also, there were significant relations of education to gender, age, ethnicity, consumption of a special diet, history of cardiovascular diseases/diabetes.

## Effect of specific dietary factors, considered separately, on inverse relation of education to SBP and DBP, US INTERMAP participants

Inclusion of six possible confounders in regression analyses on the education–BP relationship resulted in reduction in size of coefficients and Z-scores, but the inverse associations remained statistically significant (Model 2, row B, Table 2). Of the individual dietary factors considered singly, BMI accounted for the largest reduction in coefficients, that is, 36% decrease in the education–SBP coefficient and 44% decrease in the education–DBP coefficient; the latter coefficient became statistically nonsignificant (Model 3, row C, Table 2). This attenuation of the education–BP coefficient by BMI was greater for women than menF49 and 23% for SBP, 48 and 36% for DBP (gender-specific data not shown). Based on this BMI finding, Model 3 was used in each linear regression analysis on influence of an individual nutrient on education–BP coefficients.

Several specific nutrients further decreased size of education–BP coefficients by 10% or more: vegetable protein, fibre, saturated fatty acids, PFA/SFA, Keys dietary lipid score, vitamin C, thiamin, folate, riboflavin, calcium, phosphorus, magnesium, iron, urinary K and Na/K (Table 2). For most of these nutrients, findings were qualitatively similar for men and women (gender-specific data not shown). Several other nutrients produced smaller decreases in education–BP coefficients (Table 2).

## Effects of combinations of dietary factors on inverse relation of education to SBP and DBP, US INTERMAP participants

Based on the foregoing findings, effects of combinations of nutrients on the education–BP relations were assessed with BMI in the model (Table 3). The combination of BMI, urinary Na and K, alcohol intake (the INTERSALT model)<sup>16</sup> lowered the coefficients by 46 and 55%; Na, K, and alcohol-independent of BMIF16 and 20% (row D, Table 3). The combination of BMI, vegetable protein, Keys dietary lipid score decreased the coefficients by 48 and 58%; these two macronutrient variables controlled for BMI, 18 and 25% (row E, Table 3). BMI plus four minerals lowered the coefficients by 48 and 53%; the minerals with control for BMI, 19 and 16% (row F, Table 3). The combination of BMI and five vitamins lowered the coefficients by 48 and 51%; the five vitamins with control for BMI, 19 and 12% (row G, Table 3). Combinations, of up to 11 specific nutrients plus BMI, were also assessed (eg, Table 3, rows H, I, and J). In these models, the coefficients for the inverse education– BP relation were lowered by as much as 58 and 67%, to statistically nonsignificant levels. More than half of these coefficient reductions—reductions of 34 and 41% Fwere attributable to the several specific nutrients, independent of the influence of BMI. Nutrient effects were qualitatively similar for women and men, with coefficient reductions being greater overall for women than men due to greater effects of BMI in women (gender-specific data not shown).

#### Discussion

Main findings of this study on US INTERMAP participants are: (1) significant inverse relation of SBP and DBP to years of education, persistent with adjustment for several nondietary confounders (including ethnicity); (2) significant graded relations to education of BMI and multiple macro- and micronutrients, including dietary fibre, Na, and K; (3) marked reductions in the size of the education–BP relationships with inclusion in linear regression models of BMI, greater for women than men; further marked reductions in these coefficients with inclusion also in regression models of groups of dietary factors (Na, K, alcohol; macronutrients; minerals; vitamins and fibre), so that overall the diet-related coefficient reductions were as much as 58% for the inverse education–SBP relationship and 67% for the inverse education–DBP relationship, and they ceased to be statistically significant. More than half of these reductions were attributable to multiple specific nutrients, over and above effects of BMI.

These data support the concept that multiple dietary constituents account importantly for the more adverse BP levels of less educated compared to more educated Americans. Specifically, they implicate as possible contributory factors particularly the higher BMI,

higher intakes of sodium (salt) and Na/K, higher Keys dietary lipid score, and lower intakes of vegetable protein, fibre, multiple vitamins and minerals of less educated than more educated individuals.

In regard to the possible roles of more marked overweight, higher intake of salt and Na/K, lower K intake by less educated compared to more educated Americans, these INTERMAP findings (based on population samples surveyed in the US in the late 1990s) are consistent with INTERSALT results (based on population samples surveyed worldwide in the mid-1980s).<sup>16</sup> They are also concordant with findings reported by other studies, especially on BMI, but also (in a few papers) on Na, K, and Na/K.<sup>10,19</sup> As to the possible impact of alcohol intake, INTERMAP—in contrast to INTERSALT—did not find a significant graded inverse relation of education to ethanol consumption in its participants, all middle-aged. Therefore, drinking habit per se was of little account in influencing inverse education–BP associations.

By collecting dietary (as well as urinary) data, INTERMAP was able to go beyond INTERSALT and assess the role of multiple macro- and micronutrients in influencing the education–BP relation, over and above effects of BMI and dietary electrolytes (with control for alcohol intake). To our knowledge, the only other observational population-based studies of adults with related findings are from the UK, on the possible role of lower fruit and vegetable intake in accounting for higher BP of less educated people.<sup>10</sup> Lower fruit and vegetable intake generally mean less potassium, magnesium, fibre consumption and possibly less intake of iron, of vegetable protein, and of the vitamins implicated by INTERMAP as related to the inverse education–BP associations.

The strengths of the INTERMAP US data presented here derive from large sample size of the study; its inclusion of eight samples to assure diversity among participants (men and women) in ethnicity, socioeconomic status, and geographic location across the country; standardized collection of high-quality BP and nutrition data, with use of four 24-h dietary recalls and two 24-h timed urine collections to enhance reliability of dietary data and reduce regression-dilution bias:<sup>17,18</sup> collection of data on multiple possible confounders: in-depth statistical analyses; consistency of results for men and women. Limitations are possible residual underestimation of impact of dietary factors due to still-existent regression-dilution bias; possible residual confounding due to lack of data on one or more variables confounding education-BP relations; the fact that INTERMAP-like INTERSALT-is crosssectional, not prospective. In these regards, however, it is relevant to note that multiple dietary factors—Na, K, minerals, vitamins, lipids—implicated by INTERMAP as possibly accounting (over and above BMI) for the higher SBP/DBP of less educated Americans are among the factors modified in the DASH feeding trials, with consequent substantial reduction in SBP/DBP of both nonhy-pertensive and hypertensive men and women of diverse ethnicities.<sup>20,21</sup> This concordance of INTERMAP observational data with the experimental findings from the DASH controlled interventional trials lends further support to the inference that the INTERMAP results are robust and generalizable.

#### Summary and conclusion

For the 2195 US participants aged 40–59 years, from eight widely distributed population samples diverse in ethnicity and socioeconomic status, the less the education, the higher the SBP and DBP, independent of ethnicity and other possible nondietary confounders. For the less educated, BMI levels and more adverse intake patterns of multiple macro- and micronutrients accounted substantially for their higher BP levels. These findings lend further support to the strategic concept that special efforts by public health and medical care to improve nutrition of lower socioeconomic population strata can contribute importantly to prevention and control of their particularly adverse levels of BP and other major risk factors, and thereby serve significantly to overcome disparities in key health outcomes of these strata, in accordance with highest priority national health goals.<sup>22</sup>

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Table 1

Dietary and other variables by years of education: all 2195 US INTERMAP participants

Variable	≤ 11 years	12 years	13–15 years	16 years	17+ years	$\mathbf{P}^{d}$	$\mathbf{P}^p$	ΗI
Participants - Number (%)	110	429	624	489	543			2195
	5.0	19.5	28.4	22.3	24.8			100.0
Men (%)	4.9	17.0	24.5	24.3	29.3	<0.0001		100.0
Women (%)	5.1	22.1	32.4	20.2	20.2			100.0
Age (years)	51.6	49.9	49.0	48.0	49.1	<0.0001	<0.0001	49.1
African-American (%)	6.0	21.4	34.1	21.4	17.0	0.0016		100.0
Non-African-American (%)	4.8	19.2	27.3	22.5	26.3			100.0
SBP (mmHg)	123.3	120.6	119.5	117.0	116.4	<0.0001	<0.0001	118.6
DBP (mmHg)	73.5	73.9	73.8	73.2	72.7	0.2495	0.0004	73.4
Current smokers (%)	33.6	26.3	17.5	12.1	9.4	<0.0001		16.8
Ex-smokers (%)	28.2	30.8	32.9	30.7	29.3	0.6938		30.8
Never smokers (%)	38.2	42.9	49.7	57.3	61.3	<0.0001		52.4
Cigarettes/day (All)	4.9	4.4	3.1	2.0	1.2	<0.0001	<0.0001	2.7
Cigarettes/day (Current smokers)	14.6	16.7	17.7	16.5	12.9	0.0601	0.0909	16.2
CVD/DM history (%)	30.0	19.1	16.4	11.9	12.5	<0.0001		15.6
HBP/CVD drug $R_x$ (%)	34.6	31.9	25.3	17.4	18.2	<0.0001		23.6
Pulse (bpm)	75.4	74.1	74.5	72.5	71.7	<0.0001	0.0008	73.3
Height (m)	1.66	1.66	1.68	1.69	1.70	<0.0001	0.0263	1.68
Eating special diet (%)	17.3	22.4	19.6	14.7	16.9	0.0322		18.3
BMI (kg/m <sup>2</sup> )	30.4	29.8	29.7	28.3	27.6	<0.0001	<0.0001	28.9
Energy intake/(kcal)/day	2272	2231	2253	2250	2234	0.9373	0.0049	2244
Total protein (% kcal)	15.3	15.7	15.2	15.6	15.7	0.0290	0.3839	15.5
Animal protein (% kcal)	10.3	10.7	10.0	10.1	10.0	0.0050	0.0128	10.2
Vegetable protein (% kcal)	4.8	4.8	5.0	5.3	5.6	<0.0001	<0.0001	5.2
Available carbohydrate (% kcal)	48.9	48.1	49.4	49.6	50.6	<0.0001	<0.0001	49.5
Starch (% kcal)	22.0	21.8	22.3	23.1	23.9	<0.0001	<0.0001	22.8
Galactose (% kcal)	0.02	0.03	0.04	0.04	0.05	<0.0001	<0.0001	0.04
Lactose (% kcal)	1.8	2.2	2.2	2.3	2.4	0.0068	0.0029	2.3

Variable	≰ 11 years	12 years	13–15 years	16 years	17+ years	$\mathbf{b}^{q}$	$\mathbf{P}^{p}$	ИI
Sucrose (% kcal)	11.0	11.0	11.1	10.2	10.3	0.0041	0.0111	10.7
Maltose (% kcal)	0.52	0.60	0.64	0.63	0.64	0.0389	0.0341	0.62
Fibre (g/1,000kcal)	8.6	8.3	8.5	9.3	9.8	<0.0001	<0.0001	0.6
Pectins (g/1000kcal)	0.71	0.86	0.89	1.02	1.09	<0.0001	<0.0001	0.95
Total fat (% kcal)	34.0	34.2	33.4	32.7	31.5	<0.0001	<0.0001	32.9
SFA (% kcal)	11.2	11.2	10.8	10.5	10.1	<0.0001	<0.0001	10.7
MFA (% kcal)	12.8	12.7	12.3	12.1	11.6	<0.0001	<0.0001	12.2
PFA (% kcal)	9.9	7.0	7.1	7.0	6.7	0.0108	0.0532	7.0
Omega-6 F. Ac. (% kcal)	6.0	6.4	6.5	6.3	6.1	0.0143	0.0433	6.3
Trans F. Ac. (% kcal)	1.9	2.1	2.0	1.9	1.8	<0.0001	<0.0001	1.9
Cholesterol (mg/1000kcal)	163.0	146.9	134.1	123.1	117.2	<0.0001	<0.0001	131.4
PFA/SFA	0.65	0.70	0.75	0.76	0.78	<0.0001	0.0005	0.74
Keys dietary lipid score	40.0	38.5	36.5	35.4	34.1	<0.0001	<0.0001	36.2
Current drinkers (%)	60.9	65.7	65.4	75.7	74.8	<0.0001		69.8
Ex-drinkers (%)	26.4	22.1	24.4	13.7	15.5	<0.0001		19.5
Never drinkers (%)	12.7	12.1	10.3	10.6	9.8	0.7232		10.7
Alcohol (4) (% kcal—All)	1.7	1.9	2.0	2.0	2.1	0.8071	0.1875	2.0
Alcohol (4) (% kcal-current drinkers)	2.7	2.9	3.0	2.6	2.9	<0.0001	0.9273	2.8
Alcohol (14) (g/day —All)	T.T	7.6	6.1	7.2	7.0	0.4006	0.7527	6.9
Alcohol (14) (g/day-current drinkers)	12.7	11.5	9.4	9.5	9.4	<0.0001	0.0788	9.9
Vitamin A (IU/1000kcal)	2749	3542	3753	4223	4468	<0.0001	<0.0001	3943
Beta-carotene (mcg/1000 kcal)	1341	1680	1802	2097	2238	<0.0001	<0.0001	1929
Vitamin C (mg/1000kcal)	44.4	46.9	49.0	57.6	59.6	<0.0001	<0.0001	52.9
Vitamin E (mg/1000 kcal)	4.0	4.4	4.4	4.5	4.6	0.0014	0.0038	4.5
Thiamin (mg/1000kcal)	0.81	0.84	0.84	0.88	0.91	<0.0001	<0.0001	0.86
Riboflavin (mg/1000kcal)	0.87	0.91	0.89	0.92	0.94	0.0107	0.0010	0.91
Niacin (mg/1000kcal)	10.7	11.6	11.3	11.8	12.0	<0.0001	0.0005	11.6
Pantothenic Acid (mg/1000 kcal)	1.5	1.7	1.7	1.7	1.8	0.0027	0.0002	1.7
Vitamin $B_6 (mg/1000 \text{ kcal})$	0.82	0.88	0.87	0.93	0.96	<0.0001	<0.0001	0.91
Folate (mcg/1000kcal)	136.9	129.7	130.3	139.4	147.0	<0.0001	<0.0001	136.7
Calcium (mg/1000 kcal)	329.1	350.1	350.8	373.0	385.1	<0.0001	<0.0001	363.0

Page 12

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Variable	≤ 11 years	12 years	13–15 years	16 years	17+ years	$\mathbf{b}^{a}$	$\mathbf{h}^{p}$	All
Phosphorus (mg/1000kcal)	571.6	584.0	578.0	596.7	610.3	<0.0001	<0.0001	591.0
Magnesium (mg/1000kcal)	135.3	142.3	143.5	151.4	157.8	<0.0001	<0.0001	148.1
iron (mg/1000kcal)	7.0	7.4	7.5	8.0	8.3	< 0.0001	<0.0001	7.8
Copper (mg/1000kcal)	0.61	0.65	0.65	0.69	0.71	<0.0001	<0.0001	0.67
Caffeine (mg/1000kcal)	143.7	137.7	131.4	119.1	117.7	0.0396	0.0277	127.1
Urinary Na (mmol/day)	170.1	164.2	163.7	162.4	158.7	0.2699	<0.0001	162.6
Urinary K (mmol/day)	49.3	54.8	55.0	60.4	62.2	< 0.0001	<0.0001	57.7
Jrinary Na/K (mmol/mmol)	3.72	3.23	3.26	2.93	2.76	< 0.0001	< 0.0001	3.08
2+ h/day of moderate or heavy physical activity (work, leisure) (%)	74.6	59.9	50.8	36.0	36.5	< 0.0001	< 0.0001	46.9
3+ Hours/day of moderate or heavy physical activity (work, leisure) (%)	62.7	47.6	38.8	27.8	23.8	<0.0001	< 0.0001	35.4

 $^{a}P$  for ANOVA adjusted for gender and sample.

<sup>b</sup> for continuous variables is the *P*-value for years of education, in linear regression—adjusted for age, sex, and sample—to test for linear trend.

For the following variables, there was no significant linear relation to education, hence data on them are not included above: ratio of energy intake to weight (keal per day/kg), estimated total sugars, fructose, glucose, omega-3 PFA, eicosapentanoic acid, docosapentanoic acid, docosahexanoic acid, zinc, selenium, retinol, Vitamins D and B12, all expressed as caloric density. F. Ac. is fatty acids; alcohol (4) is the average of the four alcohol data from the four 24-h dietary recalls on each person; alcohol (14) is the average of the daily alcohol intake for each person from the two histories of daily alcohol consumption during the preceding 7 days.

# Table 2

Effect of single dietary variables on education-BP inverse relationship: all 2195 US INTERMAP participants

Row	Variables in multiple linear regression model	SBP	DBP
А	Model 1: Education, age, sample, gender	-0.5410 <sup>a</sup>	-0.2473 <sup>a</sup>
		$(-5.320)^{b}$	$(-3.581)^{b}$
В	Model 2: Model 1 variables+CVD disease/diabetes diagnosis,	-0.4122	-0.1920
	special diet, ethnicity (African-American)	(-4.098)	(-2.788)
C	Model 3: Model 2 variables+BMI (kg/m <sup>2</sup> )	-0.2646	-0.1073
		(-2.752)	(-1.606)
		-35.8% <sup>c</sup>	$-44.1\%^{c}$
D	Model 3+vegetable protein (% kcal)	-0.2233	-0.0843
		(-2.309)	(-1.252)
		$-15.6\%^{d}$	$-21.4\%^{d}$
Щ	Model 3+total available carbohydrate (% kcal)	-0.2485	-0.1027
		(-2.584)	(-1.534)
		-6.1%	-4.3%
Ц	Model 3+galactose (% kcal)	-0.2471	-0.1040
		(-2.561)	(-1.549)
		-6.6%	-3.1%
IJ	Model 3+Fibre (g/1000kcal)	-0.2243	-0.0893
		(-2.310)	(-1.322)
		-15.2%	-16.8%
Н	Model 3+total fat (% kcal)	-0.2567	-0.1070
		(-2.658)	(-1.594)
		-3.0%	-0.3%
I	Model 3+sat. F. Ac. (% kcal)	-0.2489	-0.0965
		(-2.578)	(-1.438)
		-5.9%	-10.1%
ſ	Model 3+monounsat. F. Ac. (% kcal)	-0.2498	-0.1072
		(-2.578)	(-1.595)

Row	Variables in multiple linear regression model	SBP	DBP
		-5.6%	-0.1%
К	Model 3+trans F.Ac. (% kcal)	-0.2569	-0.1097
		(-2.661)	(-1.634)
		-2.9%	+2.2%
L	Model 3+dietary chol. (mg/1000kcal)	-0.2502	-0.1075
		(-2.584)	(-1.596)
		-5.4%	+0.2%
M	Model 3+PFA/SFA	-0.2421	-0.0930
		(-2.515)	(-1.390)
		-8.5%	-13.3%
z	Model 3+Keys dietary lipid score	-0.2368	-0.0913
		(-2.449)	(-1.357)
		-10.5%	-14.9%
0	Model 3+vitamin A (IU/1000kcal)	-0.2475	-0.1032
		(-2.564)	(-1.537)
		-6.5%	-3.8%
Ь	Model 3+beta-carotene (mcg/1000kcal)	-0.2509	-0.1057
		(-2.598)	(-1.574)
		-5.2%	-1.5%
ð	Model 3+vitamin C (mg/1000kcal)	-0.2318	-0.1074
		(-2.386)	(-1.589)
		-12.4%	+0.1%
R	Model 3+thiamin (mg/1000kcal)	-0.2432	-0.0936
		(-2.519)	(-1.395)
		-8.1%	-12.8%
s	Model 3+vitamin B <sub>6</sub> (mg/1000kcal)	-0.2438	-0.0970
		(-2.519)	(-1.441)
		-7.9%	-9.6%
F	Model 3+folate (mcg/1000kcal)	-0.2318	-0.0915
		(-2.403)	(-1.363)

J Hum Hypertens. Author manuscript; available in PMC 2019 June 12.

Stamler et al.

L

-14.7%

-12.4%

Variables in multiple linear regression mo	Model 3+calcium (mg/1000kcal)
Row	n
	Row Variables in multiple linear regression mo

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Variables in multiple linear regressio	n model SBP	DBP
Model 3+calcium (mg/1000kcal)	-0.2371	-0.0915
	(-2.462)	(-1.370)
	-10.4%	-14.7%
Model 3+phosphorus (mg/1000 kcal)	-0.2423	-0.0910
	(-2.517)	(-1.360)
	-8.4%	-15.2%
Model 3+magnesium (mg/1000 kcal)	-0.2319	-0.0948
	(-2.394)	(-1.406)
	-12.4%	-11.6%
Model 3+iron (mg/1000kcal)	-0.2310	-0.0899
	(-2.394)	(-1.339)
	-12.7%	-16.2%
Model 3+copper (mg/1 000 kcal)	-0.2449	-0.1056
	(-2.535)	(-1.571)
	-7.4%	-1.6%
Model 3+urinary Na (mmol/24h)	-0.2624	-0.1098
	(-2.725)	(-1.639)
	-0.8%	+2.3%
Model 3+urinary K (mmol/24h)	-0.2438	-0.0920
	(-2.520)	(-1.367)

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J Hum Hypertens. Author manuscript; available in PMC 2019 June 12.

-0.0978

-0.2487

Model 3+caffeine (mg/1000kcal)

ΕĒ

-2.4%

(-1.384)

-0.0958(-1.437)

Model 3+riboflavin (mg/1000kcal)

CC

-12.9%

-10.7%-0.2481 -0.1052

Model 3+maltose (%kcal)

DD

(-1.573)-2.0%

(-2.684) -0.2582

-10.7%

-6.2%

(-2.586)

-14.3%-0.0935

-7.9%

-0.2364(-2.435)

Model 3+urinary Na/K (mmol/mmol)

BB

AA

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FF       Model 3+14-day alcohol (g/day)       (-2.583)       (-1.461)         -6.0%       -8.9%         FF       Model 3+14-day alcohol (g/day)       -0.2584       -0.1044         (-2.698)       (-1.564)       -2.7%       -2.7%         GG       Model 3+2+h/day moderate or heavy physical activity       -0.2684       -0.1166         (work, leisure)No, Yes       -0.2684       -0.1166       (-1.729)         HH       Model 3+3+h/day moderate or heavy physical activity       -0.2784       -0.1184         (work, leisure)No, Yes       (-2.767)       (-1.729)       (-1.739)         HH       Model 3+3+h/day moderate or heavy physical activity       -0.2784       -0.1184         (work, leisure)No, Yes       +6.2%       +10.3%       +5.2%       +10.3%	Row	Variables in multiple linear regression model	SBP	DBP
FF       Model 3+14-day alcohol (g/day)       -6.0%       -8.9%         FF       Model 3+14-day alcohol (g/day)       -0.2584       -0.1044         GG       Model 3+2+h/day moderate or heavy physical activity       -2.3%       -2.7%         GG       Model 3+2+h/day moderate or heavy physical activity       -0.2684       -0.1166         (work, leisure)—No, Yes       +1.4%       +8.7%         HH       Model 3+3+h/day moderate or heavy physical activity       -0.2784       -0.1184         (work, leisure)—No, Yes       +1.4%       +8.7%       +8.7%         HH       Model 3+3+h/day moderate or heavy physical activity       -0.2784       -0.1184         (work, leisure)—No, Yes       +1.4%       +8.7%       +10.3%			(-2.583)	(-1.461)
FF       Model 3+14-day alcohol (g/day)       -0.2584       -0.1044         (-2.698)       (-1.564)       (-2.698)       (-1.564)         GG       Model 3+2+h/day moderate or heavy physical activity       -0.2684       -0.1166         (work, leisure)—No, Yes       -0.2684       -0.1166       -1.729         HH       Model 3+3+h/day moderate or heavy physical activity       -0.2784       -0.1184         (work, leisure)—No, Yes       -0.2784       -0.1184       +8.7%         HH       Model 3+3+h/day moderate or heavy physical activity       -0.2784       -0.1184         (work, leisure)—No, Yes       -0.2784       -0.1184       -0.1384         (work, leisure)—No, Yes       +1.4%       +8.7%       +10.3%			-6.0%	-8.9%
(-2.698)       (-1.564)         GG       Model 3+ 2+ h/day moderate or heavy physical activity       -2.3%       -2.7%         (work, leisure)—No, Yes       -0.2684       -0.1166       (-1.729)         (work, leisure)—No, Yes       (-2.767)       (-1.729)       +1.4%         HH       Model 3+ 3+ h/day moderate or heavy physical activity       -0.2784       -0.1184         (work, leisure)—No, Yes       (-2.866)       (-1.753)	FF	Model 3+14-day alcohol (g/day)	-0.2584	-0.1044
GG       Model 3+ 2+ h/day moderate or heavy physical activity       -2.3%       -2.7%         (work, leisure)—No, Yes       -0.2684       -0.1166         (work, leisure)—No, Yes       (-2.767)       (-1.729)         HH       Model 3+ 3+ h/day moderate or heavy physical activity       -0.2784       -0.1184         (work, leisure)—No, Yes       (-2.866)       (-1.753)         +H       Model 3+ 3+ h/day moderate or heavy physical activity       -0.2784       -0.1184         (work, leisure)—No, Yes       +5.2%       +10.3%			(-2.698)	(-1.564)
GG       Model 3+ 2+ h/day moderate or heavy physical activity       -0.2684       -0.1166         (work, leisure)—No, Yes       (-2.767)       (-1.729)         HH       Model 3+ 3+ h/day moderate or heavy physical activity       -0.2784       -0.1184         (work, leisure)—No, Yes       (-2.866)       (-1.753)         HH       Model 3+ 3+ h/day moderate or heavy physical activity       -0.2784       -0.1184         (work, leisure)—No, Yes       +5.2%       +10.3%			-2.3%	-2.7%
(work, leisure)—No, Yes       (-2.767)       (-1.729)         (work, leisure)—No, Yes       +1.4%       +8.7%         (work, leisure)—No, Yes       (-2.866)       (-1.753)         +5.2%       +10.3%	GG	Model 3+ 2+ h/day moderate or heavy physical activity	-0.2684	-0.1166
+1.4%       +8.7%         HH       Model 3+ 3+ h/day moderate or heavy physical activity       -0.2784       -0.1184         (work, leisure)—No, Yes       (-2.866)       (-1.753)         +5.2%       +10.3%		(work, leisure)—No, Yes	(-2.767)	(-1.729)
HH         Model 3+ 3+ h/day moderate or heavy physical activity         -0.2784         -0.1184           (work, leisure)—No, Yes         (-2.866)         (-1.753)           +5.2%         +10.3%			+1.4%	+8.7%
(work, leisure)—No, Yes (-2.866) (-1.753) +5.2% +10.3%	ΗH	Model 3+ 3+ h/day moderate or heavy physical activity	-0.2784	-0.1184
+5.2% +10.3%		(work, leisure)—No, Yes	(-2.866)	(-1.753)
			+5.2%	+10.3%
	$b_{\mathrm{Z-score}}$	ri -		

J Hum Hypertens. Author manuscript; available in PMC 2019 June 12.

 $^{\mathcal{C}}$  Percent reduction in education–SBP coefficient compared to Model 2.

 $d_{
m Percent}$  reduction in education–SBP coefficient compared to Model 3; same for all percentages in rows E–HH.

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Effect of combinations of dietary variables on education-BP inverse relationship: all 2195 US INTERMAP participants

Row	Variables $^{a}$ in multiple linear regression model	SBP	DBP
A	Model 2: Education, age, sample, ethnicity (African-American),	-0.4122 <sup>a</sup>	-0.1920 <sup>a</sup>
	CVD disease/diabetes diagnosis, special diet, gender	(-4.098) <sup>a</sup>	(-2.788) <sup>a</sup>
В	Model 3: Model 2 + BMI	-0.2646	-0.1073
		(-2.752)	(-1.606)
		$-35.8\%^{b}$	$^{44.1\%}b$
C	Model 3+24-h urinary Na and 24-h urinary K	-0.2315	-0.0910
		(-2.378)	(-1.344)
		$-43.8\%^{b}$	$-52.6\%^{b}$
		$-12.5\%$ $^{c}$	$-15.2\%$ $^{\mathcal{C}}$
D	Model 3+24-h urinary Na and 24-h urinary K, 14-day	-0.2210	-0.0861
	alcohol intake (g/day)	(-2.279)	(-1.274)
		-46.4%	-55.2%
		-16.5%	-19.8%
Щ	Model 3+macronutrients: Vegetable Protein and Keys score	-0.2166	-0.0802
		(-2.234)	(-1.188)
		-47.5%	-58.2%
		-18.1%	-25.3%
ц	Model 3+Minerals: Mg, Ca, P, Fe	-0.2138	-0.0902
		(-2.203)	(-1.337)
		-48.1%	-53.0%
		-19.2%	-15.9%
IJ	Model 3+fibre and vitamins: C, B <sub>6</sub> , folate, thiamin, riboflavin	-0.2151	-0.0947
		(-2.207)	(-1.396)
		-47.8%	-50.7%
		-18.7%	-11.7%
Н	Model $3 + 24$ -h urinary Na and K, 14-day alcohol intake,	-0.1901	-0.0684
	Vegetable protein, and Keys dietary lipid score	(-1.950)	(-1.006)

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<ul> <li>-53.9</li> <li>Model 3+ 24-h urinary Na and K, 14-day alcohol intake, -28.2</li> <li>Vegetable protein, Keys dietary lipid score, Mg, Ca, P, Fe (-1.79</li> <li>Negetable protein, Keys dietary lipid score, Mg, Ca, P, Fe -51.5</li> <li>Model 3+ 24-h urinary Na and K, 14-day alcohol intake, -0.188</li> <li>Vegetable protein, Keys dietary lipid score, fibre, vitamins C, B<sub>6</sub>, (-1.93</li> <li>Folate, thiamin, riboflavin -54.2</li> </ul>	Row	Variables $^{a}$ in multiple linear regression model	SBP	DBP
<ul> <li>Model 3+ 24-h urinary Na and K, 14-day alcohol intake, -0.17;</li> <li>Wegetable protein, Keys dietary lipid score, Mg, Ca, P, Fe (-1.79)</li> <li>Model 3+ 24-h urinary Na and K, 14-day alcohol intake, -0.18;</li> <li>Model 3+ 24-h urinary Na and K, 14-day alcohol intake, -0.18;</li> <li>Folate, thiamin, riboflavin -54.2;</li> </ul>			-53.9%	-64.4%
I       Model 3+ 24-h urinary Na and K, 14-day alcohol intake,       -0.17;         Vegetable protein, Keys dietary lipid score, Mg, Ca, P, Fe       (-1.79         -57.57       -57.57         33.7       Model 3+ 24-h urinary Na and K, 14-day alcohol intake,       -0.18;         Vegetable protein, Keys dietary lipid score, fibre, vitamins C, B <sub>6</sub> ,       (-1.93         Folate, thiamin, riboflavin       -54.2			-28.2%	-36.3%
Vegetable protein, Keys dietary lipid score, Mg, Ca, P, Fe       (-1.79         -57.5       -53.7         -33.7       Model 3+ 24-h urinary Na and K, 14-day alcohol intake,       -0.18         Vegetable protein, Keys dietary lipid score, fibre, vitamins C, B <sub>6</sub> ,       (-1.93         Folate, thiamin, riboflavin       -54.2	I	Model 3+ 24-h urinary Na and K, 14-day alcohol intake,	-0.1753	-0.0633
<ul> <li>-57.5</li> <li>-33.7</li> <li>-33.7</li> <li>-33.7</li> <li>Model 3+ 24-h urinary Na and K, 14-day alcohol intake, -0.18</li> <li>Vegetable protein, Keys dietary lipid score, fibre, vitamins C, B<sub>6</sub>, (-1.93</li> <li>Folate, thiamin, riboflavin -54.2</li> </ul>		Vegetable protein, Keys dietary lipid score, Mg, Ca, P, Fe	(-1.795)	(-0.931)
<ul> <li>Model 3+ 24-h urinary Na and K, 14-day alcohol intake, -0.18</li> <li>Wegetable protein, Keys dietary lipid score, fibre, vitamins C, B<sub>6</sub>, (-1.93</li> <li>Folate, thiamin, riboflavin -54.2</li> </ul>			-57.5%	-67.0%
<ul> <li>Model 3+ 24-h urinary Na and K, 14-day alcohol intake, -0.18;</li> <li>Vegetable protein, Keys dietary lipid score, fibre, vitamins C, B<sub>6</sub>, (-1.93</li> <li>Folate, thiamin, riboflavin -54.2</li> </ul>			-33.7%	-41.0%
Vegetable protein, Keys dietary lipid score, fibre, vitamins C, B <sub>6</sub> , (–1.93 Folate, thiamin, riboflavin –28.7	ſ	Model 3+ 24-h urinary Na and K, 14-day alcohol intake,	-0.1886	-0.0784
Folate, thiamin, riboflavin -28.7		Vegetable protein, Keys dietary lipid score, fibre, vitamins C, $\mathbf{B}_{6}$ ,	(-1.931)	(-1.152)
-28.7		Folate, thiamin, riboflavin	-54.2%	-59.2%
			-28.7%	-26.9%

<sup>a</sup>Units for dietary variables as in Table 2.

 $^{\prime}$  Coefficient for the education–BP inverse relation in this multiple linear regression model.

 $X_{
m Z-score.}$ 

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b Percent reduction in education-SBP coefficient compared to Model 2.

cPercent reduction in education-SBP coefficient compared to Model 3.