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Relationship of Dietary Linoleic Acid to Blood Pressure:

The International Study of Macro-Micronutrients and Blood Pressure Study

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Abstract

Findings from observational and interventional studies on the relationship of dietary linoleic acid, the main dietary polyunsaturated fatty acid, with blood pressure have been inconsistent. The International Study of MacroMicronutrients and Blood Pressure is an international cross-sectional epidemiological study of 4680 men and women ages 40 to 59 years from 17 population samples in China, Japan, United Kingdom, and United States. We report associations of linoleic acid intake of individuals with their blood pressure. Nutrient intake data were based on 4 in-depth multipass 24-hour dietary recalls per person and 2 timed 24-hour urine collections per person. Systolic and diastolic blood pressures were measured 8 times at 4 visits. With several models to control for possible confounders (dietary or other), linear regression analyses showed a nonsignificant inverse relationship of linoleic acid intake (percent kilocalories) to systolic and diastolic blood pressure for all of the participants. When analyzed for 2238 "nonintervened" individuals (not on a special diet, not consuming nutritional supplements, no diagnosed cardiovascular disease or diabetes, and not taking medication for high blood pressure, cardiovascular disease, or diabetes), the relationship

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None.

was stronger. With adjustment for 14 variables, estimated systolic/diastolic blood pressure differences with 2-SD higher linoleic acid intake (3.77% kcal) were −1.42/−0.91 mm Hg (P<0.05 for both) for nonintervened participants. For total polyunsaturated fatty acid intake, blood pressure differences were −1.42/−0.98 mm Hg (P<0.05 for both) with 2 SD higher intake (4.04% kcal). Dietary linoleic acid intake may contribute to prevention and control of adverse blood pressure levels in general populations.

Keywords

blood pressure; nutrition; linoleic acid; polyunsaturated fatty acid; population study

Numerous studies have investigated relationships of intake of neutral lipids with blood pressure (BP).[1–6] Data from several epidemiological studies and intervention trials indicate that higher intake of saturated fatty acids (SFAs) and lower intake of polyunsaturated fatty acids (PFAs) are related to higher BP. However, findings are inconsistent, and the issue remains to be clarified.

For PFA, 80% to 90% comes from linoleic acid in many countries.[7] In Western countries, the intake of linoleic acid has dramatically increased during the last several decades, mainly from vegetable products (particularly vegetable oils), substituted for animal fats high in SFA.[8,9] To date, few epidemiological studies have investigated the relationship of dietary linoleic acid intake, per se, to BP; studies have reported no significant relationship of total dietary PFA intake to BP.[1–6] Some cross-sectional studies have found associations between the tissue level of linoleic acid and BP[10–13]; other studies have not.[1–4] The findings from dietary studies are understandably inconsistent for the following reasons: (1) small sample sizes with resultant low statistical power; (2) limited methods of dietary assessment, eg, a single 24-hour dietary recall, with consequent limited ability accurately to classify dietary intake of individuals; and (3) few BP measurements insufficiently standardized. Tissue measurements of linoleic acid may only partially reflect dietary linoleic acid intake. Inconsistent findings from randomized, controlled trials on BP effects of PFA or linoleic acid could also be attributable to small sample size and short duration, with consequent limitation in the ability to detect small BP differences.

The population-based International Study of MacroMicronutrients and Blood Pressure (INTERMAP) was designed to cope with such problems.[14–20] Its basic premises are that multiple nutrients have small independent influences on the BPs of individuals that, in combination, summate as sizable effects. To detect the impact of single nutrients on the BP of individuals, it is essential to collect standardized, high-quality data on large samples of diverse populations. Accordingly, INTERMAP surveyed in-depth 4680 men and women ages 40 to 59 years from 17 population samples in Japan, People’s Republic of China, United Kingdom, and United States. The data enable INTERMAP to address the unanswered question on linoleic acid intake and BP. INTERMAP hypothesized that dietary linoleic acid intake of individuals is inversely related to their BP.[14] Findings are reported here.

Methods

Population Samples, Field Methods (1996–1999)

INTERMAP included men and women ages 40 to 59 years from population random samples in Japan (4 samples), People's Republic of China (3 samples), the United Kingdom (2 samples), and the United States (8 samples).[14] Participants were selected randomly from population lists, stratified by age and gender. Staff were trained and certified for BP measurement by international and/or national senior colleagues based on a common standardized protocol.[14] Each participant attended 4 times, with visits 1 and 2 on consecutive days and visits 3 and 4 on consecutive days on average 3 weeks later. For BP measurement, each participant (having emptied his or her bladder) was seated comfortably for 5 minutes, feet flat on the floor, in a quiet room, with no physical activity in the preceding half hour. Korotkoff sounds I and V were criteria for systolic BP (SBP) and diastolic BP (DBP). BP was measured twice at each visit with a random 0 sphygmomanometer; BP at each visit was the average of the 2 readings. Measurements of height and weight and questionnaire data on daily alcohol consumption over the previous 7 days were obtained at 2 visits (14 days total). Dietary data were collected at each visit by a trained certified interviewer with use of the in-depth multipass 24-hour recall method.[15] All of the foods and drinks consumed in the previous 24 hours, including dietary supplements, were recorded. Questionnaire data were obtained on demographic and other possible confounders. Quality control throughout the field surveys was ongoing and extensive at the international, national, and local levels.[14,15]

Each participant provided two 24-hour urine collections, start and end timed at the research center (visits 1 to 2 and 3 to 4); measurements included urinary volume, sodium, potassium, and creatinine[14]; 8% of urine samples were split locally and sent blind to the central laboratory to estimate technical error.

Individuals were excluded if they did not attend all 4 of the visits; diet data were considered unreliable; energy intake from any 24-hour dietary recall was <500 or >5000 kcal/d for women or 8000 kcal for men; 2 urine collections were not available; or if data on other variables were incomplete or indicated protocol violation (total exclusions: 215 people). The study received institutional ethics committee approval for each site; all of the participants gave written informed consent.

Statistical Methods

Food data of individuals were converted into nutrients (83 nutrients) with use of enhanced country-specific food tables, standardized across countries by the University of Minnesota Nutrition Coordinating Center.[15,16] For nutrients supplying energy, intake was calculated as the percentage of total energy; for others, as intake per 1000 kcal; nutrients were calculated also as amounts per 24 hours. Food data were used to assess main food groups supplying linoleic acid and total PFA. Urinary values per 24 hours were calculated as products of urinary concentrations and timed volume standardized to 24 hours. Measurements per person were averaged, for BP and nutrient variables, across the 4 visits and for urinary excretions across the 2 collections. For descriptive statistics, means and SDs, numbers, and

percentages were calculated by country and study wide. The reliability of SBP, DBP, and dietary nutrient intakes from the mean of the 4 visits was estimated from the formula 1/[1 + (ratio/ 4)]×100, where the ratio is intraindividual variance:interindividual variance, estimated separately for 8 gender and/or country strata and pooled by weighting each stratum-specific estimate by (sample size −1). This gives a first approximation of reliability, ie, an estimate of the size of an observed coefficient as a percentage of the theoretical coefficient in a univariate regression analysis.[21,22] Reliability of urinary sodium and potassium excretion from the mean of the 2 measurements was estimated from the formula 1/[1+ (ratio/2)]×100.

Associations among nutritional variables were explored by partial correlation, adjusted for sample, age, and gender, and pooled across countries, weighted by sample size. Multiple regression analyses were used to examine the relationships of dietary linoleic acid (percentage of kilocalories) of individuals to their SBP and DBP. These analyses were done for 2 cohorts: all 4680 participants and 2238 “nonintervened” persons who were not on a special diet, not consuming nutritional supplements, with no diagnosed cardiovascular disease (CVD) and/or diabetes, and not taking medication for high BP, cardiovascular disease, or diabetes (ie, exclusion of people whose data might bias the dietary linoleic acid-BP relationship). Adjustment for confounders was done sequentially: for sample, age, gender, height, weight, reported special diet, dietary supplement intake, moderate and/or heavy physical activity (h/d), history of cardiovascular disease or diabetes, and family history of hypertension (model 1); plus 24-hour urinary sodium, potassium, and 7-day alcohol intake (model 2); plus dietary cholesterol, SFA, and calcium (model 3); plus dietary phosphorus (model 4).

Regression models were fit separately by country and coefficients pooled across countries, weighted by inverse of variance, to estimate overall association; cross-country heterogeneity was tested; interactions were assessed for age and gender. Regression coefficients were expressed as millimeters of mercury for a 2-SD difference in dietary linoleic acid from the pooled within-country SDs weighted by sample size.

Sensitivity analyses involved: inclusion of energy intake with nutrient densities; use of grams per day intakes adjusted for energy; inclusion separately in model 4 of multiple other dietary variables (expressed as nutrient density), each instead of dietary phosphorus; and exclusion of people with marked intraindividual variability in intake of nutrients and/or SBP/DBP (detailed methods have been reported).[14] All of the analyses were done also for dietary total PFA. Analyses were done with SAS 8.02 (by Q.C. and I.J.B.).

Results

Descriptive Statistics

Average SBP ranged from 117.2 (Japan) to 121.3 mmHg (People’s Republic of China) and average DBP from 73.2 (People’s Republic of China) to 77.3 mmHg (United Kingdom) (Table S1, available in the online data supplement at http://hyper.ahajournals.org). Mean body mass index and energy intake were lower for Japanese (23.4 kg/m^2) and People’s Republic of China participants (23.1 kg/m^2) and highest for American (28.9 kg/m^2). Mean total PFA intake from foods (grams per 24 hours and percentage of kilocalories) was highest

in the United States (7.0% kcal) and lowest in the People's Republic of China (5.8% kcal). Mean linoleic acid intake (grams per 24 hours and percentage of kilocalories) was highest in the United States (6.2% kcal) and lowest in Japan (4.9% kcal); linoleic acid was ≈86% of total PFA (range: 77% for Japanese to 90% for Chinese). The main food group supplying linoleic acid was oil (49%, People's Republic of China; 30%, Japan; 28%, United States; and 17%, United Kingdom). Linoleic acid was also consumed in table spreads, salad dressings, nuts or nut butters, and breads, rolls, biscuits, and related products.

Univariate estimates for reliability of lipid intake by individuals based on means of four 24-hour recalls were for all of the 4680 participants: the linoleic acid (percentage of kilocalories) observed coefficient was 56.5% of theoretical coefficient, and total PFA was 54.6% (Table 1). Subcohort reliability data were similar, eg, for the 2238 nonintervened persons, linoleic acid was 64.2%. These estimates varied across countries, eg, linoleic acid (all 4680 participants) was from 48.6% in Japan to 75.2% in the People's Republic of China. BP reliability estimates (all 4680 participants) were 94.3% for SBP, 93.0% for DBP, and similar for the nonintervened subcohort, uniformly high in each country.

Partial Correlation Data

Dietary linoleic acid (percentage of kilocalories) correlated directly with omega-3 PFA (partial r=0.48), monounsaturated fatty acid (MFA) (partial r=0.50), oleic acid (partial r=0.53), vitamin E (partial r=0.56), and SFA (partial r= 0.21) and inversely with available carbohydrate (partial r=−0.40) and sugars (partial r=−0.27). Correlations were small with arachidonic acid, animal protein, vegetable protein, calcium, magnesium, phosphorus, urinary sodium, and potassium (partial r values= −0.09 to +0.06).

Relation of Dietary Linoleic Acid to BP

All 4680 Participants—Consistently, dietary linoleic acid was inversely related to SBP and DBP (P>0.05; Table 2). With 2 SD higher linoleic acid (3.766% kcal=≈9.0 g/d), the estimated difference in SBP was −0.4 to −0.5 mmHg; in DBP, it was −0.3 to −0.5 mmHg. There were no statistically significant interactions with age or gender. Although all of the tests for cross-country heterogeneity were nonsignificant, the inverse linoleic acid-BP relation was stronger for US participants, eg, in model 4, the estimated SBP difference was −0.99 mm Hg, with 2-SD higher linoleic acid (z score: −1.93; P>0.05), and DBP was −0.72 mmHg (z score: −2.01; P<0.05). Corresponding analyses with control for urinary Na/creatinine and K/creatinine (instead of 24-hour Na and K excretion), and for linoleic acid from both foods and dietary supplements yielded similar findings (data not tabulated).

Nonintervened Subcohort—The percentage of persons with untreated high BP in this subcohort (n=2238) was 11.8% (men) and 5.6% (women). Estimated SBP and DBP differences were consistently greater than for all of the participants, eg, in model 4, the SBP difference was −1.42 mmHg (z score: −2.26; P<0.05), and the DBP difference was −0.91 mmHg (z score: −2.14; P<0.05), with 2-SD higher linoleic acid (Table 2). There were no significant interactions with age, gender, or body mass index. Although all of the tests for cross-country heterogeneity were nonsignificant, BP differences were non-significantly larger for the United Kingdom and Japan participants (SBP: −3.18 and −2.49 mmHg; DBP:

−2.17 and −1.35 mm Hg; model 4), whereas for the United States and People's Republic of China, SBP was −1.40 and 0.09 mm Hg and DBP was −1.26 and 0.14 mm Hg. Analyses with control for urinary Na/creatinine and K/creatinine yielded similar findings, eg, in model 4, SBP difference was −1.40 mm Hg (*z* score: −2.23; $P<0.05$), and DBP difference was −0.90 mmHg (*z* score: −2.11; $P<0.05$) with 2-SD higher linoleic acid (data not tabulated).

Sensitivity Analyses—Multiple other regression models yielded results qualitatively similar to the foregoing, eg, modifications A through C of model 4 (Table 3). With model C, excluding people with high day-to-day variability in SBP, DBP, and/or nutrient intakes, BP differences and *z* scores were greater than for all of the nonintervened persons (model A; SBP: −1.67 mmHg [z score: −2.32; $P<0.05$];DBP: −1.17 mmHg [*z* score: −2.35; $P<0.05$]). Inclusion singly (model 4) of fiber, magnesium, animal and/or vegetable protein, oleic acid, arachidonic acid, and total sugars (instead of phosphorus) had little effect on SBP/DBP differences; with omega-3 PFA included, differences were smaller (SBP: −1.01 mmHg; DBP: −0.39 mmHg); with total carbohydrate or starch, differences were larger, and they were largest with total carbohydrates (SBP: −1.84 mmHg; DBP: −1.05 mmHg; data not tabulated).

Relation of Dietary Total PFA to BP

For all 4680 of the participants and the nonintervened subcohort, relations of dietary total PFA to BP were similar to those of dietary linoleic acid (Table 4). Thus, for nonintervened participants, estimated SBP and DBP differences with 2-SD higher intake (4.044% kcal=≈9.7 g/d) were −1.42 mmHg (*z* score: −2.30; $P<0.05$) and −0.98 mmHg (*z* score: −2.31; $P<0.05$; model 4). Although all of the tests for cross-country heterogeneity were nonsignificant, data for nonintervened United Kingdom and Japan participants showed nonsignificantly larger estimated SBP differences, eg, in model 4, data showed differences of −2.85 and −2.33 mmHg.

Discussion

The main findings of this population-based study on dietary linoleic acid of individuals and their BP are as follows: (1) independent inverse relations of dietary linoleic acid to SBP/DBP, which is stronger in nonintervened persons; (2) estimated effect sizes of ≈1.4 mmHg SBP and 0.9 mmHg DBP with 2-SD higher linoleic acid intake (9.0 g/d); and (3) similar inverse relations of total PFA intake to SBP/DBP.

To the best of our knowledge, these INTERMAP data are the first comprehensive population-based findings on this matter. In a population study of 722 Finnish men with dietary intake assessed by a 4-day food record, no significant cross-sectional relation of linoleic acid to BP was found.[23] In that study, mean SFA intake was higher (60.6 g/d) and linoleic acid intake lower (9.9 g/d) than in INTERMAP. Other cross-sectional studies reporting no significant relations of total PFA intake to BP were based on a single 24-hour dietary recall,[24,25] use of only 1 or 2 BP measure- ments,[25–27] or small sample sizes.[25–27]

An additional reason for inconsistent results on this issue is that individuals detected as having adverse cardiovascular risk factors, including high BP, tend to increase PFA (mainly

linoleic acid) intake and to reduce SFA intake to reduce serum cholesterol level and to prevent atherosclerosis. These behaviors would cause underestimation of an inverse relationship between linoleic acid intake and BP. Therefore, it is reasonable that we observed stronger linoleic acid-BP relationships in nonintervened participants.

There have been several randomized, controlled trials to investigate BP-lowering effects of diets with different total fat content, including different PFA/SFA ratio, MFA, and PFA levels.[1–4] Inconsistent results from these studies may be attributable to short duration and small sample sizes, resulting in insufficient statistical power to detect small differences in BP. Two small randomized trials demonstrated the BP-lowering effect with linoleic acid supplementation compared with paraffin[28] or oleic acid[29] supplementation. Four-week supplementation with safflower oil capsules (4 g of linoleic acid per day) for 22 participants reduced SBP/DBP by 4.0/2.0 mmHg (supine) and 1.0/2.0 mmHg (standing) more than for 22 control individuals.[28] In another study, 17 adults consumed 23 g/d of linoleic acid or oleic acid for 4 weeks; SBP/DBP of the linoleic acid group was reduced by 2.5/ 2.1 mm Hg more than for the oleic acid group, a nonsignificant difference.[29] Given low statistical power, such nonsignificant results are not definitive evidence as to effect of dietary linoleic acid intake on BP. Also, this latter trial may have been confounded by use of oleic acid in the control group, because this MFA apparently lowers BP.[30]

BP-lowering effects of linoleic acid may be mediated through changes in prostaglandin (PG) metabolism.[4] In animal studies of diets enriched with n-6 PFA, the vasodilator PGs (PGI_2 and PGE_2) increased in kidney, aorta, blood, or urine. In humans, there is evidence that PG production in kidney and other tissues from dietary PFA is involved in BP regulation.[4]

Limitations of the INTERMAP findings include the following: their cross-sectional nature, although they are the only available extensive, high-quality population-based data on dietary linoleic acid and BP; underestimation of effect size because of limited reliability in measurement of nutrients (regression dilution bias), despite multiple standardized state- of-the-art measurements; and limited ability to fully control for higher-order collinearity (eg, linoleic acid with omega-3 PFA), consequently, limited ability to address definitively the matter of a causal relation of linoleic acid intake with BP.

If feasible intakes of dietary linoleic acid influence BP favorably for people in the general population, effect size is apparently small, based on our results. This finding, anticipated by INTERMAP,[14] needs to be kept in perspective. First, with multiple nutrients having “small” independent influences, the combined effect becomes sizable, ie, improved nutrition is capable of preventing or lowering unfavorable BP levels for most people, as the Dietary Approaches to Stop Hypertension and Optimal Macronutrient Intake Trial to Prevent Heart Disease feeding trial results indicate.[30–32] Second, long-term BP effects of habitual eating patterns, from early life into middle age, may be greater, as data on salt intake and BP indicate.[33,34] Third, lowering of the population average SBP by small amounts (eg, 2 mm Hg) is estimated to reduce mortality rates by 6% for stroke and 4% for coronary heart disease.[33] Fourth, enhanced linoleic acid intake from vegetable products instead of SFA and/or cholesterol from animal products may decrease the risk of coronary heart disease and/or CVD not only by modestly lowering BP but also by favorably influencing the serum

cholesterol level.[8,9,35] Fifth, INTERMAP data also indicate low-order independent favorable influence of food omega-3 PFA, vegetable protein, and other nutrients on the BP of individuals in general populations.[17–20]

In conclusion, there was an inverse relationship of dietary linoleic acid intake to BP with control for multiple possible confounders. This finding was stronger for persons not experiencing dietary and/or medical intervention, ie, was stronger after removing sources of possible bias, a result consistent with the inference that the linoleic acid-BP relationship may be etiologically significant.

Perspectives

Recent research indicates that multiple improvements in dietary pattern lower BP of adults, both prehypertensive and hypertensive. Nutrients possibly accounting for these favorable effects include minerals (calcium, magnesium, and phosphorus), vegetable protein, PFAs, and reduced intake of total fat, SFAs, cholesterol, and sugars over and above the known favorable BP effects of reduced salt, increased potassium, prevention and/or correction of overweight/obesity, and excess alcohol intake. Findings here indicate a favorable influence of linoleic acid and total PFA intake on the BP of individuals from general population samples. These results on a major coronary heart disease/CVD risk factor lend support to current recommendations for increased ingestion of PFA from vegetable sources.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Reliability of BP, Dietary Nutrient Intake, and Urinary Electrolyte Excretion Measurements by Country

Variable	Japan (n=1145)	People's Republic of China (n=839)	United Kingdom (n=501)	United States (n=2195)	All (n=4680)
SBP, mm Hg	94.9	94.5	94.4	94.0	94.3
DBP, mm Hg	93.7	92.6	92.8	92.9	93.0
Linoleic acid, % kcal	48.6	75.2	58.8	55.5	56.5
Total PFA, % kcal	44.1	72.0	57.1	55.7	54.6
Total SFA, % kcal	64.0	70.1	73.6	67.9	67.8
7-d alcohol, g/24 h	89.7	89.5	87.3	87.5	88.4
Cholesterol, mg/1000 kcal	43.8	58.0	41.1	54.1	50.1
Calcium, mg/1000 kcal	70.5	54.7	72.6	74.5	68.9
Phosphorus, mg/1000 kcal	66.4	83.5	76.1	70.5	72.0
Urinary sodium, mmol/24 h	63.3	72.9	56.7	59.2	62.0
Urinary potassium, mmol/24 h	74.5	64.0	67.3	76.8	72.5

Values are estimates of the size of an observed coefficient as a percentage of the theoretical coefficient in a univariate regression analysis.

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Table 2.

Estimated Mean Difference in BP and Dietary Linoleic Acid Higher by 2 SDs (Sequential Regression Models)

Model	Other Variables, Added Subsequently*	SBP		DBP	
		Difference, mm Hg	*z* Score	Difference, mm Hg	*z* Score
All of the participants (n=4680)					
1		−0.45	−1.12	−0.34	−1.26
2	Urinary Na, urinary K, alcohol	−0.39	−0.96	−0.31	−1.12
3	Cholesterol, total SFA, calcium	−0.45	−1.60	−0.54	−1.24
4	Phosphorus	−0.44	−1.56	−0.50	−1.14
Nonintervened participants (n=2238)					
1		− 1.54	−2.56†	−0.92	−2.28†
2	Urinary Na, urinary K, alcohol	− 1.36	−2.25†	−0.83	−2.02†
3	Cholesterol, total SFA, calcium	− 1.39	−2.23†	−0.92	−2.17†
4	Phosphorus	− 1.42	−2.26†	−0.91	−2.14†

Units are millimoles per 24 hours (urinary Na and urinary K), grams per 24 hours (alcohol), milligrams per 1000 kcal (calcium, phosphorus, and cholesterol), and percentage of kilocalories (SFA). All of the nutrients are from foods only, exclusive of amounts from dietary supplements. The 2-SD difference in dietary linoleic acid is 3.766 %kcal. All of the tests for cross-country heterogeneity were nonsignificant ($P>0.05$).

*Model 1 includes sample, age, gender, height, weight, physical activity, family history of high BP, special diet, supplement intake, and CVD-diabetes diagnosis (the latter 3 variables were not included in model 1 for nonintervened participants). From models 2 to 4, variables listed are added to each previous model. Special diet indicates weight loss, weight gain, vegetarian, salt reduced, diabetic, fat modified, or any other special diet. CVD-diabetes indicates history of heart attack, other heart disease, stroke, or diabetes. Supplement intake indicates taking any dietary supplement at the time of the study.

†$P<0.05$.

Table 3.

Sensitivity Analyses: Estimated Mean Difference in BP and Dietary Linoleic Acid Higher by 2 SDs for Model 4 in Table 2 for Nonintervened Participants (n=2238)

	SBP		DBP	
Modification of Model 4	**Difference, mm Hg**	***z* Score**	**Difference, mm Hg**	***z* Score**
A, %kcal with inclusion of energy intake (kcal/24 h; n=2238)	−1.43	−2.27*	−0.89	−2.07*
B, g/24 h adjusted for energy intake (kcal/24 h; n=2238)	−1.61	− 1.93	−0.82	− 1.45
C, %kcal with exclusion of people with high day-to-day variability of SBP, DBP, and/or nutrient intakes (n=1598)	−1.67	−2.32*	−1.17	−2.35*

The 2-SD difference in dietary linoleic acid is 3.766 %kcal (rows A and C) or 12.789 g/24 h (row B). All of the tests for cross-country heterogeneity were nonsignificant ($P>0.05$).

*$P<0.05$.

Table 4.

Estimated Mean Difference in BP and Dietary Total PFAs Higher by 2 SDs (Sequential Regression Models)

Model	Other Variables, Added Subsequently*	SBP		DBP	
		Difference, mm Hg	*z* Score	Difference, mm Hg	*z* Score
All participants (n=4680)					
1		−0.46	−1.17	−0.38	−1.43
2	Urinary Na, urinary K, alcohol	−0.38	−0.97	−0.34	−1.25
3	Cholesterol, total SFA, calcium	−0.58	−1.42	−0.48	−1.73
4	Phosphorus	−0.59	−1.45	−0.47	−1.70
Nonintervened participants (n=2238)					
1		−1.53	−2.57†	−0.98	−2.44†
2	Urinary Na, urinary K, alcohol	−1.35	−2.25†	−0.88	−2.18†
3	Cholesterol, total SFA, calcium	−1.42	−2.29†	−0.99	−2.35†
4	Phosphorus	−1.42	−2.30†	−0.98	−2.31†

Units are millimoles per 24 hours (urinary Na and urinary K), grams per 24 hours (alcohol), milligrams per 1000 kcal (calcium, phosphorus, and cholesterol), and percentage of kilocalories (SFA). All of the nutrients are from foods only, exclusive of the amounts from dietary supplements. The 2-SD difference in dietary total polyunsaturated fatty acids is 4.044 %kcal.

*Model 1 includes sample, age, gender, height, weight, physical activity, family history of high BP, special diet,supplement intake, and CVD-diabetes diagnosis (the latter 3 variables were not included in model 1 for nonintervened participants). From models 2 to 4, variables listed are added to each previous model. Special diet indicates weight loss, weight gain, vegetarian, salt reduced, diabetic, fat modified, or any other special diet. CVD-diabetes indicates history of heart attack, other heart disease, stroke, or diabetes. Supplement intake indicates taking any dietary supplement at the time of the study. All of the tests for cross-country heterogeneity were nonsignificant ($P>0.05$).

†$P<0.05$.