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Relationship of dietary monounsaturated fatty acids to blood pressure: the international study of macro/micronutrients and blood pressure

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Abstract

Objective—In short-term feeding trials, replacement of other macronutrients with monounsaturated fatty acid reduces blood pressure. However, observational studies have not clearly demonstrated a relationship between monounsaturated fatty acid intake and blood pressure.

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Conflicts of interest
The authors have no conflicts of interest.

We report associations of monounsaturated fatty acid intake of individuals with blood pressure in a cross-sectional study.

Methods—The International Study of Macro/Micronutrients and Blood Pressure is a cross-sectional epidemiologic study of 4680 men and women ages 40–59 years from 17 population samples in China, Japan, UK and USA. Nutrient intake data were based on four in-depth multipass 24-h dietary recalls/person and two-timed 24-h urine collections/person. Blood pressure was measured eight times at four visits.

Results—Mean monounsaturated fatty acid intake ranged from 8.1%kcal (China) to 12.2%kcal (USA). With sequential models to control for possible confounders (dietary, other), linear regression analyses showed significant inverse relationship of total monounsaturated fatty acid intake with DBP for all participants; for 2238 'nonintervened' individuals, the relationship was stronger. Estimated DBP differences with 2-SD higher monounsaturated fatty acids (5.35%kcal) were −0.82mmHg ($P<0.05$) for all participants and −1.70mmHg ($P<0.01$) for nonintervened individuals. Inverse associations of dietary total oleic acid (main monounsaturated) with blood pressure in nonintervened individuals were not significant, but those of oleic acid from vegetable sources were stronger and significant ($P<0.05$).

Conclusion—Dietary monounsaturated fatty acid intake, especially oleic acid from vegetable sources, may contribute to prevention and control of adverse blood pressure levels in general populations.

Keywords

blood pressure; monounsaturated fatty acids; nutrition; oleic acid; population study

INTRODUCTION

A Mediterranean diet has been reported to reduce cardiovascular disease risk [1]. A major characteristic of a Mediterranean diet is a high proportion of energy from monounsaturated fatty acids (MFAs), mainly from olive oil. Dietary intake of MFA has been hypothesized to have a favourable effect on blood pressure (BP). Data from short-term feeding trials have documented that MFA replacement of saturated fatty acids (SFAs), polyunsaturated fatty acids (PFAs) or carbohydrate lowered BP [2–5]. However, findings from observational studies, cross-sectional and longitudinal, have been inconsistent [6–12]. Thus, effects of dietary MFA on BP in the general population merit further study. Possible reasons for inconsistencies across studies include limitations in methods of dietary assessment, for example, a single 24-h dietary recall, or use of food frequency questionnaires, with consequent limited ability to classify dietary intake of individuals accurately; BP measurements insufficiently standardized; and small sample sizes with resultant low statistical power.

The population-based International Study of Macro/Micronutrients and Blood Pressure (INTERMAP) was designed to address these problems [13–25]. Its basic premise is that multiple nutrients have small independent influences on BP of individuals that in combination summate as sizable effects. To detect the impact of single nutrients or foods on 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 40–59 years, from 17 population samples in Japan, Peoples Republic of China, UK and USA. INTERMAP investigators hypothesized that intakes of total MFA and its main constituent oleic acid by individuals are inversely related to their BP [13].

MATERIALS AND METHODS

Population samples, field methods (1996–1999)

INTERMAP included 4680 men and women ages 40–59 years from population samples in Japan (four samples), People's Republic of China (PRC, three), UK (two) and USA (eight) [13]. Participants were selected randomly from population lists, stratified by age/sex. Staff were trained, standardized and certified for BP measurement by international/national senior colleagues on the basis of a common protocol [13]. Each participant attended four visits, visits 1 and 2 on consecutive days, visits 3 and 4 on consecutive days on average 3 weeks later. For BP measurement, each participant – having emptied his/her bladder – was seated comfortably for 5min, 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 SBP and DBP. BP was measured twice at each visit with a random zero sphygmomanometer; BP at each visit was the average of the two readings. Measurements of height and weight, and questionnaire data on daily alcohol consumption over the previous 7 days were obtained at two visits (14 days total). Dietary data were collected at each visit by a trained certified interviewer with use of the in-depth multipass 24-h recall method [14]. All foods and drinks consumed in the previous 24 h, including dietary supplements, were recorded. Questionnaire data were obtained on demographic, biomedical and other possible confounders. Quality control throughout the field surveys was ongoing and extensive at the international, national and local levels [13,14].

Each participant provided two 24-h urine collections, start and end timed at the research centre (visits 1–2 and 3–4); measurements included urinary volume, sodium, potassium, creatinine [13]; 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 four visits; diet data were considered unreliable; energy intake from any 24-h dietary recall was below 500 kcal/day or greater than 5000 kcal/day for women, 8000 kcal/day for men; two urine collections were not available; 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 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 Nutrition Coordinating Center, University of Minnesota [14,15]. For nutrients supplying energy, intake was calculated as percentage total energy (%kcal) whereas for others, as intake/1000 kcal;

nutrients were calculated also as amounts/24 h. Food data were used to assess main food groups supplying total MFA and its main component oleic acid. Urinary values/24 h were calculated as products of urinary concentrations and timed volumes standardized to 24 h. Measurements/person were averaged, for BP and nutrient variables, across the four visits and for urinary excretions across the two collections. For descriptive statistics, means and standard deviations, numbers and percentages were calculated by country and study-wide.

Associations among nutritional variables were explored by partial correlation, adjusted for sample, age, sex; pooled across countries, weighted by sample size. Multiple linear regression analyses were used to examine relationships of dietary MFA and oleic acid (%kcal) of individuals to their SBP andDBP. These analyses were done for two cohorts: all 4680 participants and 2238 ‘nonintervened’ persons not being on a special diet, not consuming nutritional supplements, not diagnosed with cardiovascular disease/diabetes and not taking medication for high BP, cardiovascular disease or diabetes, that is, exclusion of people whose data might bias the dietary MFA–BP relationship. Adjustment for confounders was done sequentially for sample, age, sex, BMI, moderate/heavy physical activity (hours/day), smoking status (current smoker or not), family history of hypertension, reported special diet, dietary supplement intake, history of cardiovascular disease or diabetes (model A), along with 24-h urinary sodium, potassium and 7-day alcohol intake (model B), as well as dietary cholesterol, total SFA and calcium (model C). Models D1–D3 were adjusted for model C variables along with each stipulated nutrient, that is dietary fibre (model D1), dietary phosphorus (model D2) and vegetable protein (model D3). Corresponding analyses were done for dietary total oleic acid, oleic acid from animal sources and oleic acid from vegetable sources (%kcal) instead of dietary MFA. For these analyses, model E involved adjustment for nonheme iron [20] and glutamic acid [21] in addition to model D3 variables.

Regression models were fit separately by country and coefficients pooled across countries, weighted by inverse of variance, to estimate overall associations; cross-country heterogeneity was tested; interactions were assessed for age and sex. Regression coefficients were expressed as mmHg for two standard deviation (SD) difference in dietary MFA or oleic acid, from pooled within-country standard deviations weighted by sample size. Adjusted mean BPs by quartiles of dietary MFA were also calculated and plotted in a figure.

Analyses were carried out with SAS version 9.2 (SAS Institute Inc., Cary, North Carolina, USA).

RESULTS

Descriptive statistics

Average SBP ranged from 117.2 (Japan) to 121.3mmHg (PRC) and average DBP from 73.2 (PRC) to 77.3 (UK)mmHg (Online Table 1, http://links.lww.com/HJH/A247). Mean BMI and energy intake were lower for Japanese and PRCparticipants and highest forAmerican participants.Mean total MFA intake from foods was highest in USA (31.9 g/day, 12.2%kcal) and lowest in PRC (18.5 g/day, 8.1%kcal). Mean oleic acid intake was highest in USA (29.8 g/day, 11.6%kcal) and lowest in PRC (15.4 g/day, 6.7%kcal); oleic acid was about 91% of

total MFA (range across countries: 83%, PRC to 95%, USA). Main food groups supplying MFA were, first, fats/oils/margarines (51%, PRC; 32%, USA; 31%, UK; 26%, Japan), and, second, meat (26%, USA; 21%, UK; 20%, PRC; 20%, Japan) (Online Table 2, http://links.lww.com/HJH/A247). MFA was also consumed in milk/cheese, cakes/puddings/cookies/other sweet snacks, fish, condiments/seasonings and pasta/rice/noodles.

Partial correlation data

High direct correlations prevailed for dietary MFA (%kcal) with SFA (partial $r = 0.73$), PFA (0.52), n-6 PFA (0.51) and dietary cholesterol (0.37), whereas inverse correlations with vegetable protein (−0.33), fibre (−0.29) and magnesium (−0.28) (Online Table 3, http://links.lww.com/HJH/A247). MFA correlations were small with calcium, urinary sodium, potassium and 7-day alcohol (partial r values −0.09 to +0.09). All the foregoing correlations prevailed also for total oleic acid; oleic acid from animal sources correlated directly with total SFA (partial $r = 0.73$); oleic acid from vegetable sources correlated directly with total PFA (0.63) and n-6 PFA (0.63).

Relation of dietary monounsaturated fatty acid to blood pressure

All 4680 participants—In models A and B, dietary MFA was not related to SBP and DBP (Table 1). In model C with further adjustment also for dietary cholesterol, total SFA and calcium, dietary MFA was significantly and inversely related to DBP; results were similar with additional adjustment for fibre, phosphorus or vegetable protein (models D1–D3). With two SD higher MFA (5.35%kcal = about 12.8 g/day), estimated difference in average DBP was approximately −0.8mmHg. Interactions with age or sex were not statistically significant in most models. Although all tests for cross-country heterogeneity were nonsignificant for DBP, the inverse MFA–BP relationship was largest for Chinese participants, for example, model D3, estimated DBP difference −2.70mmHg with 2 SD higher MFA (Z-score −2.35; $P<0.05$) (Online Table 4, http://links.lww.com/HJH/A247). Corresponding analyses with control for urinary Na/creatinine and K/creatinine (instead of 24-h Na and K excretion) yielded similar findings (data not tabulated). SBP was not associated with MFA in any models.

Multivariate-adjusted mean values of DBP by quartiles of dietary MFA showed a linear inverse relation (P for trend = 0.036) (Fig. 1). Adjusted mean DBP was 73.7mmHg in the first quartile and 71.1mmHg in the fourth quartile.

'Nonintervened' subcohort (n = 2238)—In this subcohort, the percentage of persons with untreated high BP was 11.8% (men) and 5.6% (women). Dietary MFA was inversely related to SBP and DBP, significantly to DBP (Table 1). Estimated SBP and DBP differences were consistently greater than for all participants, for example, in model D3, SBP difference was −1.29mmHg (Z-score −1.39; $P = 0.16$), whereas DBP difference was −1.70mmHg Z-score −2.65; $P<0.01$) with 2 SD higher MFA. Interactions with age or sex were not significant in most models. Although tests for cross-country heterogeneity were nonsignificant, BP differences were larger for Chinese participants, SBP −2.31, DBP −3.17mmHg, and for UK participants, SBP −4.12, DBP −2.15mmHg (model D3) (Online Table 4, http://links.lww.com/HJH/A247). Analyses with control for urinary Na/creatinine

and K/creatinine yielded similar findings, for example, in model D3, SBP difference was −1.22mmHg (*Z*-score −1.32; *P* = 0.18) and DBP difference was −1.68mmHg (*Z*-score −2.63; *P*<0.01) with 2 SD higher MFA (data not tabulated).

Relation of dietary oleic acid to blood pressure

Total dietary oleic acid—For all 4680 participants, dietary total oleic acid was nonsignificantly inversely related to DBP in multivariate-adjusted models (Table 2). For the nonintervened subcohort, dietary total oleic acid tended to relate inversely nonsignificantly to SBP and DBP; estimated SBP and DBP differences with 2 SD higher intake were larger than for all participants.

Dietary oleic acid from vegetable sources—Dietary oleic acid from vegetable sources was related inversely with SBP and DBP in all participants (Table 2): SBP difference −0.70 mmHg, DBP difference −0.57mmHg (*Z*-score −2.01; *P*<0.05), with 2 SD higher oleic acid from vegetable sources (4.12%kcal = about 9.8 g/day) (model E). The relationships were stronger for nonintervened participants; estimated SBP and DBP differences with 2 SD higher intake were −1.26mmHg (Z-score −1.97; *P*<0.05) and −1.02mmHg (*Z*-score −2.32; *P*<0.05) (model E).

Dietary oleic acid from animal sources—In contract to the inverse relationship of dietary oleic acid from vegetable sources with BP, dietary oleic acid from animal sources was positively associated with SBP and DBP for all participants and nonintervened participants (Table 2), with relationships weaker for nonintervened participants, nonsignificant in models D3 and E for both SBP and DBP.

DISCUSSION

Main findings of this population-based study are independent inverse relations of dietary MFA and oleic acid (principal MFA) to DBP, estimated effect size −0.8 to −1.7mmHg DBP with 2 SD higher MFA intake (approximately 13 g/day). These results are consistent with those from the DASH and OMNIHEART feeding trials and other studies [2–5,26,27]. In INTERMAP, relations to BP of oleic acid from vegetable sources were stronger than those of total oleic acid intake. Also, a direct (not inverse) association with BP was observed for oleic acid from animal sources.

In INTERMAP, over 90% of dietary total MFA intake was oleic acid (*cis* C18 : 1 n-9) (range in countries from 83%, PRC to 95%, USA); 58% of oleic acid was from vegetable sources. Some vegetable oils contain much MFA (over 70% in olive oil and over 60% in canola oil), whereas other vegetable oils differ (e.g. less than 30% in corn oil and sunflower oil). MFA makes up over 40% of animal fats (e.g. lard, chicken fat, beef tallow) [28]. Therefore, relation of MFA or oleic acid to BP in free-living people in observational studies differs potentially from that in intervention studies in which MFA is usually from supplemental vegetable oil, mainly olive oil.

In the present study, DBP was significantly and SBP tended to be related inversely to total MFA intake, especially in nonintervened participants who are presumably less likely to have

changed their dietary habit intentionally. Previous observational studies, cross-sectional and longitudinal, showed no or direct association between MFA intake and BP in US populations [8,9] and inverse association in Mediterranean countries where olive oil consumption is higher [10–12]. Our findings from East Asian and Western population samples lend support to the concept of a favourable effect of MFA intake on BP.

In our study, oleic acid from vegetable – but not animal – sources was inversely related to SBP and DBP. Data from previous observational [10–12] and intervention studies [2–5] suggest a BP-lowering effect of MFA from vegetable oils, mostly olive oil. Other components in oleic acid rich vegetable oils (e.g. polyphenols and vitamins with antioxidant effect) may be contributing to lower BP [29,30].

Reasons are unclear for the unexpected direct relationship to BP of oleic acid from animal sources. It was significant – especially for SBP – with control for multiple possible confounders systemically/routinely considered by INTERMAP, and with further control for others as well (correlates of oleic acid from animal products) in total participants. However, the relationship was no longer significant after adjustment for vegetable protein in nonintervened participants. Oleic acid in these analyses includes both *cis* and *trans*-isomers, for example elaidic acid (C18 : 1 *trans* n-9) and vaccenic acid (C18 : 1 *trans* n-7); the latter is the most common *trans* isomer in beef and dairy products. Possible residual confounding by factors such as *trans*-MFA could not be controlled in our study.

Limitations of the INTERMAP findings include, first, the cross-sectional study design. However, our data are the only available extensive high-quality population-based data on dietary MFA and BP. Second concern is underestimation of effect size due to limited reliability in measurement of nutrients (regression dilution bias), despite multiple standardized state-of-the-art measurements. Third, because of high-order collinearity (e.g. MFA with SFA or PFA), we have limited ability to control for the BP effects of these nutrients. Fourth, four current 24-h dietary recalls may not for some persons yield accurate data on individual's long-term dietary intake of MFA.

The apparently small effect of MFA on BP, anticipated by INTERMAP [13], needs to be kept in perspective: First, with multiple nutrients having 'small' independent influences, the combined effect is potentially quite sizable, that is improved nutrition is capable of preventing or lowering unfavourable BP levels for most people, as the INTERMAP, as well as DASH and OMNIHEART feeding trial, results indicate [5,26]. 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 [31]. Third, lowering of population average SBP by 'small' amounts (e.g. 2mmHg) is estimated to reduce mortality rates, 6% for stroke and 4% for CHD [31]. Fourth, INTERMAP data also indicate low-order independent favourable influences on BP of food n-3 and n-6 PFA, vegetable protein, calcium, phosphorus, magnesium, nonheme iron, potassium and other nutrients on BP, as well as lower sodium intake, avoidance of heavy alcohol consumption and prevention and control of overweight/obesity, adding up to estimated sizable combined effect for general populations [16–25,32].

In conclusion, there was an inverse relationship of dietary MFA intake to BP with control for multiple possible confounders. This finding was stronger for dietary oleic acid intake from vegetable sources and in persons not experiencing dietary/medical intervention. Dietary MFA intake, especially oleic acid from vegetable sources, may contribute to prevention and control of adverse BP levels in general populations. These results lend support to current recommendations for increased ingestion of MFA from vegetable sources.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

MFA	monounsaturated fatty acid
SFA	saturated fatty acid
PFA	polyunsaturated fatty acid
INTERMAP	the International Study of Macro/Micronutrients and Blood Pressure

REFERENCES

1. Martinez-Gonzalez MA, Sanchez-Villegas A. The emerging role of Mediterranean diets in cardiovascular epidemiology: monounsaturated fats, olive oil, red wine or the whole pattern? Eur J Epidemiol. 2004; 19:9–13. [PubMed: 15012018]
2. Thomsen C, Rasmussen OW, Hansen KW, Vesterlund M, Hermansen K. Comparison of the effects on the diurnal blood pressure, glucose, and lipid levels of a diet rich in monounsaturated fatty acids with a diet rich in polyunsaturated fatty acids in type 2 diabetic subjects. Diabet Med. 1995; 12:600–606. [PubMed: 7554782]
3. Ruiz-Gutierrez V, Muriana FJ, Guerrero A, Cert AM, Villar J. Plasma lipids, erythrocyte membrane lipids and blood pressure of hypertensive women after ingestion of dietary oleic acid from two different sources. J Hypertens. 1996; 14:1483–1490. [PubMed: 8986934]
4. Ferrera LA, Raimondi AS, d'Episcopo L, Guida L, Dello Russo A, Marotta T. Olive oil and reduced need for antihypertensive medications. Arch Intern Med. 2000; 160:837–842. [PubMed: 10737284]
5. Appel LJ, Sacks FM, Carey VJ, Obarzanek E, Swain JF, Miller ER 3rd, et al. OmniHeart Collaborative Research Group. Effects of protein, monounsaturated fat, carbohydrate intake on blood pressure and serum lipids: results of the OmniHeart randomized trial. JAMA. 2005; 294:2455–2464. [PubMed: 16287956]
6. Witteman JC, Willett WC, Stampfer MJ, Colditz GA, Sacks FM, Speizer FE, et al. A prospective study of nutritional factors and hypertension among US women. Circulation. 1989; 80:1320–1327. [PubMed: 2805268]

7. Ascherio A, Hennekens C, Willett WC, Sacks F, Rosner B, Manson J, et al. Prospective study of nutritional factors, blood pressure, and hypertension among US women. Hypertension. 1996; 27:1065–1072. [PubMed: 8621198]
8. Stamler J, Liu K, Ruth KJ, Pryer J, Greenland P. Eight-year blood pressure change in middle-aged men: relationship to multiple nutrients. Hypertension. 2002; 39:1000–1006. [PubMed: 12019283]
9. Stamler J, Caggiula A, Grandits GA, Kjelsberg M, Cutler JA. Relationship to blood pressure of combinations of dietary macronutrients. Findings of the Multiple Risk Factor Intervention Trial (MRFIT). Circulation. 1996; 94:2417–2423. [PubMed: 8921782]
10. Psaltopoulou T, Naska A, Orfanos P, Trichopoulos D, Mountokalakis T, Trichopoulou A. Olive oil, the Mediterranean diet, and arterial blood pressure: the Greek European Prospective Investigation into Cancer and Nutrition (EPIC) study. Am J Clin Nutr. 2004; 80:1012–1018. [PubMed: 15447913]
11. Trevisan M, Krogh V, Freudenheim J, Blake A, Muti P, Panico S, et al. Consumption of olive oil, butter, and vegetable oils and coronary heart disease risk factors. The Research Group ATS-RF2 of the Italian National Research Council. JAMA. 1990; 263:688–692. [PubMed: 2296124]
12. Alonso A, Martínez-González MA. Olive oil consumption and reduced incidence of hypertension: the SUN study. Lipids. 2004; 39:1233–1238. [PubMed: 15736920]
13. Stamler J, Elliott P, Dennis B, Dyer AR, Kesteloot H, Liu K, et al. for the INTERMAP Research Group. INTERMAP: background, aims, design, methods, and descriptive statistics (nondietary). J Hum Hypertens. 2003; 17:591–608. [PubMed: 13679950]
14. Dennis B, Stamler J, Buzzard M, Conway R, Elliott P, Moag-Stahlberg A, et al. for the INTERMAP Research Group. INTERMAP: the dietary data – process and quality control. J Hum Hypertens. 2003; 17:609–622. [PubMed: 13679951]
15. Schakel SF, Dennis BH, Wold AC, Conway R, Zhao L, Okuda N, et al. for the INTERMAP Research Group. Enhancing data on nutrient composition of foods eaten by participants in the INTERMAP Study in China, Japan, the United Kingdom and the United States. J Food Comp Anal. 2003; 16:395–408.
16. Stamler J, Elliott P, Appel L, Chan Q, Buzzard M, Dennis B, et al. for the INTERMAP Cooperative Research Group. Higher blood pressure in middle-aged American adults with less education – role of multiple dietary factors: The INTERMAP Study. J Hum Hypertens. 2003; 17:655–664. [PubMed: 13679955]
17. Elliott P, Stamler J, Dyer AR, Appel L, Dennis B, Kesteloot H, et al. for the INTERMAP Cooperative Research Group. Association between protein intake and blood pressure: the INTERMAP Study. Arch Intern Med. 2006; 166:79–87. [PubMed: 16401814]
18. Ueshima H, Stamler J, Elliott P, Chan Q, Brown IJ, Carnethon MR, et al. for the INTERMAP Research Group. Food omega-3 fatty acid intake of individuals (total, linolenic acid, long-chain) and their blood pressure: INTERMAP study. Hypertension. 2007; 50:313–319. [PubMed: 17548718]
19. Miura K, Stamler J, Nakagawa H, Elliott P, Ueshima H, Chan Q, et al. for the INTERMAP Research Group. Relationship of dietary linoleic acid to blood pressure: the International Study of Macro- Micronutrients and Blood Pressure. Hypertension. 2008; 52:408–414. [PubMed: 18606902]
20. Tzoulaki I, Brown IJ, Chan Q, Van Horn L, Ueshima H, Zhao L, et al. for the International Collaborative Research Group on Macro-/Micronutrients, Blood Pressure. Relation of iron and red meat intake to blood pressure: cross sectional epidemiological study. BMJ. 2008; 337:a258. [PubMed: 18632704]
21. Stamler J, Brown IJ, Daviglus ML, Chan Q, Kesteloot H, Ueshima H, et al. for the INTERMAP Research Group. Glutamic acid, the main dietary amino acid, and blood pressure: the INTERMAP Study. Circulation. 2009; 120:221–228. [PubMed: 19581495]
22. Elliott P, Kesteloot H, Appel LJ, Dyer AR, Ueshima H, Chan Q, et al. for the INTERMAP Research Group. Dietary phosphorus and blood pressure: INTERMAP study. Hypertension. 2008; 51:669–675. [PubMed: 18250363]
23. Brown IJ, Elliott P, Robertson CE, Chan Q, Daviglus ML, Dyer AR, et al. for the INTERMAP Research Group. Dietary starch intake of individuals and their blood pressure: the international

study of macronutrients and micronutrients and blood pressure. J Hypertens. 2009; 27:231–236. [PubMed: 19155780]

24. Sakurai M, Stamler J, Miura K, Brown IJ, Nakagawa H, Elliott P, et al. for the INTERMAP Research Group. Relationship of dietary cholesterol to blood pressure: the INTERMAP study. J Hypertens. 2011; 29:222–228. [PubMed: 21045731]
25. Brown IJ, Stamler J, Van Horn L, Robertson CE, Chan Q, Dyer AR, et al. Sugar-sweetened beverage, sugar intake of individuals, and their blood pressure: International Study of Macro/Micronutrients and Blood Pressure. Hypertension. 2011; 57:695–701. [PubMed: 21357284]
26. Appel LJ, Moore TJ, Obarzanek E, Vollmer WM, Svetkey LP, Sacks FM, et al. for the DASH Collaborative Research Group. A clinical trial of the effects of dietary patterns on blood pressure. N Engl J Med. 1997; 336:1117–1124. [PubMed: 9099655]
27. Shah M, Adams-Huet B, Garg A. Effect of high-carbohydrate or highcis-monounsaturated fat diets on blood pressure: a meta-analysis of intervention trials. Am J Clin Nutr. 2007; 85:1251–1256. [PubMed: 17490960]
28. Reeves, JB., III; Weihrauch, JL. Consumer and Food Economics Institute. Agriculture Handbook No. 8-4. USDA Science and Education Administration. Washington, DC: US Government Printing Office; 1979. Composition of foods: fats and oils raw, processed, prepared. [Revised June 1979]
29. Alonso A, Ruiz-Gutierrez V, Martinez-Gonzalez MA. Monounsaturated fatty acids, olive oil and blood pressure: epidemiological, clinical and experimental evidence. Public Health Nutr. 2006; 9:251–257. [PubMed: 16571180]
30. Degirolamo C, Rudel LL. Dietary monounsaturated fatty acids appear not to provide cardioprotection. Curr Atheroscler Rep. 2010; 12:391–396. [PubMed: 20725810]
31. Stamler J, Rose G, Stamler R, Elliott P, Dyer A, Marmot M. INTERSALT study findings: public health and medical care implications. Hypertension. 1989; 14:570–577. [PubMed: 2807518]
32. Stamler, J. Improved nutrition: key to solving the populationwide blood pressure problem – conclusions from a quarter century of research. In: Mancini, M.; Ordovas, J.; Riccardi, G.; Rubba, P.; Strazzullo, P., editors. Cardiovascular disease: nutritional and metabolic. Oxford: Blackwell Publishing; 2009.

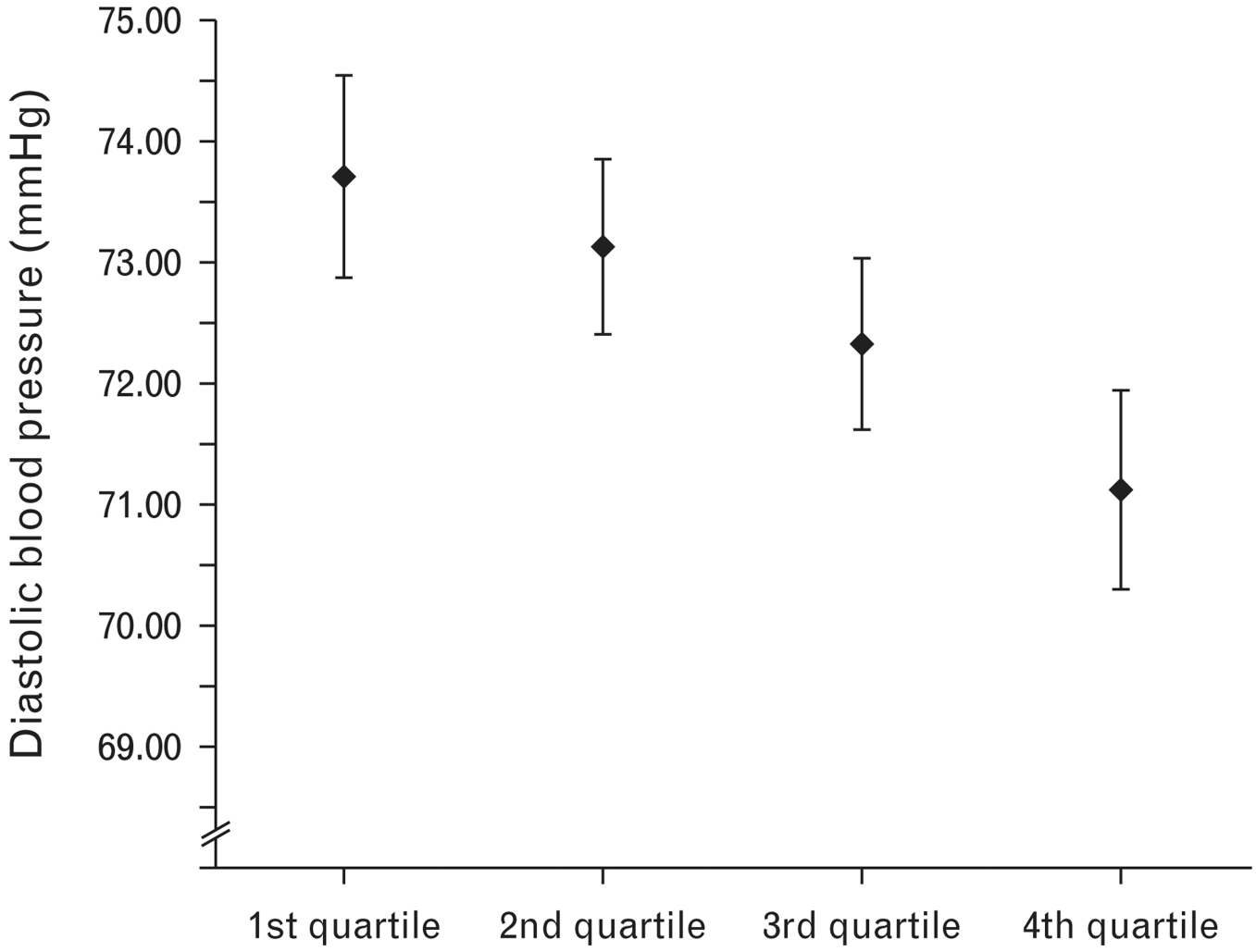

FIGURE 1.

Adjusted mean values of DBP by quartiles of total monounsaturated fatty acid intake (%kcal) in all participants (n = 4680). Mean values were adjusted for variables in model D3 (see Table 1 for variables). Cut-off values of the quartiles are 8.31, 10.48 and 12.72%kcal. P value for trend was 0.036.

TABLE 1

Estimated mean difference in blood pressure (mmHg) associated with total monounsaturated fatty acids (%kcal) higher by two standard deviations[a] (sequential regression models), the International Study of Macro/Micronutrients and Blood Pressure

		SBP		DBP	
Model	**Variables added sequentially[b]**	**Difference (mmHg)**	**Z-score**	**Difference (mmHg)**	**Z-score**
		All participants (n = 4680)			
A		0.28[c]	0.71	−0.11	−0.39
B	Urinary Na, urinary K, alcohol	0.32[c]	0.78	−0.08	−0.28
C	Cholesterol, total SFA, calcium	0.05	0.08	−0.84	−2.02*
D1	Fibre	0.09	0.15	−0.83	−2.00*
D2	Phosphorus	−0.005	−0.01	−0.84	−2.02*
D3	Vegetable protein	0.12	0.20	−0.82	−1.97*
		Nonintervened participants (n = 2238)			
C	Cholesterol, total SFA, calcium	−1.22	−1.33	−1.54	−2.43*
D3	Vegetable protein	−1.29	−1.39	−1.70	−2.65**

Special diet: Weight loss, weight gain, vegetarian, salt reduced, diabetic, fat modified or any other special diet. CVD-DM: History of heart attack, other heart disease, stroke or diabetes. Supplement intake: Taking any dietary supplement at time of the study. SFA, saturated fatty acid.

*P<0.05,

**P<0.01.

[a]Two standard deviation difference is 5.35%kcal for monounsaturated fatty acids.

[b]Model A includes sample, age, sex, BMI, physical activity, smoking status, family history of hypertension, special diet, supplement intake and CVD-DM diagnosis (the latter 3 variables were not included in models for nonintervened participants). From models B to C, variables listed are added to each prior model. Models D1–D3 are adjusted for model C variables along with each stipulated nutrient.

[c]Test for cross-country heterogeneity significant at P<0.05.

TABLE 2

Estimated mean difference in blood pressure (mmHg) associated with oleic acid (%kcal) higher by two standard deviations[a] (sequential regression models), the International Study of Macro/Micronutrients and Blood Pressure

		SBP		DBP	
Model	**Variables added sequentially[b]**	**Difference (mmHg)**	**Z-score**	**Difference (mmHg)**	**Z-score**
Total oleic acid (%kcal)					
		All participants (n = 4680)			
C	Cholesterol, total SFA, calcium	0.07	0.12	−0.57	−1.35
D3	Vegetable protein	0.21	0.34	−0.50	−1.19
E	Nonheme iron, glutamic acid	0.20	0.32	−0.54	−1.27
		Nonintervened participants (n = 2238)			
C	Cholesterol, total SFA, calcium	−1.02	−1.08	−0.99	−1.49
D3	Vegetable protein	−1.01	−1.07	−1.08	−1.61
E	Nonheme iron, glutamic acid	−1.07	−1.11	−1.11	−1.64
Oleic acid from vegetable sources (%kcal)					
		All participants (n = 4680)			
C	Cholesterol, total SFA, calcium	−0.84	−2.06*	−0.65	−2.33*
D3	Vegetable protein	−0.74	−1.79	−0.59	−2.10*
E	Nonheme iron, glutamic acid	−0.70	−1.69	−0.57	−2.01*
		Nonintervened participants (n = 2238)			
C	Cholesterol, total SFA, calcium	−1.28	−2.05*	−1.01	−2.36*
D3	Vegetable protein	−1.24	−1.97*	−1.01	−2.33*
E	Nonheme iron, glutamic acid	−1.26	−1.97*	−1.02	−2.32*
Oleic acid from animal sources (%kcal)					
		All participants (n = 4680)			
C	Cholesterol, total SFA, calcium	2.47	3.73**	0.94	2.07*

J Hypertens. Author manuscript; available in PMC 2014 July 24.

Model	Variables added sequentially[b]	SBP		DBP	
		Difference (mmHg)	Z-score	Difference (mmHg)	Z-score
D3	Vegetable protein	2.37	3.58**	0.86	1.91
E	Nonheme iron, glutamic acid	2.43	3.50**	0.80	1.68
		Nonintervened participants (n = 2238)			
C	Cholesterol, total SFA, calcium	1.80	1.88	1.22	1.86
D3	Vegetable protein	1.71	1.78	1.09	1.67
E	Nonheme iron, glutamic acid	1.79	1.77	1.14	1.67

All tests for cross-country heterogeneity are not significant. SFA, saturated fatty acid.

[a] Two standard deviation differences are 5.10%kcal for total oleic acid, 4.12%kcal for oleic acid from vegetable sources and 3.86%kcal for oleic acid from animal sources.

[b] See Table 1 for variables adjusted in each model. Models E are controlled for model D3 variables along with nonheme iron and glutamic acid.

* P<0.05.

** P<0.01.

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