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Relation of Nutrient Intake to Microalbuminuria in Nondiabetic Middle-Aged Men and Women: International Population Study on Macronutrients and Blood Pressure (INTERMAP)

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Abstract

Background: Microalbuminuria (MA) is a risk factor for cardiovascular and renal disease. However, little is known about the relation of nutritional factors to MA, especially in individuals without diabetes.

Methods: Data collected by the International Population Study on Macronutrients and Blood Pressure from 1997 to 1999 were used to assess relations of multiple dietary factors (energy intake, macronutrients, and micronutrients) independent of lifestyle related cardiovascular risk factors to MA (urinary albumin excretion, 30 to <300 mg/24 h). The study population included 4,381 Chinese, Japanese, UK, and US men and women without diabetes aged 40 to 59 years (17 population samples) without macroalbuminuria.

Results: MA prevalences ranged from 3.1% to 5.5% for men and 2.6% to 4.6% for women in the 4 countries. With adjustment for age and country, the following nutrients considered singly (of 29) were related in logistic regression analyses to MA prevalence ($P < 0.05$): for men, inversely, iron, vitamin C and E, estimated total simple sugar, ω−6 fatty acid, polyunsaturated fatty acid, and calcium (all expressed as caloric density) intake; for women, directly, 24-hour urinary sodium excretion and alcohol intake. In multivariate analyses, sugar, iron, polyunsaturated fats, and vitamin C and E intake (in men) and alcohol intake (women only) remained associated with MA ($P < 0.05$). MA also was related directly to body mass index ($P < 0.05$), blood pressure ($P < 0.001$), and smoking ($P > 0.05$) and inversely to education ($P < 0.05$ in women).

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Conclusion: In cross-sectional analyses, several nutrients were related to MA among men. Additional studies are required to confirm these findings. *Am J Kidney Dis* 45:256–266.

INDEX WORDS

Population study; nutrient intake; lifestyles; cardiovascular risk factors; microalbuminuria (MA)

MICROALBUMINURIA(MA), urinary albumin excretion of 30 to less than 300 mg/d, is associated with increased risk for renal and cardiovascular disease (CVD) morbidity and mortality in both diabetic and hypertensive individuals.[1–5] In individuals with diabetes, MA, a clinical sign of nephropathy, was associated with major CVD risk factors.[6,7] In studies including persons without diabetes, MAwas related to diet-dependent major CVD risk factors (blood pressure [BP], serum cholesterol level, and body mass index [BMI]) and other lifestyle factors (cigarette smoking, alcohol consumption),[7–11] as well as future CVD and non-CVD mortality.[5,12,13]

Previous studies[14–20] of relations of dietary factors to MA have focused on the impact of dietary protein intake, particularly in persons with diabetes.[14–19] No study systematically explored relations of multiple nutrients to MA independent of CVD risk factors and other lifestyle factors among men and women without diabetes. It remains undetermined whether MA reflects early vascular damage attributable in part to adverse dietary traits associated with cardiovascular risk.

This report describes relationships of MA with multiple nutrients (macronutrients and micronutrients) in population-identified middle-aged men and women without diabetes from 4 countries (China, Japan, the United Kingdom, and the United States).

METHODS

Participants

The International Population Study on Macronutrients and Blood Pressure (INTERMAP) is a cross-sectional investigation of relations between nutrients and BP. It includes 4,680 men and women aged 40 to 59 years from 17 diverse population samples in Japan (4 samples), the People's Republic of China (3 samples), the United Kingdom (2 samples), and the United States (8 samples).[21] Each sample was selected randomly from an age- and sex-stratified population list to give approximately equal numbers (69 people) in each of four 10-year age and sex groups (men, women, and ages 40 to 49 and 50 to 59 years). The protocol received institutional review board approval at each center before commencement of the study.

Data Collection

Each participant attended the local INTERMAP research center on 4 occasions: 2 visits on consecutive days with an additional 2 visits on consecutive days 3 to 6 weeks later. When possible, 1 visit by each participant included a weekend day (or an equivalent rest day) according to work schedule. All data were collected by trained and certified staff using high-quality standardized methods. Written informed consent was obtained from each participant.

BP and other data.—BP of the seated participant was measured twice per visit (4 different days) using a random zero sphygmomanometer after at least 5 minutes' rest.[21] Pulse was measured 3 times per visit. Height and weight without shoes were measured at the first and third visits. BMI was calculated as weight divided by height squared (kilograms/square meters). Data for demographic and other factors, including education, leisure-time and work-related physical activity, smoking, previous medical history, current special diet (ie, nonhabitual diet for weight loss or gain, salt- or fat-modified diet, or vegetarian or diabetic diet), and medication use were collected by interviewer-administered questionnaires.

Dietary data.—Dietary data were collected at each of the 4 visits by using the multiple-pass 24-hour recall method.[22] All foods and beverages consumed in the previous 24 hours were recorded in an interview by trained and certified staff, predominantly dieticians. To aid accurate recall, fresh foods of varied standardized portion sizes, food and drink models, containers of various types and sizes, and photographs, specific to each country and standardized within country, were used. Interviewers used neutral probing techniques and such details as brands of foods, quantities, processing methods, additions in cooking and/or at table, and amounts left on plate to check for completeness of items reported. In the United States, dietary information was directly computerized with the use of a program to guide on-screen coding. In the other 3 countries, data were entered onto standard forms and coded, then computerized twice by 2 separate trained staff members. Discrepancies were adjudicated, and final corrections were made. Nutrient intakes of participants were calculated from special country-specific food tables compiled and enhanced from national food tables for each country and made comparable by the Nutrition Coordinating Center in Minneapolis, MN.[23] The Nutrition Coordinating Center provided nutrient content of foods not included in national nutrient databases in each of the 4 countries and checked and updated data for other foods. Daily alcohol consumption (amount and type of alcoholic beverage) during the previous 7 days and, for abstainers, information on previous drinking were obtained by interview twice, at the first and third visits. These data were in addition to data for alcohol intake from the 4 dietary recalls.

Multiple methods were used for standardization and ongoing quality control of dietary data collection and processing at the local, national, and international levels.[22] These included central training and certification for all dietary interviewers, a dry run before the start of field work, monitoring of interviewers during field work, audiotape recording of all interviews and review of randomly selected tapes by site and country nutritionists, and recoding of a 10% random sample of dietary records by country nutritionists.

Urinary data.—Two timed 24-hour urine specimens were collected for measurement of urinary albumin, sodium, potassium, creatinine, urea nitrogen, and multiple other metabolites. Timed collections were started at the research center on the first and third visits and completed at the center the next day. Urine aliquots were stored frozen at [H11002]20°C before being shipped frozen to the Central Laboratory in Leuven, Belgium, where analyses were performed using strict internal and external quality control. Urinary samples were thawed to room temperature, homogenized manually, and pretested for albumin by using

Albustix (Bayer, Brussels, Belgium). Urinary albumin was quantitatively determined by means of immunoturbidimetric assay using automated clinical chemistry analyzers (Roche/Hitachi 717; Roche Diagnostics, Indianapolis, IN). The lowest detectable level of albumin was 1 mg/L. Sodium and potassium were measured by means of emission flame photometry; creatinine, by means of the modified Jaffé method; and urea nitrogen, by means of autoanalyzer, with use of an adaptation of the Fearon condensation method. Individual excretion values were calculated as the product of concentrations in urine and urinary volumes corrected to 24 hours. The average of the 2 excretion values was used.

Exclusions

Of 4,680 participants, 299 individuals were excluded for the following reasons: missing data for MA (n = 2) and diagnosis of diabetes or on antidiabetic treatment (n = 276). Of the latter, 35 persons (12.7%) had MA and 16 persons (5.8%) had macroalbuminuria (urinary albumin excretion ≥ 300 mg/d). An additional 21 participants without diabetes with macroalbuminuria (0.5%) also were excluded, leaving 4,381 individuals (2,200 men, 2,181 women; 35.7% non-Hispanic whites, 7.6% blacks, 30.3% Japanese, 19.1% Chinese, and 5.6% Hispanics).

Statistical Analyses

All analyses were conducted separately for men and women. Prevalence rates of MA were calculated for each country and the entire sample. Mean values for urinary albumin excretion, other urinary measures, risk factors, and dietary factors were calculated for 2 strata of urinary albumin excretion: MA-negative (ie, albumin < 30 mg/d) and MA-positive (ie, albumin ≥ 30 to < 300 mg/d). Age- and country-adjusted and multivariate-adjusted logistic regression analyses were used to estimate the odds of MA (yes, no) in relation to nutrient intake. Variables in the final multivariate models were selected on the basis of prior literature on risk factors for MA or their significance in the age- and country-adjusted univariate logistic results. Because of a paucity of prior population-based data, analyses on relations of macronutrients and micronutrients to MA are considered exploratory, rather than hypothesis testing. *P* values are given as guides to interpretation.

RESULTS

MA, Demographic, and Risk Factor Data by Sex and Country

For these middle-aged population samples, MA prevalences were similar for men (3.8%) and women (3.9%). Mean urinary albumin excretion for persons with MA was 94.6 ± 63.5 mg/24 h for men and 87.7 ± 61.6 mg/24 h for women. Table 1 lists prevalence of MA, mean urinary albumin excretion for persons with MA, and known risk factors for MA by sex and country. MA prevalence was highest in Japanese men (5.5%) and lowest in British women (2.6%). On average, Chinese participants had notably lower educational levels, smoked more cigarettes per day (men only), and had greater mean levels of physical activity than participants from other countries. Alcohol intake was greatest among Japanese men. Both mean BMI and educational attainment levels were greatest among US participants.

Descriptive Characteristics for Men and Women With and Without MA

Participants with MA were on average slightly younger (particularly women), had fewer mean years of education, a greater mean BMI, and considerably greater systolic and diastolic BP. Mean systolic BP levels were 131.3 and 120.1 mm Hg for men and 126.0 and 116.2 mm Hg for women with and without MA, respectively. The percentage of participants administered antihypertensive medication also was greater among persons with MA (men, 31.3% with MA compared with 13.2% without MA; women, 27.9% with MA and 14.1% without MA). A greater proportion of men with MA were current smokers and drinkers (results not tabulated). Table 2 lists nutrient intake and urinary characteristics for men and women without and with MA. Differences in dietary variables between those without and with MA were small. Individuals with MA had greater dietary cholesterol and alcohol intake and lower (particularly in men) fiber, sugar, calcium, magnesium, and vitamin C intake. Urinary volume and sodium excretion in 24 hours were greater in individuals with than without MA.

Age- and Country-Adjusted Univariate Analyses

Table 3 lists age- and country-adjusted odds ratios (ORs) and *P* from logistic regression analyses for the relation of each nutrient (considered singly) to MA for men and women. Sodium and potassium values were based on urinary measurements, generally recognized to be more valid than dietary measures. In men, total estimated sugar, ω−6 fatty acid, polyunsaturated fatty acid, calcium, vitamin E ($P < 0.05$), vitamin C, and iron intake ($P < 0.01$) were associated inversely with MA; special diet was related directly to MA ($P < 0.01$). Vegetable protein, fiber, and vitamin A intake also were related inversely, and urinary sodium level and sodium-potassium ratio were related directly to MA (*P* ranging from 0.079 to 0.334). In women, urinary sodium level and alcohol intake were related directly to MA ($P < 0.05$). Total estimated sugar, ω−6 fatty acid, fiber, and vitamin C and E intake also were related inversely, and special diet and urinary sodium-potassium ratio were related directly to MA (*P* ranged from 0.057 to 0.637).

Because dietary intake may vary by ethnicity and associations of dietary factors with MAmay be affected by both ethnicity and smoking status, we tested for interactions of these factors with dietary variables in relation to MA. Significant interactions ($P < 0.05$) were found between ethnicity and both alcohol intake (grams per day) and use of a special diet in men and between ethnicity and alcohol intake (both as percentage of kilocalories and grams per day) in women. Also, in men, there was a significant interaction ($P < 0.05$) between cigarette smoking and use of a special diet.

In age- and country-adjusted analyses, BMI, BP (systolic, diastolic, and use of antihypertensive medication), and urinary volume (men only) were associated directly with MA ($P < 0.001$) and education was associated inversely with MA ($P = 0.008$ for women). Other results are listed in Table 3 footnotes. Cigarette smoking was associated directly with MA ($P = 0.319$ for men and $P = 0.576$ for women).

Multivariate Analyses

Based on the foregoing results, multivariate analyses were performed for selected variables (Table 4). With the inclusion of systolic BP and cigarette smoking (model I), associations of sugar, polyunsaturated fatty acid, iron, and vitamin C and E intake and special diet with MA persisted in men. The inclusion of BMI (model II), education, or physical activity (hours of moderate/heavy activity per day, variables associated with specific nutrients and potentially representing overadjustment, especially BMI and education, did not substantially alter the foregoing relationships. Additional adjustment for education or physical activity yielded similar associations with MA for vitamin C (OR, 0.74; $P = 0.048$; OR, 0.72; $P = 0.035$, respectively) and vitamin E (OR, 0.67; $P = 0.015$; OR, 0.65; $P = 0.010$, respectively). Adjustment for antihypertensive drug treatment (model III), which may affect urinary albumin excretion, had little effect on the findings. Associations of vitamin C and E, sugar, polyunsaturated fat, and iron intake with MA apparently were robust. In women, alcohol intake was associated with MAwith adjustment for education ($P = 0.042$). BMI and systolic BP remained associated positively with MAin all models ($P < 0.05$ and $P < 0.001$, respectively).

DISCUSSION

The findings of this study of middle-aged adults without diabetes from 4 countries are as follows. (1) MA prevalence was similar for men and women; it varied slightly by country of origin. (2) In analyses controlled for age and country, several nutrients considered singly were related to MA ($P < 0.05$): inversely, sugar, iron, ω−6 fatty acid, polyunsaturated fatty acid, calcium, and vitamin C and E intake (all for men only); directly, 24-hour urinary sodium excretion and alcohol intake (for women only). (3) In multivariate analyses, sugar, iron, polyunsaturated fat, and vitamin C and E intake (all for men only) were related inversely and alcohol intake (for women only) was associated directly with MA ($P < 0.05$). Additionally, in age- and country-adjusted analyses, BMI, BP (systolic, diastolic, or antihypertensive medication use), and urinary volume (men only) were directly related and education (women only) was inversely related ($P < 0.01$) to MA. Cigarette smoking also was (nonsignificantly) associated directly with MA. In multivariate analyses, systolic BP remained associated positively with MA ($P < 0.01$).

Previous reports of MA prevalence in various adult populations have ranged widely from 23% to 50% in individuals with diabetes and 2% to 13% in those without diabetes.[13,24–26] Data from the Third National Health and Nutrition Examination Survey showed that in 4,229 US adults aged 40 to 59 years, the prevalence of MA determined from a single untimed (spot) urine sample was approximately 6%; for those free of diabetes, hypertension, CVD, and elevated serum creatinine levels, MA prevalence was approximately 3%.[26] In our study, the prevalence of MA (defined as mean urinary albumin excretion from two 24-hour urine collections) in men and women without diabetes was, in general, less than previously reported.

Studies of dietary factors and MA to date have involved mainly individuals with diabetes; results have been conflicting. A cross-sectional study of 178 Tasmanian adults (mean age, 39.4 ± 12.8 years) with insulin-dependent diabetes mellitus, with usual dietary intake

measured by means of a food frequency questionnaire, reported that dietary saturated fat intake was associated positively and dietary protein intake was associated inversely with MA, after adjustment for age, sex, diabetes duration, insulin therapy, glycated hemoglobin level, BMI, serum high-density lipoprotein cholesterol level, exercise frequency, and smoking status. Compared with the lowest quintile of intake (percentage of total energy) of saturated fat (<13.1%) and protein (<16.5%), ORs for MA for the highest quintile of saturated fat (≥19.2%) and protein intake (≥20.5%) were 4.9 (95% confidence interval [CI], 1.2 to 20.0; $P = 0.03$) and 0.10 (95% CI, 0.02 to 0.56; $P = 0.01$), respectively. For participants with and without MA, mean protein intake (percentage of energy) was 18.2 ± 2.1 and 18.9 ± 3.0, and mean saturated fat intake (percentage of energy) was 17.2 ± 3.7 and 16.0 ± 3.2. There were no significant associations between MA and intake of carbohydrates or monounsaturated or polyunsaturated fat.[14] Conversely, in a cross-sectional study of 2,696 European men and women aged 15 to 60 years with insulin-dependent diabetes, mean albumin excretion rate was less than 20 μg/min (~30 mg/24 h) for persons with protein intake of 20% or less of total energy intake and was elevated in persons with dietary protein intake greater than 20% of total energy intake. Dietary intake was ascertained by means of a standardized 3-day dietary record, with individuals instructed by dietitians on how to report all foods and beverages consumed during 3 days (2 work days and a Sunday).[15] Other studies using 3-day diet recalls[16] or 7-day diet histories to assess food intake[17] reported no significant differences in dietary protein intake in individuals with insulin-dependent diabetes with and without MA. Findings for dietary fat intake also have been conflicting.[16,17]

The few reports of healthy populations also have been inconsistent, with results differing from those in persons with diabetes and/or hypertension. In the Third National Health and Nutrition Examination Survey, MA prevalence was not associated with dietary total protein intake (expressed as percentage of total energy intake and assessed from only one 24-hour dietary recall) in healthy participants without diabetes and without hypertension (n = 8,421; OR, 0.74; 95% CI, 0.45 to 1.23) for the highest (≥19.0%) versus the lowest quintile (<11.7%) of protein intake or in those with isolated systolic hypertension (n = 2,792; OR, 1.12; 95% CI, 0.66 to 1.92) or diabetes (n = 526; OR, 1.19; 95% CI, 0.31 to 4.60). However, in 634 individuals with both diabetes and hypertension, high dietary protein intake was associated significantly with MA (OR, 3.31; 95% CI, 1.39 to 7.84).[18] In 638 men and women aged 50 to 75 years (including persons with diabetes and normal and impaired glucose tolerance) from the Hoorn Study in The Netherlands, there was a positive association between dietary protein intake and prevalence of MA after adjustment for age, sex, hypertension, glucose tolerance status, and homocysteine level. Each 0.1g/kg/d greater protein intake was associated with a 20% greater risk for MA (OR, 1.20; 95% CI, 1.08 to 1.32). The association remained significant after exclusion of persons with diabetes. Dietary protein intake was measured by using a self-administered semi quantitative food frequency questionnaire.[19] In a report by Metcalf et al[20] on the relation between diet and slight albuminuria in 5,416 men and women aged 40 to 78 years from New Zealand, usual dietary intake during the preceding 3 months was assessed by using a food frequency questionnaire (modified to include local food items). Age-, sex-, and ethnicity-adjusted relative risks for small elevations in urinary albumin levels were significantly greater in persons reporting

dietary cholesterol consumption greater than 226 mg/d and significantly lower in those who consumed more than 26 g/d of fiber compared with others. A direct nonsignificant relation was reported with dietary protein.[20] In multivariate analyses, significant regression coefficients were observed for dietary fiber and dietary cholesterol independent of age, sex, ethnicity, BMI, diastolic BP, serum triglyceride level, and other variables. Although protein intake was significantly greater in persons with slight albuminuria, in multivariate regression analyses, dietary protein did not remain significant after adjustment for dietary cholesterol. These results may have been influenced by the inclusion of individuals with diabetes.[20] No significant relation was noted for difference in sugar intake to MA.

We found significant inverse associations between sugar consumption and MA in men. The direction of our other findings generally was consistent with those of the New Zealand study, [20] ie, MA was associated inversely with fiber intake and directly with dietary cholesterol and protein; however, *P* for these associations (age-, sex-, and country-adjusted) were greater than 0.10. No previous study systematically examined their relations with MA in men and women; we registered *P* less than 0.05 for age- and country-adjusted inverse associations of sugar, iron, ω–6 fatty acid, polyunsaturated fatty acid, calcium, and vitamin C and E intake with MA in men and for direct associations of alcohol intake and sodium excretion with MA in women.

In our study, we assessed relations of MA with urinary sodium excretion as an indicator of sodium intake. Measurement of sodium excretion in a 24-hour urine collection has been reported to represent approximately 85% to 90% of sodium intake estimated by dietary recall[27] and likely is the more reliable estimate of sodium intake.[28] Previous studies reporting the relation of sodium intake with urinary albumin excretion also relied on urinary sodium excretion to estimate sodium intake. In a cross-sectional study of 7,850 men and women aged 25 to 78 years from The Netherlands, dietary sodium intake (estimated by means of urinary sodium excretion from morning urine samples) was related positively to urinary albumin excretion independent of other cardiovascular risk factors and other food constituents (calcium, potassium, and protein), especially in overweight and obese individuals.[29] Similarly, du Cailar et al[30] reported that sodium intake (measured by means of urinary sodium excretion from 2 consecutive 24-hour urine collections) was a strong and independent determinant of urinary albumin excretion in 839 men and women aged 15 to 70 years.

Dietary factors are thought to have a role in the production of increased urinary albumin excretion, but few mechanisms have been postulated, eg, dietary protein restriction reduces excretion of urinary albumin and high-protein diets increase renal workload and proteinuria in people with renal disease.[31] Our study suggests independent associations of several nutrient intakes with MA among men. Although findings generally were similar in women, *P* values mostly were greater than 0.05. Although additional studies are required to validate these results, the high-quality INTERMAP dietary data, a result of meticulous data collection methods (including multiple recalls that enabled measurement of intraindividual variability in nutrient intake and use of mean values yielding greater reliability for each person, as well as reduced interindividual measurement variability) and multiple quality control procedures make it unlikely that findings are false-positive results.

Previous studies that examined individuals without diabetes found significant associations of MA with BP,[8–10] cigarette smoking,[8] serum cholesterol level,[8] and BMI.[8,9] Another study of the New Zealand cohort reported significant associations of MAwith heavy alcohol consumption; however, the cohort included a small proportion (~3%) of individuals with diabetes.[11] The association of alcohol consumption and MA in this cohort possibly may have been mediated by alcohol-induced hypertriglyceridemia because this finding was no longer significant after adjustment for serum triglyceride levels, and another report of the same cohort also described strong relationships between slight albuminuria and serum triglyceride level.[32] Our study confirms previous findings showing that BP, BMI, and alcohol consumption (women only) are directly related and education is inversely and independently related to MA in middle-aged populations without diabetes. In 1,567 nondiabetic middle-aged men and women from the Gubbio study, logarithm-transformed alcohol intake was significantly associated with logarithm-transformed albumin excretion in univariate analyses for women only, similar to our findings. However, in multivariate analyses, there was no significant association of alcohol intake with albumin excretion, possibly because of the inclusion of plasma triglyceride level in the models.[8] Our results also show a direct relationship of cigarette smoking with MA, although findings were not significant in men or women ($P > 0.05$), possibly because of a low prevalence of cigarette smoking among INTERMAP participants. BMI and BP are both diet-dependent major CVD risk factors that stem from adverse dietary habits, as well as lack of physical activity. The association of BMI with MA is of great public health importance because overweight and obesity, a major independent CVD risk factor,[33] has increased markedly in men and women of all ages, ethnicities, and socioeconomic backgrounds in the United States and other countries during the last few decades.[34–36] As a result, the incidence and prevalence of diabetes, a risk factor for MA, also has increased.[37,38]

One limitation of our study is the unavailability of data for specific foods and food groups. Hence, the relationship of MA to specific foods could not be explored. In addition, it was not possible to conduct meaningful analyses using albumin excretion as a continuous variable because of the highly skewed distribution of albumin levels. However, MA defined by using similar cutoff values in persons without diabetes previously was associated with nondietary risk factors (BP and serum cholesterol level) and BMI in middle-aged individuals.[8]

In conclusion, exploration for nutritional factors related to MA in a large, multicultural, diverse group of individuals without diabetes identified several independent associations in men. Our findings on the associations of MA with BP, BMI, education, and smoking are consistent with results of prior studies. Control of these factors likely is important for the prevention of MA.

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Table 1.

MA, Demographic, and Risk Factor Data by Sex and Country for 4,381 INTERMAP Participants

	Men				Women			
Characteristics (unit)	**Japan (n = 531)**	**China (n = 410)**	**United Kingdom (n = 259)**	**United States (n= 1,000)**	**Japan (n = 553)**	**China (n = 409)**	**United Kingdom (n = 231)**	**United States (n = 988)**
MA [*] (%)	5.5	3.7	3.1	3.1	3.3	4.2	2.6	4.6
Urinary albumin (mg/24 h) [†]	97.3 ± 60.0	93.4 ± 73.0	90.5 ± 87.9	93.8 ± 57.9	117.1 ± 76.3	70.9 ± 46.4	98.6 ± 76.6	81.0 ± 55.8
Age (y)	49.3 ± 5.3	49.0 ± 6.0	49.6 ± 5.6	48.9 ± 5.4	49.2 ± 5.3	48.9 ± 5.6	48.6 ± 5.6	49.0 ± 5.4
Education (y)	12.4 ± 2.1	6.5 ± 2.4	13.2 ± 3.1	15.5 ± 3.1	11.6 ± 2.0	4.3 ± 2.9	12.2 ± 2.9	14.6 ± 2.8
BMI (kg/m^2) [‡]	23.7 ± 2.7	22.4 ± 2.7	27.6 ± 3.9	28.8 ± 5.0	23.1 ± 3.0	23.8 ± 3.7	27.1 ± 5.3	28.3 ± 6.5
Systolic BP (mm Hg) [§]	120.1 ± 13.0	120.9 ± 17.2	123.7 ± 14.3	119.7 ± 12.3	113.9 ± 3.8	121.5 ± 17.9	116.4 ± 13.7	116.1 ± 14.2
Systolic BP (mm Hg) [§]	76.8 ± 10.1	73.7 ± 10.3	80.8 ± 9.0	75.6 ± 9.5	70.4 ± 9.5	121.5 ± 17.9	73.2 ± 9.3	71.2 ± 9.1
Drug treatment for hypertension	30 (5.7)	22 (5.4)	35 (13.5)	180(18.0)	34 (6.2)	38 (9.3)	27 (11.7)	204 (20.7)
Smoking status								
Never	124 (23.4)	67 (16.3)	120 (46.3)	458 (45.8)	497 (89.9)	385 (94.1)	141 (61.0)	597 (60.4)
Former	135(25.4)	63 (15.4)	95 (36.7)	354 (35.4)	9 (1.6)	4 (1.0)	48 (20.8)	247 (25.0)
Current	272 (51.2)	280 (68.3)	44 (17.0)	188 (18.8)	47 (8.5)	20 (4.9)	42 (18.2)	144 (14.6)
No. of cigarettes/d	11.5 ± 13.1	15.2 ± 13.9	2.5 ± 6.9	3.2 ± 8.4	1.0 ± 3.8	0.7 ± 3.3	2.3 ± 6.0	2.1 ± 6.2
Physical activity (h/d)	1.5 ± 3.6	5.2 ± 3.8	2.5 ± 6.9	3.2 ± 8.4	1.0 ± 3.8	0.7 ± 3.3	2.1 ± 2.1	3.0 ± 3.0
Drinking status								
Never	12 (2.3)	81 (19.8)	9 (3.5)	57 (5.7)	67 (12.1)	320 (78.2)	23 (10.0)	156 (15.8)
Former	4 (0.8)	30 (7.3)	11 (4.3)	169 (16.9)	22 (4.0)	10 (2.4)	12 (5.1)	189 (19.1)
Current	515 (97.0)	299 (72.9)	239 (92.3)	774 (77.4)	464 (83.9)	79 (19.3)	196 (84.9)	643 (65.1)
Alcohol intake (g/d)	30.0 ± 24.5	17.1 ± 28.1	20.5 ± 22.8	10.6 ± 16.9	3.8 ± 8.0	0.5 ± 2.2	8.6 ± 11.6	3.6 ± 7.6

NOTE. Values expressed as mean ± SD or number (percent).

[*] Defined as urinary albumin excretion (the mean of two 24-hour urine collections) of 30.0 to less than 300.0 mg/24 h.

[†] Data presented for persons with MA only.

[‡] BMI, computed as weight in kilograms divided by square of height in meters, is the mean of 2 measurements over 2 visits about 3 to 6 weeks apart.

[§] Systolic and diastolic BPs are the mean of 8 readings over 4 visits.

Table 2.

Nutritional and Urinary Characteristics for 4,381 INTERMAP Participants by Sex and Urinary Albumin Excretion

	Urinary Albumin Excretion* (mg/24 h)			
	Men		Women	
Characteristics (unit)	<30 (n = 2,117)	30–299.9 (n = 83)	<30 (n = 2,095)	30–299.9 (n = 86)
Dietary characteristics†				
Total energy intake (%kcal)15.0	2,468.8 ± 611.9	2,445.2 ± 733.3	1,820.9 ± 427.0	1,871.1 ± 493.8
Animal protein (%kcal)	15.0 ± 3.0	15.3 ± 2.7	15.1 ± 3.0	15.0 ± 3.5
Animal protein (%kcal)	8.4 ± 4.1	8.7 ± 3.8	8.2 ± 4.0	8.3 ± 4.6
Vegetable protein (%kcal)	6.5 ± 2.3	6.5 ± 2.5	6.8 ± 2.2	6.6 ± 2.4
Total protein (g/d)	90.9 ± 26.3	92.1 ± 28.8	67.5 ± 18.5	70.1 ± 24.3
Animal protein (g/d)	51.4 ± 27.9	53.5 ± 28.8	37.1 ± 19.6	39.8 ± 24.9
Vegetable protein (g/d)	38.8 ± 15.0	37.8 ± 15.3	30.1 ± 11.2	29.8 ± 13.3
Total available carbohydrate (%kcal)	51.8 ± 10.0	51.3 ± 11.4	55.2 ± 9.8	54.8 ± 11.1
Total fat (%kcal)	28.5 ± 8.2	27.0 ± 9.0	28.3 ± 8.0	28.3 ± 8.7
Saturated fatty acids (%kcal)	8.7 ± 3.6	8.2 ± 4.0	8.8 ± 3.6	8.7 ± 3.8
Polyunsaturated fatty acids (%kcal)	6.5 ± 2.0	6.0 ± 1.8	6.5 ± 2.0	6.5 ± 2.0
Monounsaturated fatty acids (%kcal)	10.5 ± 3.2	10.1 ± 3.4	10.4 ± 3.1	10.4 ± 3.3
ω−3 Fatty acids (%kcal)	0.8 ± 0.4	0.9 ± 0.5	0.9 ± 0.5	0.9 ± 0.4
ω−6 Fatty acids (%kcal)	5.7 ± 2.0	5.1 ± 1.6	5.7 ± 1.9	5.6 ± 2.0
Cholesterol (mg/1,000 kcal)	137.6 ± 73.9	146.0 ± 74.0	135.3 ± 74.6	143.3 ± 84.3
Keys dietary lipid score‡	31.7 ± 11.7	31.6 ± 11.8	31.5 ± 11.9	31.8 ± 12.2
Total fiber (g/1,000 kcal)	9.5 ± 3.8	8.7 ± 4.5	10.7 ± 4.1	10.4 ± 4.0
Starch (%kcal)	31.8 ± 14.0	33.7 ± 16.1	33.1 ± 14.7	33.4 ± 16.1
Total estimated sugars (%kcal)	19.8 ± 9.7	17.5 ± 9.3	22.0 ± 9.3	21.3 ± 8.7
Alcohol intake (%kcal)	4.7 ± 6.6	6.5 ± 7.4	1.3 ± 3.2	1.9 ± 4.7
Calcium (mg/1,000 kcal)	300.6 ± 138.0	262.5 ± 126.4	337.0 ± 156.8	334.0 ± 177.6
Magnesium (mg/1,000 kcal)	142.5 ± 36.7	136.2 ± 33.2	150.7 ± 39.8	148.8 ± 37.4
Phosphorus (mg/1,000 kcal)	552.0 ± 127.8	537.0 ± 119.9	572.4 ± 135.6	578.3 ± 157.8
Iron (mg/1,000 kcal)	6.9 ± 2.4	6.0 ± 1.7	7.1 ± 2.2	7.3 ± 2.6
Retinol (μg/1,000 kcal)	172.0 ± 248.9	131.3 ± 133.8	179.7 ± 235.5	195.4 ± 263.8
Vitamin A (RE/1,000 kcal)	352.0 ± 300.7	271.9 ± 268.6	409.5 ± 388.2	430.4 ± 410.9
Vitamin C (mg/1,000 kcal)	47.4 ± 32.4	39.3 ± 24.4	58.6 ± 36.9	54.5 ± 38.7
Vitamin E (mg/1,000 kcal)	4.8 ± 1.8	4.4 ± 1.4	5.1 ± 2.0	5.0 ± 1.7
β-Carotene (μg/1,000 kcal)	1,425.3 ± 1,315.7	1,249.2 ± 1,388.7	1,810.4 ± 1,742.2	1,823.5 ± 1,705.5
Special diet (%)§	8.3	15.7	13.8	16.3
Urinary characteristics*				
Urine volume (mL/24 h)	1,818.3 ± 753.7	2,162.3 ± 1025.3	1,688.5 ± 720.4	1,825.8 ± 790.7
Sodium (mmol/24 h)	196.2 ± 74.0	213.2 ± 87.0	162.8 ± 64.2	179.2 ± 92.9
Potassium (mmol/24 h)	57.0 ± 21.7	55.9 ± 22.9	48.9 ± 16.9	49.1 ± 19.7

	Urinary Albumin Excretion* (mg/24 h)			
	Men		Women	
Characteristics (unit)	<30 (n = 2,117)	30–299.9 (n = 83)	<30 (n = 2,095)	30–299.9 (n = 86)
Sodium-potassium ratio (mmol/mmol)	4.0 ± 2.2	4.5 ± 2.7	3.8 ± 2.0	4.2 ± 2.4
Urea nitrogen (g/24 h)	10.1 ± 2.8	10.3 ± 2.9	7.9 ± 2.0	8.2 ± 2.6
Creatinine (mmol/24 h)	14.4 ± 3.6	14.4 ± 4.2	9.4 ± 2.2	9.7 ± 2.3

NOTE. Values expressed as mean ± SD unless otherwise indicated.

Abbreviation: RE, retinol equivalence.

*Urinary albumin excretion and other urinary variables are the mean of two 24-hour urine collections.

†Dietary measures are the mean of four 24-hour recalls, 2 series of 2 consecutive days about 3 to 6 weeks apart.

‡Keys dietary lipid score was calculated as: 1.35 (2 saturated fatty acids – polyunsaturated fatty acids) + 1.5 cholesterol$^{1/2}$, where saturated and polyunsaturated fatty acids are percentage of kilocalories and cholesterol is milligrams per 1,000 kcal.

§Special diet indicates nonhabitual diet for weight loss or gain, salt- or fat-modified diet, or vegetarian or diabetic diet.

Table 3.

Age- and Country-Adjusted Logistic Regression Analyses of Nutrients, Each Considered Individually, Associated With MA by Sex

	Men			Women		
Variable	**Δ***	**OR**	***P***	**Δ***	**OR**	***P***
Total energy intake (kcal/d)	616.7	1.01	0.915	429.8	1.09	0.409
Total available carbohydrate (%kcal)	10.1	0.88	0.330	9.9	0.92	0.595
Total protein (%kcal)	3.0	1.11	0.402	3.0	1.04	0.773
Vegetable protein (%kcal)	2.3	0.83	0.334	2.2	0.88	0.483
Animal protein (%kcal)	4.0	1.18	0.258	4.1	1.08	0.617
Total protein (g/d)	26.4	1.09	0.467	18.8	1.18	0.143
Vegetable protein (g/d)	15.0	0.83	0.225	11.3	0.99	0.933
Animal protein (g/d)	27.9	1.21	0.166	19.8	1.26	0.097
Total fat (%kcal)	8.2	0.88	0.413	8.0	0.95	0.692
Saturated fatty acids (%kcal)	3.7	1.00	0.987	3.6	0.96	0.788
Polyunsaturated fatty acids (%kcal)	2.0	0.77	0.039	2.0	0.97	0.777
Monounsaturated fatty acids (%kcal)	3.2	0.95	0.714	3.1	0.94	0.640
ω−3 Fatty acids (%kcal)	0.4	0.88	0.399	0.5	1.19	0.149
ω−6 Fatty acids (%kcal)	2.0	0.75	0.039	1.9	0.94	0.568
Cholesterol (mg/1,000 kcal)	73.9	1.01	0.907	75.0	1.21	0.103
Keys dietary lipid score†	11.7	1.12	0.449	11.9	1.07	0.627
Total fiber (g/1,000 kcal)	3.9	0.81	0.199	4.1	0.92	0.576
Starch (%kcal)	14.1	1.15	0.481	14.8	1.27	0.344
Sugars (%kcal)	9.7	0.67	0.029	9.3	0.79	0.135
Alcohol intake (%kcal)	6.6	1.19	0.082	3.3	1.17	0.085
Alcohol intake (g/d)	24.2	1.20	0.060	8.9	1.20	0.024
Calcium (mg/1,000 kcal)	137.8	0.65	0.015	157.6	1.03	0.825
Magnesium (mg/1,000 kcal)	36.6	0.87	0.280	39.7	0.97	0.762
Phosphorus (mg/1,000 kcal)	127.6	0.89	0.402	136.5	1.12	0.346
Iron (mg/1,000 kcal)	2.4	0.60	0.007	2.2	1.05	0.676
Retinol (μg/1,000 kcal)	245.6	0.74	0.139	236.6	1.06	0.558
Vitamin A (RE/1,000 kcal)	299.8	0.74	0.090	389.1	1.01	0.956
Vitamin C (mg/1,000 kcal)	32.2	0.66	0.009	37.0	0.91	0.462
β-Carotene (μg/1,000 kcal)	1.80.6	0.86	0.287	1,740.4	0.99	0.945
Vitamin E (mg/1,000 kcal)	1.8	0.67	0.011	2.0	0.94	0.637
Sodium (mmol/24 h)‡	74.6	1.22	0.079	65.6	1.35	0.009
Potassium (mmol/24 h)‡	21.7	1.05	0.732	17.0	1.06	0.638
Sodium-potassium ratio‡	2.2	1.26	0.097	2.0	1.25	0.080
Urea nitrogen (g/24 h)‡	2.8	1.12	0.339	2.0	1.17	0.136
Creatinine (mmol/24 h)‡	3.6	1.12	0.422	2.2	1.12	0.343
Special diet (yes/no)§	0/1	2.38	0.007	0/1	1.22	0.057

NOTE. In a model including only age and country, ORs for age were 0.97 ($P = 0.803$) for men and 0.88 ($P = 0.257$) for women. For men, ORs for other variables, with adjustment for age and country, were systolic BP (per 13.8 mm Hg), 1.93 ($P < 0.001$); diastolic BP (per 10.0 mm Hg), 1.75 ($P < 0.001$); BMI (per 4.9 kg/m^2), 1.66 ($P < 0.001$); antihypertensive medication (yes versus no), 3.77 ($P < 0.001$); education (per 4.3 years), 0.71 ($P = 0.07$); current smoker (versus never smoker), 1.18 ($P = 0.502$); former smoker (versus never smoker), 0.79 ($P = 0.379$); cigarette smoking (per 11.6 cigarettes/d), 1.12 ($P = 0.319$); current drinker (versus never drinker), 1.19 ($P = 0.614$); former drinker (versus never drinker), 1.20 ($P = 0.643$); heavy or moderate physical activity (per 3.7 h/d), 1.00 ($P = 0.998$); and urinary volume (per 768.2 mL/h), 1.54 ($P < 0.001$). For women, ORs for other variables, with adjustment for age and country, were systolic BP (per 15.0 mm Hg), 1.83 ($P < 0.001$); diastolic BP (per 9.5 mm Hg), 1.66 ($P < 0.001$); BMI (per 5.7 kg/m^2), 1.49 ($P < 0.001$); antihypertensive medication (yes versus no), 3.77 ($P < 0.001$); education (per 4.6 years), 0.60 ($P = 0.008$); current smoker (versus never smoker), 1.37 ($P = 0.314$); former smoker (versus never smoker), 0.82 ($P = 0.565$); cigarette smoking (per 5.2 cigarettes/d), 1.06 ($P = 0.576$); current drinker (versus never drinker), 1.08 ($P = 0.761$); former drinker (versus never drinker), 0.64 ($P = 0.276$); heavy or moderate physical activity (per 3.5 h/d), 1.04 ($P = 0.752$); and urinary volume (per 723.6 mL/h), 1.17 ($P = 0.125$). Dietary measures are the mean of four 24-hour recalls, 2 series of 2 consecutive days about 3 to 6 weeks apart.

Abbreviation: RE, retinol equivalent.

*Differences for calculation of ORs are approximately 1 SD for continuous variables; for special diet, difference from persons not following special diet.

†Keys dietary lipid score was calculated as: 1.35 (2 saturated fatty acids [H11002] polyunsaturated fatty acids) [H11001] 1.5 cholesterol$^{1/2}$, where saturated and polyunsaturated fatty acids are percentage of kilocalories and cholesterol is milligrams per 1,000 kcal.

‡From urinary measurements.

§Special diet indicates nonhabitual diet for weight loss or gain, salt- or fat-modified diet, or vegetarian or diabetic diet.

Table 4.

Multivariate-Adjusted Logistic Regression Analyses for Association of Nutrients With MA

	Model I		Model II		Model III	
Dietary Factors	**OR**	***P***	**OR**	***P***	**OR**	***P***
Men						
ω−6 Fatty acids (%kcal)	0.76	0.053	0.75	0.044	0.76	0.053
Total estimated sugars (%kcal)	0.69	0.046	0.70	0.052	0.70	0.048
Alcohol intake (%kcal)	1.11	0.335	1.12	0.279	1.12	0.271
Alcohol intake (g/d)	1.12	0.271	1.12	0.248	1.14	0.211
Vitamin C (mg/1,000 kcal)	0.72	0.035	0.73	0.039	0.73	0.039
Vitamin E (mg/1,000 kcal)	0.66	0.011	0.65	0.010	0.65	0.010
Special diet (yes *v* no) *	2.32	0.011	2.11	0.025	1.93	0.053
Sodium (mmol/24 h) †	1.17	0.189	1.08	0.537	1.15	0.227
Calcium (mg/1,000 kcal)	0.72	0.064	0.70	0.051	0.72	0.062
Polyunsaturated fatty acids (%kcal)	0.77	0.049	0.76	0.039	0.77	0.047
Iron (mg/1,000 kcal)	0.66	0.036	0.67	0.046	0.65	0.027
Women						
ω−6 Fatty acids (%kcal)	0.95	0.644	0.95	0.632	0.95	0.632
Total estimated sugars (%kcal)	0.79	0.143	0.78	0.137	0.79	0.152
Alcohol intake (%kcal)	1.13	0.188	1.15	0.129	1.13	0.171
Alcohol intake (g/d)	1.17	0.065	1.17	0.053	1.17	0.057
Vitamin C (mg/1,000 kcal)	0.97	0.783	0.99	0.944	0.96	0.776
Vitamin E (mg/1,000 kcal)	0.95	0.654	0.96	0.716	0.94	0.649
Special diet (yes *v* no) *	1.15	0.642	1.10	0.762	1.10	0.756
Sodium (mmol/24 h)†	1.20	0.123	1.13	0.309	1.18	0.163
Calcium (mg/1,000 kcal)	1.11	0.462	1.11	0.429	1.12	0.412
Polyunsaturated fatty acids (%kcal)	0.97	0.815	0.97	0.788	0.97	0.787
Iron (mg/1,000 kcal)	1.12	0.313	1.15	0.209	1.12	0.308

NOTE. Model I was adjusted for age, country, systolic BP, and cigarettes per day. Model II was adjusted as model I plus BMI. Model III was adjusted as model I plus hypertensive drug treatment. Each cell (under the columns on ORs) represents a separate model with covariates as listed and 1 additional dietary variable (indicated by the row heading). For men, ORs for variables in model I (without other variables in the same model) were age (per 5.5 years), 0.85 ($P = 0.171$); systolic BP (per 13.8 mm Hg), 1.92 ($P < 0.001$); and cigarette smoking (per 11.9 cigarettes/d), 1.09 ($P = 0.448$). For women, ORs for variables in model I (without other variables in the same model) were age (per 5.4 years), 0.75 ($P = 0.015$); systolic BP (per 15 mm Hg), 1.83 ($P < 0.001$); and cigarette smoking (per 5.2 cigarettes/d), 1.04 ($P = 0.673$). Based on all models conducted, for women, *P* were consistently less than 0.05 for age, less than 0.001 for systolic BP, less than 0.05 for BMI, and greater than 0.05 for cigarette smoking, physical activity, and hypertensive drug treatment. For men, *P* were consistently greater than 0.05 for age, less than 0.001 for systolic BP, less than 0.01 for BMI, greater than 0.05 for cigarette smoking and physical activity, and less than 0.01 for hypertensive drug treatment. Dietary measures are the mean of four 24-hour recalls, 2 series of 2 consecutive days about 3 to 6 weeks apart. ORs presented are associated with approximately 1 SD difference for continuous variables (Table 3), and for special diet, difference from those not following special diet.

* Special diet indicates nonhabitual diet for weight loss or gain, salt- or fat-modified diet, or vegetarian or diabetic diet.

† From urinary measurements.