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

Katsuyuki Miura[1], Jeremiah Stamler[2], Ian J Brown [3], Hirotsugu Ueshim[1], Hideaki Nakagawa[4], Masaku Sakura[4], Queenie Chan[3], Lawrence J Appel[5], Akira Okayama[6], Nagako Okuda[7], J David Curb[8,9], Beatriz L Rodriguez8, Claire Robertson10, Liancheng Zhao11, Paul Elliott[3,12], for the INTERMAP Research Group

[1]Department of Health Science, Shiga University of Medical Science, Otsu, Japan
[2]Department of Preventive Medicine, Feinberg School of Medicine, Northwestern University, Chicago, IL, USA
[3]Department of Epidemiology and Public Health, Faculty of Medicine, St Mary's Campus, Imperial College London, UK
[4]Department of Epidemiology and Public Health, Kanazawa Medical University, Ishikawa, Japan
[5]Welch Center for Prevention, Epidemiology and Clinical Research, Johns Hopkins University, Baltimore, MD, USA
[6]First Institute of Health Service, Japan Anti-Tuberculosis Association, Tokyo, Japan
[7]Department of Nutritional Education, National Institute of Health and Nutrition, Tokyo, Japan
[8]John A. Burns School of Medicine, University of Hawaii at Manoa, Honolulu, HI, USA
[9]Deceased on January 8th, 2012
[10]School of Life Sciences, University of Westminster, London, UK
[11]State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, People's Republic of China
[12]MRC-HPA Centre for Environment and Health, Imperial College London, UK

This is an author's accepted manuscript of an article published in the Journal of Hypertension, 31 (6). pp. 1144-1150, June 2013. The final definitive version is available online at:

http://dx.doi.org/10.1097/HJH.0b013e3283604016

Relationship of Dietary Monounsaturated Fatty Acids to Blood Pressure: The International Study of Macro/Micronutrients and Blood Pressure

Short title: Monounsaturated Fat and Blood Pressure

Katsuyuki MIURA [a], Jeremiah STAMLER [b], Ian J BROWN [c], Hirotsugu UESHIMA [a], Hideaki NAKAGAWA [d], Masaku SAKURAI [d], Queenie CHAN [c], Lawrence J APPEL [e], Akira OKAYAMA [f], Nagako OKUDA [g], J David CURB [h,i], Beatriz L RODRIGUEZ [h], Claire ROBERTSON [j], Liancheng ZHAO [k], Paul ELLIOTT [c,l], for the INTERMAP Research Group

[a] Department of Health Science, Shiga University of Medical Science, Otsu, Japan

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

[c] Department of Epidemiology and Public Health, Faculty of Medicine, St Mary’s Campus, Imperial College London, UK

[d] Department of Epidemiology and Public Health, Kanazawa Medical University, Ishikawa, Japan

[e] Welch Center for Prevention, Epidemiology and Clinical Research, Johns Hopkins University, Baltimore, MD, USA

[f] First Institute of Health Service, Japan Anti-Tuberculosis Association, Tokyo, Japan

[g] Department of Nutritional Education, National Institute of Health and Nutrition, Tokyo, Japan

[h] John A. Burns School of Medicine, University of Hawaii at Manoa, Honolulu, HI, USA

[i] Deceased on January 8th, 2012

[j] School of Life Sciences, University of Westminster, London, UK

[k] State Key Laboratory of Cardiovascular Disease, Fuwai Hospital, National Center for Cardiovascular Diseases, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing, People's Republic of China

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

SOURCES OF FUNDING

This research is supported by grant 2-RO1-HL50490 from the U.S. National Heart, Lung, and Blood Institute, National Institutes of Health (NIH) and by the NIH Office on Dietary Supplements, Bethesda, Maryland; and by national agencies in China, Japan (the Ministry of Education, Science, Sports, and Culture, Grant-in-Aid for Scientific Research [A], No. 090357003), and the U.K. P.E.'s research is supported in part by a grant from the National Institute of Health Research (NIHR) Biomedical Research Centre, Imperial College Healthcare NHS Trust. P.E. is an NIHR Senior Investigator.

CONFLICT OF INTEREST DISCLOSURES

None.

Correspondence and reprint requests to:

Katsuyuki Miura, MD, PhD
Department of Health Science, Shiga University of Medical Science
Seta-Tsukinowa-cho, Otsu, Shiga, 520-2192, Japan.
Tel: +81-77-548-2191 Fax: +81-77-543-9732 E-mail: miura@belle.shiga-med.ac.jp

Total word count: 4,680 words (excluding tables, captions, and online supplement tables)

Two tables, one figure, four online supplementary tables

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. 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 4,680 men and women ages 40-59 from 17 population samples in China, Japan, United Kingdom, and United States. Nutrient intake data were based on four in-depth multi-pass 24-hour dietary recalls/person and two timed 24-hour 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 (United States). With sequential models to control for possible confounders (dietary, other), linear regression analyses showed significant inverse relationship of total monounsaturated fatty acid intake with diastolic blood pressure for all participants; for 2,238 “non-intervened” individuals, the relationship was stronger. Estimated diastolic blood pressure differences with 2-SD higher monounsaturated fatty acids (5.35 %kcal) were -0.82 mm Hg (P<0.05) for all participants and -1.70 mm Hg (P<0.01) for non-intervened individuals. Inverse associations of dietary total oleic acid (main monounsaturated) with blood pressure in non-intervened individuals were not significant, but those of oleic acid from vegetable sources were stronger and significant (P<0.05).

Conclusions: 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.

Condensed Abstract

The associations of monounsaturated fatty acid intake of individuals with blood pressure was investigated in a cross-sectional epidemiologic study of 4,680 men and women ages 40-59 from 17 population samples in China, Japan, United Kingdom, and United States. Linear regression analyses showed significant inverse relationship of total monounsaturated fatty acid intake with diastolic blood pressure. Inverse associations of dietary total oleic acid from vegetable sources with blood pressure in non-intervened individuals were stronger and significant. 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.

Key words: Blood pressure; nutrition; monounsaturated fatty acids; oleic acid; population study

Abbreviations:

MFA, monounsaturated fatty acids; SFA, saturated fatty acids; PFA, polyunsaturated fatty acids; INTERMAP, the International Study of Macro/Micronutrients and Blood Pressure.

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 (MFA), mainly from olive oil. Dietary intake of MFA has been hypothesized to have a favorable effect on blood pressure (BP). Data from short term feeding trials have documented that MFA replacement of saturated fatty acids (SFA), polyunsaturated fatty acids (PFA), 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, e.g., 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 4,680 men and women, ages 40-59, from 17 population samples in Japan, Peoples Republic of China, United Kingdom, and United States. INTERMAP investigators hypothesized that intakes of total MFA and its main constituent oleic acid by individuals are inversely related to their blood pressure [13].

METHODS

Population Samples, Field Methods (1996-1999)

INTERMAP included 4,680 men and women ages 40-59 years from population samples in Japan (four samples), People's Republic of China (PRC, three), United Kingdom (UK, two), and United States (USA, eight) [13]. Participants were selected randomly from population lists, stratified by age/gender. Staff were trained, standardized, and certified for BP measurement by international/national senior colleagues based on 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 five 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 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 seven 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 multi-pass 24-hr recall method [14]. All foods and drinks consumed in the previous 24 hours, including dietary supplements, were recorded. Questionnaire data were obtained on demographic, biomedical, and other possible confounders. Quality control throughout the field surveys was on-going and extensive at the international, national, and local levels [13, 14].

Each participant provided two 24-hour urine collections, start and end timed at the research center (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-hour dietary recall was below 500 kcal/day or greater than 5,000 kcal/day for women, 8,000 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 percent total energy (%kcal); for others, as intake/1,000 kcal; nutrients were calculated also as amounts/24 hours. Food data were used to assess main food groups supplying total MFA and its main component oleic acid. Urinary values/24 hours were calculated as products of urinary concentrations and timed volumes standardized to 24 hours. 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, gender; 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 and DBP. These analyses were done for two cohorts: all 4,680 participants and 2,238 “non-intervened” 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; i.e., exclusion of people whose data might bias the dietary MFA-BP relationship. Adjustment for confounders was done sequentially: for sample, age, gender, body mass index (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); plus 24-hour urinary sodium, potassium, and 7-day alcohol intake (model B); plus dietary cholesterol, total SFA, calcium (model C). Models D1–D3 were adjusted for model C variables plus each stipulated nutrient; i.e., dietary fiber (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, oleic acid from vegetable sources (%kcal) instead of dietary MFA. For these analyses, model E involved adjustment for non-heme 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 gender. Regression coefficients were expressed as mm Hg 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 with SAS version 9.2 (SAS Institute Inc., Cary, NC, USA).

RESULTS

Descriptive Statistics

Average SBP ranged from 117.2 (Japan) to 121.3 mm Hg (PRC); average DBP, from 73.2 (PRC) to 77.3 (UK) mm Hg (Online Table 1). Mean BMI and energy intake were lower for Japanese and PRC participants, highest for American 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). 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), dietary cholesterol (0.37); inverse correlations with vegetable protein (-0.33), fiber (-0.29), and magnesium (-0.28) (Online Table 3). MFA correlations were small with calcium, urinary sodium, potassium, 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 MFA to Blood Pressure

All 4,680 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 fiber, phosphorus, or vegetable protein (models D1-3). With two SD higher MFA (5.35 %kcal = about 12.8 grams/day), estimated difference in average DBP was approximately -0.8 mm Hg. Interactions with age or gender were not statistically significant in most models. While all tests for cross-country heterogeneity were non-significant for DBP, the inverse MFA-BP relation was largest for Chinese participants, e.g., model D3, estimated DBP difference -2.70 mm Hg with 2 SD higher MFA (Z-score -2.35; $P<0.05$) (Online Table 4). Corresponding analyses with control for urinary Na/creatinine and K/creatinine (instead of 24-hour 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) (Figure). Adjusted mean DBP was 73.7 mm Hg in the 1st quartile and 71.1 mm Hg in the 4th quartile.

“Non-intervened” subcohort (n = 2,238): 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, e.g., model D3, SBP difference -1.29 mm Hg (Z-score -1.39; *P*=0.16), DBP difference -1.70 mm Hg (Z-score -2.65; *P*<0.01) with 2 SD higher MFA. Interactions with age or gender were not significant in most models. While tests for cross-country heterogeneity were non-significant, BP differences were larger for Chinese participants, SBP -2.31 mm Hg, DBP -3.17 mm Hg, and for UK participants, SBP -4.12 mm Hg, DBP -2.15 mm Hg (model D3) (Online Table 4). Analyses with control for urinary Na/creatinine and K/creatinine yielded similar findings, e.g., model D3, SBP difference -1.22 mm Hg (Z-score -1.32; P=0.18) and DBP difference -1.68 mm Hg (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 4,680 participants, dietary total oleic acid was non-significantly inversely related to DBP in multivariate-adjusted models (Table 2). For the non-intervened subcohort, dietary total oleic acid tended to relate inversely non-significantly 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 mm Hg, DBP difference -0.57 mm Hg (Z-score -2.01; *P*<0.05) with 2 SD higher oleic acid from vegetable sources (4.12 %kcal = about 9.8 grams/day) (model E). The relationships were stronger for non-intervened participants; estimated SBP and DBP differences with 2 SD higher intake were -1.26 mm Hg (Z-score -1.97; *P*<0.05) and -1.02 mm Hg (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 non-intervened participants (Table 2), with relationships weaker for non-intervened participants, non-significant 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 -1.7 mm Hg DBP with 2 SD higher MFA intake (approximately 13 grams/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), 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 where 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 non-intervened 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 favorable 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 non-intervened participants. Oleic acid in these analyses includes both *cis*- and *trans*-isomers, e.g., 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 such factors as *trans*-MFA could not be controlled in our study.

Limitations of the INTERMAP findings include the cross-sectional study design. However, our data are the only available extensive high-quality population-based data on dietary MFA and BP. Another 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-hr 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, i.e., improved nutrition is capable of preventing or lowering unfavorable 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., 2 mm Hg) is estimated to reduce mortality rates 6% for stroke, 4% for CHD [31]. Fourth, INTERMAP data also indicate low-order independent favorable influences on BP of food n-3 and n-6 PFA, vegetable protein, calcium, phosphorus, magnesium, non-heme 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 monounsaturated fatty acid intake, especially oleic acid from vegetable sources, may contribute to prevention and control of adverse blood pressure levels in general populations. These results lend support to current recommendations for increased ingestion of MFA from vegetable sources.

ACKNOWLEDGEMENTS

It is a pleasure to express appreciation to all INTERMAP staff at local, national, and international centers for their invaluable efforts; a partial listing of these colleagues is given in reference No. 13 of this paper.

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Table 1. Estimated mean difference in blood pressure (mm Hg) associated with total monounsaturated fatty acids (%kcal) higher by two standard deviations [a] (sequential regression models), INTERMAP.

		Systolic blood pressure		Diastolic blood pressure	
Model	Variables added sequentially [b]	Difference (mm Hg)	Z-score	Difference (mm Hg)	Z-score
		All participants (n=4,680)			
A		0.28 [c]	0.71	-0.11	-0.39
B	Urinary Na, urinary K, alcohol	0.32 [d]	0.78	-0.08	-0.28
C	Cholesterol, total SFA, calcium	0.05	0.08	-0.84	-2.02 [e]
D1	Fiber	0.09	0.15	-0.83	-2.00 [e]
D2	Phosphorus	-0.005	-0.01	-0.84	-2.02 [e]
D3	Vegetable protein	0.12	0.20	-0.82	-1.97 [e]
		Non-intervened participants (n = 2,238)			
C	Cholesterol, total SFA, calcium	-1.22	-1.33	-1.54	-2.43 [e]
D3	Vegetable protein	-1.29	-1.39	-1.70	-2.65 [f]

Na, sodium; K, potassium; SFA, saturated fatty acids.

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

[b] Model A includes sample, age, gender, body mass index, 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 non-intervened participants).

From model B to C, variables listed are added to each prior model. Models D1–D3 are adjusted for model C variables plus each stipulated nutrient.

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.

Test for cross-country heterogeneity significant at [c] $P<0.01$, [d] $P<0.05$.

[e] $P<0.05$, [f] $P<0.01$.

Table 2. Estimated mean difference in blood pressure (mm Hg) associated with oleic acid (%kcal) higher by two standard deviations [a] (sequential regression models), INTERMAP.

		Systolic blood pressure		Diastolic blood pressure	
Model	Variables added sequentially [b]	Difference (mm Hg)	Z-score	Difference (mm Hg)	Z-score
Total oleic acid (%kcal)					
	All participants (n=4,680)				
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	Non-heme iron, glutamic acid	0.20	0.32	-0.54	-1.27
	Non-intervened participants (n = 2,238)				
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	Non-heme iron, glutamic acid	-1.07	-1.11	-1.11	-1.64
Oleic acid from vegetable sources (%kcal)					
	All participants (n=4,680)				
C	Cholesterol, total SFA, calcium	-0.84	-2.06 [c]	-0.65	-2.33 [c]
D3	Vegetable protein	-0.74	-1.79	-0.59	-2.10 [c]
E	Non-heme iron, glutamic acid	-0.70	-1.69	-0.57	-2.01 [c]
	Non-intervened participants (n = 2,238)				
C	Cholesterol, total SFA, calcium	-1.28	-2.05 [c]	-1.01	-2.36 [c]

D3	Vegetable protein	-1.24	-1.97 [c]	-1.01	-2.33 [c]
E	Non-heme iron, glutamic acid	-1.26	-1.97 [c]	-1.02	-2.32 [c]
Oleic acid from animal sources (%kcal)					
	All participants (n=4,680)				
C	Cholesterol, total SFA, calcium	2.47	3.73 [d]	0.94	2.07 [c]
D3	Vegetable protein	2.37	3.58 [d]	0.86	1.91
E	Non-heme iron, glutamic acid	2.43	3.50 [d]	0.80	1.68
	Non-intervened participants (n = 2,238)				
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	Non-heme iron, glutamic acid	1.79	1.77	1.14	1.67

Na, sodium; K, potassium; SFA, saturated fatty acids.

[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 plus non-heme iron and glutamic acid.

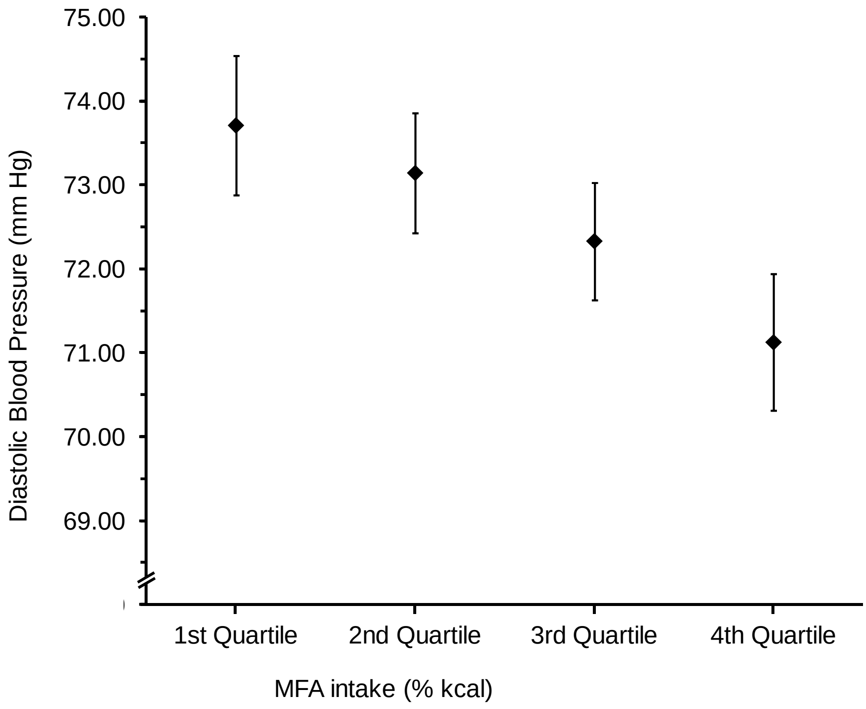
[c] *P*<0.05, [d] *P*<0.01.

All tests for cross-country heterogeneity are not significant.

Figure legends

Figure. Adjusted mean values of diastolic blood pressure by quartiles of total monounsaturated fatty acid intake (%kcal) in all participants (n=4,680). Mean values were adjusted for variables in model D3 (see Table 1 for variables). Cut-off values of the quartiles are 8.31%kcal, 10.48%kcal, and 12.72%kcal. *P* for trend was 0.036.

Figure.


75.00
74.00
73.00
72.00
71.00
70.00
69.00
Diastolic Blood Pressure (mm Hg)
1st Quartile
2nd Quartile
3rd Quartile
4th Quartile
MFA intake (% kcal)

Online Table 1. Descriptive statistics, mean (SD) or number (%), by country, men and women combined, INTERMAP.

Variable	Japan (n=1,145)		P. R. China (n=839)		UK (n=501)		USA (n=2,195)		All (n=4,680)	
	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)	Mean	(SD)
Age (years)	49.4	(5.3)	49.0	(5.8)	49.1	(5.6)	49.1	(5.4)	49.2	(5.5)
Systolic BP (mm Hg)	117.2	(13.8)	121.3	(17.4)	120.4	(14.6)	118.6	(13.9)	118.9	(14.7)
Diastolic BP (mm Hg)	73.6	(10.3)	73.2	(10.2)	77.3	(9.9)	73.4	(9.7)	73.8	(10.0)
Energy (kcal/24hr)	2038.6	(449.0)	2035.8	(576.8)	2167.8	(631.8)	2244.2	(698.7)	2148.4	(624.5)
Total fat (%kcal)	24.9	(5.0)	20.0	(6.1)	32.8	(6.5)	32.9	(6.9)	28.6	(8.2)
Total MFA (%kcal)	9.0	(2.2)	8.1	(2.8)	11.0	(2.5)	12.2	(2.9)	10.5	(3.2)
Oleic acid (%kcal)	8.0	(2.0)	6.7	(2.8)	10.0	(2.3)	11.6	(2.8)	9.6	(3.2)
Oleic acid from vegetable sources (%kcal)	4.7	(1.6)	4.0	(1.6)	5.8	(2.2)	6.7	(2.3)	5.6	(2.3)
Oleic acid from animal sources (%kcal)	3.3	(1.2)	2.7	(1.9)	4.2	(1.9)	4.9	(2.1)	4.0	(2.1)
Total SFA (%kcal)	6.6	(1.8)	5.0	(2.0)	12.1	(3.3)	10.7	(2.8)	8.8	(3.6)
Total PFA (%kcal)	6.4	(1.5)	5.8	(2.2)	6.2	(1.9)	7.0	(2.2)	6.5	(2.1)

continued on next page

Online Table 1 continued, page 2

Total fat (g/day)	56.8	(16.6)	45.9	(20.4)	81.0	(31.7)	84.4	(33.9)	70.4	(32.3)
Total MFA (g/day)	20.6	(6.7)	18.5	(8.6)	27.3	(11.0)	31.9	(13.5)	26.2	(12.5)
Oleic acid (g/day)	18.3	(6.2)	15.4	(8.2)	24.8	(10.0)	29.8	(12.6)	23.8	(12.0)
Oleic acid from vegetable souces (g/day)	10.7	(4.3)	9.3	(5.3)	14.4	(7.1)	17.3	(8.5)	13.9	(7.8)
Oleic acid from animal souces (g/day)	7.6	(3.4)	6.1	(5.6)	10.3	(6.2)	12.5	(7.1)	9.9	(6.6)
Total TFA (%kcal)	0.44	(0.30)	0.18	(0.34)	1.36	(0.61)	1.94	(0.80)	1.20	(0.98)
PFA/SFA ratio	1.09	(0.31)	1.39	(0.57)	0.60	(0.26)	0.74	(0.29)	0.93	(0.45)
Cholesterol (mg/1,000 kcal)	197.2	(66.9)	89.0	(85.9)	120.4	(48.3)	131.4	(58.8)	138.7	(75.0)
Animal protein (%kcal)	8.9	(2.4)	2.5	(2.4)	9.8	(3.3)	10.2	(3.2)	8.4	(4.1)
Vegetable protein (%kcal)	7.1	(1.1)	9.9	(1.3)	6.1	(1.4)	5.2	(1.6)	6.6	(2.2)
Glutamic acid (% total protein)	17.8	(1.4)	24.1	(4.4)	20.5	(1.6)	19.8	(1.7)	20.1	(3.1)
Calcium (mg/1,000 kcal)	305.6	(108.7)	149.3	(56.2)	445.4	(118.7)	363.0	(142.0)	319.4	(149.1)
Magnesium (mg/1,000 kcal)	134.4	(25.2)	154.6	(46.6)	153.3	(35.0)	148.1	(40.0)	146.5	(38.5)
Phosphorus (mg/1,000 kcal)	562.6	(94.4)	438.9	(113.2)	661.6	(126.1)	591.0	(124.6)	564.4	(132.7)

continued on next page

Online Table 1 continued, page 3

Non-heme iron (mg/1,000 kcal)	4.8	(1.1)	7.5	(1.6)	5.8	(1.5)	7.3	(2.7)	6.6	(2.3)
Fiber (g/1,000 kcal)	7.9	(2.3)	14.2	(3.8)	12.2	(3.8)	9.0	(3.4)	10.0	(4.0)
Vitamin E (mg/1,000 kcal)	4.9	(1.4)	5.3	(1.6)	4.5	(1.6)	4.5	(1.8)	4.7	(1.7)
7-Day alcohol [a] (g/24hr)	17.0	(22.6)	8.6	(21.4)	14.7	(19.2)	6.9	(13.7)	10.5	(18.8)
7-Day alcohol among drinkers [a] (g/24hr)	18.8	(23.0)	18.9	(28.4)	16.6	(19.6)	9.9	(15.4)	14.5	(20.7)
Urinary sodium (mmol/24hr)	198.3	(56.2)	227.5	(100.3)	145.2	(49.1)	162.6	(59.4)	181.1	(72.4)
Urinary potassium (mmol/24hr)	48.9	(13.6)	38.3	(12.7)	68.2	(20.1)	57.7	(20.9)	53.2	(20.0)
Height (m)	1.61	(0.09)	1.59	(0.08)	1.69	(0.09)	1.68	(0.10)	1.65	(0.10)
Weight (kg)	61.2	(10.2)	58.9	(10.0)	78.2	(15.3)	82.3	(19.6)	72.5	(19.0)
Body Mass Index (kg/m^2)	23.4	(2.9)	23.1	(3.4)	27.5	(4.6)	28.9	(5.9)	26.4	(5.5)
	n	(%)	n	(%)	N	(%)	n	(%)	n	(%)
Family history of hypertension in any first degree relative										
-Yes	528	(46.1)	298	(35.5)	242	(48.3)	1,491	(67.9)	2,559	(54.7)
-Unknown	406	(35.5)	188	(22.4)	188	(37.5)	489	(22.3)	1,271	(27.2)

continued on next page

Online Table 1 continued, page 4

Current alcohol drinkers	1,039	(90.7)	382	(45.5)	444	(88.6)	1,533	(69.8)	3,398	(72.6)
Current cigarette smokers	346	(30.2)	305	(36.4)	87	(17.4)	369	(16.8)	1,107	(23.7)
Special diet: weight loss, weight gain, vegetarian, salt reduced, diabetic, fat modified, or other	76	(6.6)	45	(5.4)	106	(21.2)	401	(18.3)	628	(13.4)
Taking dietary supplement	243	(21.2)	34	(4.1)	191	(38.1)	1,136	(51.8)	1,604	(34.3)
High blood pressure [b]	153	(13.4)	145	(17.3)	116	(23.2)	595	(27.1)	1,009	(21.6)
History of heart attack, other heart disease, stroke, or diabetes	131	(11.4)	59	(7.0)	54	(10.8)	343	(15.6)	587	(12.5)
Taking prescribed drug treatment for high BP, CVD [c], diabetes, or affecting cardiovascular system	124	(10.8)	86	(10.3)	98	(19.6)	644	(29.3)	952	(20.3)

BP, blood pressure; PFA, polyunsaturated fatty acids; SFA, saturated fatty acids; MFA, monounsaturated fatty acids; TFA, trans fatty acids; CVD, cardiovascular diseases.

[a] Average daily alcohol intake, from two histories per person of daily alcohol intake during the preceding 7 days.

[b] Systolic BP ≥140 mm Hg or diastolic BP ≥90 mm Hg or reporting use of medication for high BP

[c] Includes lipid-lowering drugs

Online Table 2. Foods contributing >1% of total monounsaturated fatty acid intake.

Japan (n=1145)			P. R. China (n=839)			UK (n=501)			USA (n=2195)		
Food source	**g/day**	**%**	**Food source**	**g/day**	**%**	**Food source**	**g/day**	**%**	**Food source**	**g/day**	**%**
Fats, oils & margarines	5.3	25.5	Fats, oils & margarines	9.4	50.5	Fats, oils & margarines	8.4	30.7	Fats, oils & margarines	10.3	32.3
Meats	4.1	19.8	Meats	3.7	20.0	Meats	5.8	21.1	Meats	8.2	25.8
Fish	1.9	9.2	Pasta, rice & noodles	1.3	6.7	Cakes, puddings, cookies & other sweet snacks	4.1	15.1	Milk & cheese	2.4	7.5
Condiments & seasonings	1.8	8.5	Eggs	0.9	5.0	Milk & cheese	2.4	8.7	Condiments & seasonings	2.0	6.2
Eggs	1.7	8.1	Grains & flour	0.9	4.9	Savoury snacks	1.0	3.8	Cakes, puddings, cookies & other sweet snacks	1.9	5.9
Milk & cheese	1.2	5.6	Nuts & seeds	0.9	4.8	Bread, rolls, biscuits	1.0	3.6	Nuts & seeds	1.8	5.5
Cakes, puddings, cookies & other sweet snacks	1.1	5.3	Bread, rolls, biscuits	0.6	3.0	Eggs	0.7	2.5	Bread, rolls, biscuits	1.4	4.3
Vegetarian meat substitutes	1.0	4.6	Cakes, puddings, cookies & other sweet snacks	0.3	1.5	Soup, gravy & sauces	0.7	2.4	Eggs	1.1	3.3
Pasta, rice & noodles	0.7	3.6	Vegetarian meat substitutes	0.3	1.5	Nuts & seeds	0.6	2.3	Ice-cream & frozen treats	0.6	1.9
Bread, rolls, biscuits	0.6	2.9	Fish	0.2	1.1	Condiments & seasonings	0.5	1.7	Savoury snacks	0.6	1.9
Nuts & seeds	0.6	2.8				Fish	0.4	1.5	Other dairy products	0.4	1.1
Other dairy products	0.3	1.5				Other dairy products	0.4	1.4			
						Vegetables & beans	0.4	1.3			

	Cereals	0.3	1.1

Online Table 3. Partial correlation coefficients [a] of monounsaturated fatty acids, oleic acid with other variables.

Variable	Total MFA	Oleic acid	Oleic acid from vegetable sources	Oleic acid from animal sources
Total MFA	1	0.98	0.64	0.60
Oleic acid	0.98	1	0.68	0.58
Oleic acid from vegetable sources	0.64	0.68	1	-0.20
Oleic acid from animal sources	0.60	0.58	-0.20	1
Total energy	0.16	0.15	0.11	0.08
Total fat	0.94	0.93	0.58	0.60
Total SFA	0.73	0.72	0.22	0.73
Total PFA	0.52	0.54	0.63	0.03
Total n-3 PFA	0.34	0.27	0.30	0.04
Total n-6 PFA	0.51	0.54	0.63	0.02
PFA/SFA ratio	-0.18	-0.17	0.26	-0.52
Keys score	0.55	0.53	-0.04	0.76
Dietary cholesterol	0.37	0.35	-0.04	0.52
Total TFA	0.45	0.46	0.42	0.15
Animal protein	0.19	0.17	-0.18	0.42
Vegetable protein	-0.33	-0.31	-0.01	-0.40
Glutamic acid	-0.03	-0.04	-0.14	0.13
Calcium	-0.09	-0.10	-0.10	-0.02
Magnesium	-0.28	-0.27	-0.09	-0.25
Phosphorus	-0.13	-0.14	-0.19	0.04
Non-heme iron	-0.15	-0.14	-0.03	-0.14

Fiber	-0.29	-0.27	-0.06	-0.29
Vitamin E	0.26	0.26	0.43	-0.12
7-day alcohol	-0.09	-0.09	-0.11	0.00
Urinary Na	0.09	0.09	0.01	0.11
Urinary K	-0.08	-0.08	-0.03	-0.06
Urinary Na/K ratio	0.13	0.13	0.02	0.14
Height	0.06	0.05	0.05	0.02
Weight	0.13	0.12	0.02	0.14
BMI	0.11	0.10	0.00	0.14

MFA, monounsaturated fatty acids; SFA, saturated fatty acids; PFA, polyunsaturated fatty acids; TFA, trans fatty acids; Na, sodium; K, potassium; BMI, body mass index.

Variables are %kcal (total MFA, oleic acid, total fat, total SFA, total PFA, n-6 PFA, n-3 PFA, TFA, animal protein, vegetable protein, glutamic acid), kcal (energy), mg/1,000 kcal (cholesterol, calcium, magnesium, phosphorus, vitamin E), g/1,000 kcal (fiber), g/24-h (7-day alcohol), mmol/24-h (urinary Na, urinary K), m (height), kg (weight), kg/m^2 (BMI).

[a] Pooled by country (weighted by n), adjusted for age, gender, centre.

Online Table 4. Country specific estimated mean difference in blood pressure (mm Hg) associated with total monounsaturated fatty acids (%kcal) higher by two standard deviations [a] (model D3 [b]), INTERMAP.

Country	n	Systolic blood pressure		Diastolic blood pressure	
		Difference (mm Hg)	Z-score	Difference (mm Hg)	Z-score
All participants (n=4,680)					
Japan	1145	-0.34	-0.23	-0.38	-0.35
PRC	839	-1.18	-0.60	-2.70	-2.35 [c]
UK	501	0.86	0.47	0.73	0.58
USA	2195	0.32	0.42	-0.80	-1.49
Non-intervened participants (n = 2,238)					
Japan	695	-1.16	-0.66	-0.25	-0.19
PRC	691	-2.31	-1.11	-3.17	-2.55 [c]
UK	204	-4.12	-1.40	-2.15	-1.13
USA	648	-0.23	-0.16	-1.43	-1.39

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

[b] See Table 1 for variables adjusted in model D3.

[c] $P<0.05$