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ORIGINAL CONTRIBUTION

Nutrient and food intakes of middle-aged adults at low risk of cardiovascular disease: the international study of macro-/micronutrients and blood pressure (INTERMAP)

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Abstract
Purpose Individuals with favorable levels of readily measured cardiovascular disease (CVD) risk factors (low risk, LR) experience low long-term rates of CVD mortality and greater longevity. The purpose of the current study was to compare nutrient/food intakes of LR participants with participants not LR in the INTERMAP study.
Methods Men and women (40–59 years) from 17 population samples in four countries (China, Japan, UK, US) provided four 24-h dietary recalls and two timed 24-h urine collections. LR was defined as meeting all of the following CVD risk criteria: systolic/diastolic blood pressure (BP) $\leq$120/$\leq$80 mmHg; no drug treatment for high BP, hyperlipidemia, or CVD; non-smoking; BMI <25.0 kg/m^2 (US, UK) or <23.0 kg/m^2 (China, Japan); alcohol consumption <26.0 g/day (men)/<13.0 g/day (women); and no history of diabetes or CVD. Multivariate logistic regression was used to examine associations of nutrient/food intakes with LR.
Results LR individuals reported higher intake of vegetable protein, fiber, magnesium, non-heme iron, potassium; lower energy intake; lower intake of cholesterol, saturated fatty acids, animal protein; and lower 24-h urinary sodium compared with individuals not LR. With regard to foods, LR individuals reported higher intake of fruits, vegetables, grains, pasta/rice, fish; lower intakes of meats, processed meats, high-fat dairy, and sugar-sweetened beverages than individuals not LR.
Conclusions Lower energy intake and differential intake of multiple specific nutrients and foods are characteristic of individuals at low risk for developing CVD. Identification of dietary habits associated with LR is important for further

This study is conducted for the INTERMAP Research Group.

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development of public health efforts aimed at reduction/prevention of CVD.

Keywords Cardiovascular disease · Diet · Foods · Low cardiovascular risk · Nutrients · Risk factors

Introduction

Individuals with favorable levels of readily measured major cardiovascular (CVD) risk factors (low CVD risk, LR) experience notably lower long-term rates of CVD mortality, greater longevity, and better health-related quality of life than those not LR [1–4]. Only a small percentage (generally <10%) of adults middle-aged and older without CVD meet the LR criteria of untreated blood pressure (BP) ≤120/≤80 mmHg, body mass index (BMI) <25.0 kg/m^2, untreated serum cholesterol <200 mg/dL, no cigarette use, and no diabetes [4–6].

Extensive research data—epidemiologic (within/across populations), metabolic ward, clinical, controlled trial, animal-experimental, anthropologic—support the conclusion that multiple dietary traits are associated with elevated CVD risk (i.e., higher intakes of saturated and trans fatty acids, dietary cholesterol, animal protein, sugars, salt, calories, and inadequate intakes of vitamins, minerals, vegetable protein, and fiber from vegetables, fruits, legumes, whole grain products, and nuts) [7–12]. Although independent relationships between dietary factors and level of CVD risk have been established, limited information is available regarding nutritional intake of individuals characterized at having low CVD risk, particularly in cross-cultural settings.

Here we report energy, nutrient, and food intakes of LR and not LR individuals from the International Study of Macro-/Micronutrients and Blood Pressure (INTERMAP) and test whether these individuals differ in intake of specific nutrients/foods.

Materials and methods

Population samples and field methods

Background, aims, design, methods, and descriptive statistics of the INTERMAP Study have been reported in detail [13]. Briefly, in 1996–1999, INTERMAP surveyed 4,680 men and women ages 40–59 years from Japan (4 samples), the People's Republic of China (PRC, 3 samples), the United Kingdom (UK, 2 samples), and the United States (US, 8 samples). At two pairs of visits on average 3 weeks apart, trained staff recorded eight standardized BP measurements (2 per visit), measured height and weight, and collected information regarding daily alcohol consumption over the previous 7 days. Trained interviewers collected dietary data (including dietary supplement use) at each of the four visits via the in-depth multi-pass 24-h recall method [14]. Demographic and biomedical information and other possible confounders were also collected by interview. Each participant also provided two timed 24-h urine collections; urinary calcium, creatinine, magnesium, potassium, sodium, and urea nitrogen were measured centrally. Written informed consent was given by all participants, and the study design, data collection, and analyses were performed in accordance with the ethical standards of the supervising institutional review boards of all centers in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

Low cardiovascular disease risk criteria

LR was defined as meeting all of the following CVD risk criteria: systolic/diastolic blood pressure (BP) ≤120/≤80 mmHg, no drug treatment for high blood pressure (BP) or CVD (including lipid lowering medications); no current smoking; body mass index (BMI) <25.0 kg/m^2 (US and UK) or <23.0 kg/m^2 (Japan and PRC); no heavy alcohol consumption (<26 g/day for men or <13 g/day for women), and no history of diabetes, CHD or stroke [15, 16]. There is evidence that CVD risk is increased at lower BMI levels in Asian populations compared with Western populations [17]. Therefore, a BMI cut point of 23.0 kg/m^2 was utilized to define overweight in the participants from PRC and Japan, while 25.0 kg/m^2 was used to define overweight in UK and US participants. Blood samples were not obtained in most of the 17 INTERMAP population samples.

Statistical methods

For macronutrients (nutrients supplying energy), intake was calculated as percentage of total energy (%kcal) or intake/1,000 kcal as appropriate. For foods/food subgroups, intake was calculated as grams/1,000 kcal. Constituent amino acids from protein intake were also calculated as percentage of total protein. Urinary values were calculated as products of urinary concentrations and timed volume standardized to 24 h. Keys Dietary Lipid Score, a method of expressing the qualitative lipid content of the diet, was calculated as 1.35 (2 SFA–PFA) + 1.5 CHOL$^{1/2}$ where SFA is percent energy from saturated fatty acids, PFA is percent energy from polyunsaturated fatty acids, and CHOL is dietary cholesterol per 1,000 kcal. Within-person measurements were averaged for BP and dietary variables across the four visits. Within-person measurements for urinary excretions were averaged across the two 24-h collections. For descriptive statistics, means and standard deviations, or frequencies and percentages, were calculated by region (Eastern and Western), country, sex, and

LR status. Univariate differences by LR status were evaluated using a Student's *t* test, Mann–Whitney *U* test, or Chi-Square test as appropriate. Logistic regression analyses were used to assess associations of energy intake and individual nutrients with LR. For the examination of nutrients, regression models were used adjusted for sample, age, sex, use of a special diet for medical or weight loss purposes (yes/no), dietary supplement use at time of study (yes/no), and moderate/heavy physical activity (h/day). Logistic regression models were additionally adjusted for 24-h urinary sodium and potassium excretion (mmol/24-h), saturated fatty acids (SFA) (% kcal), and dietary cholesterol (mg/1,000 kcal) in supplemental analyses. Odds ratios were calculated for differences according to 1 sex-specific standard deviation. For the examination of foods/food subgroups, all food intakes were ranked and generalized linear models were used to assess significant differences in intake by LR status using ranked values. All models were adjusted for age, sex and country. All *P* values reported are 2-sided.

In a subsample of INTERMAP participants of Japanese ancestry from Japan and the US (Hawaii) (672 men, 676 women), serum total cholesterol and HDL cholesterol (HDL-C) were measured for an ancillary investigation [18]. Non-fasting blood was drawn; serum and plasma were centrifuged within 30 min of blood drawing and stored immediately under refrigeration. All specimens were frozen and stored locally at −70 °C. Serum lipids and other variables were measured in a central laboratory approximately 6–12 months later. Samples from Hawaii and the Japanese centers were shipped to the central laboratory in Japan on dry ice. Individual samples from all centers were allocated for analyses randomly to avoid systematic measurement bias. Additional sensitivity analyses were performed to examine the influence of inclusion of serum total cholesterol <200 mg/dL and/or HDL-C >40 mg/dL (men) or >50 mg/dL (women) in the LR definition. Prevalence of LR and the associations between nutrient intake and LR were examined using the modified LR criteria for the subsample with these serum cholesterol measures. Also, sensitivity analyses were performed on the influence of underweight (BMI <18.5 kg/m^2) using the original LR definition (not including serum cholesterol) with exclusion of underweight participants from these analyses. Analyses were performed with SAS 9.2 (SAS Institute, Cary, North Carolina, USA) by C.M.S.

Results

Descriptive statistics

Characteristics of INTERMAP participants by LR status are displayed in Table 1; additional data by LR status, sex, country, and region—Eastern (Japan and PRC) and Western (US and UK)—are displayed in Online Resource Tables 1–3. Overall, only 757 (16.2%) INTERMAP participants were classified as LR (Table 1). LR participants were younger and lower proportions of LR participants were men and reported a family history of hypertension compared with those who were not LR. A lower proportion of LR participants were on a special diet compared with participants not LR. Level of education (years) was similar between LR and those not LR in East Asia (Online Resource Table 2); however, LR individuals from Western regions had higher educational attainment compared with those not LR (Online Resource Table 3). Levels of physical activity were similar between LR and individuals not LR overall and in Western regions; however, LR participants in East Asia (particularly PRC) exhibited higher levels of physical activity compared with participants not LR. Unadjusted country- and sex-specific mean values of dietary nutrients by LR status are provided in Online Resource Tables 4–7. Partial correlation coefficients between nutrients adjusted for age, sex, and sample are provided in Online Resource Tables 8–10.

Association of individual nutrients and urinary measures with low cardiovascular disease risk

Odds ratios (OR) for relation of individual micronutrient intakes and urinary measures to LR status overall and by sex are presented in Table 2. For men and women, greater intake of several micronutrients was associated with higher probability (OR) of being LR, including vitamins A, C, and E, beta carotene, calcium, magnesium, phosphorus, total and non-heme iron (iron originating mainly from vegetable sources). Higher heme iron and dietary cholesterol intake were associated with lower probability of being LR. Urinary urea nitrogen (a measure of total protein intake) and urinary sodium (a measure of dietary sodium intake) were also inversely associated with LR status, while a higher urinary sodium/potassium ratio was associated with greater odds of being LR. These associations remained significant with adjustment for special diet, dietary supplement use, and moderate/heavy physical activity. Findings were similar with adjustment for additional possible confounders (Online Resource Tables 11 and 12).

ORs for relation of total energy intake and individual macronutrient intakes to LR status overall and by sex are presented in Table 3. For men and women, greater intake of several macronutrients was associated with higher probability (OR) of being LR, including dietary fiber, vegetable protein (% total protein), total carbohydrate, starch, and sugar. Higher polyunsaturated/saturated fatty acid ratio was associated with higher odds of LR only in men. Lower energy intake and lower intake of several

Table 1 Characteristics of participants by low cardiovascular disease risk status[a], all participants (Japan, People's Republic of China, United Kingdom, United States), 1996–1999: The INTERMAP Study ($N = 4,680$)

Variable	Not low CVD risk	Low CVD risk	*P* value
Number (%)	3,923 (83.8)	757 (16.2)	
Age (years)	49.4 (5.4)	48.1 (5.5)	<0.001
Male (*n*, %)	2,162 (55.1)	197 (26.0)	<0.001
Education (years)	12.3 (4.4)	12.1 (4.9)	0.28
Systolic blood pressure (mmHg)	121.3 (14.6)	106.7 (7.3)	
Diastolic blood pressure (mmHg)	75.4 (9.9)	66.0 (6.2)	
Body mass index (kg/m^2)	27.3 (5.5)	21.7 (1.8)	
Family history of hypertension (*n*, %)	2,239 (57.1)	320 (42.3)	<0.001
Dietary supplement use (*n*, %)	1,334 (34.0)	292 (38.6)	0.02
Moderate/heavy physical activity (hours/day), median (IQR)	2.0 (0.5, 6.0)	2.0 (0.5, 7.0)	0.16
Special diet (*n*, %)[b]	555 (14.2)	73 (9.6)	<0.001

CVD cardiovascular disease, *IQR* interquartile range

Data presented as mean (SD) unless otherwise noted

Univariate differences by low-risk status evaluated using a Student's *t* test, Mann–Whitney *U* test, or Chi-Square test as appropriate

[a] Low CVD risk defined as having all of the following traits: untreated systolic/diastolic blood pressure (BP) ≤120/≤80 mmHg, no drug treatment for high blood pressure (BP) or CVD; no current smoking; body mass index (BMI) <25.0 kg/m^2 (United States and United Kingdom) or <23.0 kg/m^2 (Japan and People's Republic of China); no heavy alcohol consumption (<26 g/day for men or <13 g/day for women), and no history of diabetes or CVD

[b] Special diet defined as current dietary modification for medical or weight loss purposes

macronutrients were associated with lower odds of being LR, including animal protein (% total protein), glycine (% total protein), and total and saturated fatty acids (SFA).

Sensitivity analyses, underweight and subsample with serum cholesterol data

A sensitivity analysis was performed to examine the influence of underweight (BMI <18.5 kg/m^2) on the observed association between nutrient intakes and LR. Of the overall INTERMAP sample, 44 (5.8%) LR participants and 36 (0.9%) participants not LR were underweight. With exclusion of underweight participants, multivariate associations of LR with nutrient and food intakes remained similar in direction and magnitude (data not shown).

An additional sensitivity analysis was performed to examine the influence of serum cholesterol on the association between nutrient and food intakes with LR. Of the 1,348 participants of Japanese ancestry from Japan and the US (Hawaii) with available serum cholesterol measurements [18], 272 (20.2%) participants were LR based on the original LR definition. When both serum total cholesterol <200 mg/dL and HDL-C >40 mg/dL (men) or >50 mg/dL (women) were included in the LR definition, 144 (53.0%) LR participants were reclassified as not LR resulting in a LR prevalence of 9.5%. With total cholesterol and HDL-C as part of the LR criteria, multivariate associations of LR with nutrient intakes were similar to those for all participants in direction and magnitude (data not shown).

Food and food subgroup intake by low cardiovascular risk status

LR participants consumed significantly higher amounts (g/1,000 kcal) of fruits, vegetables, grains, and fish compared with participants who were not LR (Table 4). LR participants also exhibited lower intake of higher fat dairy foods, meats, poultry, processed meats, eggs, alcoholic and non-alcoholic beverages, and sugar-sweetened beverages compared with individuals not LR.

Discussion

The main findings from this investigation are that both energy intake and intake of specific macro-/micronutrients and food subgroups are associated with low CVD risk. Compared to participants with one or more CVD risk factors at adverse levels, LR individuals consume a diet higher in fiber, vitamins and minerals, non-heme iron, vegetable protein, and carbohydrates, lower in animal protein, sodium, cholesterol, SFA, and heme iron. LR individuals also consume a diet higher in nutrient-dense foods (e.g., fruits, vegetables, grains, fish) and lower in high-calorie foods (e.g., higher fat dairy, meats fresh and processed, eggs, sugar-sweetened beverages). This dietary pattern results in lower energy intake observed among LR individuals. These findings lend support to the concept that both nutrient/food quality and energy intake are associated

Table 2 Odds ratios[a] for the relation of individual micronutrient intakes and urinary measures to low cardiovascular risk status[b], East Asia (Japan, People's Republic of China) and West (United Kingdom, United States), 1996–1999: The INTERMAP Study ($N = 4,680$)

Variable	All participants		Men		Women	
	OR[c]	95% CI	OR[d]	95% CI	OR[d]	95% CI
Vitamin A (RE/1,000 kcal)[e]	1.20	(1.11–1.30)	1.26	(1.09–1.40)	1.14	(1.06–1.30)
Vitamin C (mg/1,000 kcal)	1.25	(1.15–1.35)	1.40	(1.23–1.59)	1.15	(1.04–1.28)
Vitamin E (mg/1,000 kcal)	1.11	(1.03–1.21)	1.09	(0.95–1.24)	1.11	(1.00–1.22)
Beta carotene (μg/1,000 kcal)	1.20	(1.12–1.30)	1.21	(1.08–1.37)	1.19	(1.07–1.31)
Retinol (μg/1,000 kcal)	1.00	(0.91–1.09)	1.00	(0.94–1.23)	1.00	(0.86–1.08)
Calcium (mg/1,000 kcal)	1.23	(1.10–1.36)	1.16	(0.97–1.38)	1.21	(1.06–1.38)
Magnesium (mg/1,000 kcal)[e]	1.41	(1.29–1.55)	1.65	(1.41–1.94)	1.27	(1.13–1.43)
Phosphorus (mg/1,000 kcal)[e]	1.25	(1.13–1.39)	1.37	(1.15–1.64)	1.16	(1.02–1.32)
Iron (mg/1,000 kcal)	1.30	(1.19–1.42)	1.27	(1.11–1.45)	1.30	(1.16–1.45)
Heme–iron (mg/1,000 kcal)	0.74	(0.66–0.83)	0.64	(0.52–0.80)	0.78	(0.68–0.88)
Non-heme–iron (mg/1,000 kcal)	1.35	(1.24–1.48)	1.33	(1.16–1.51)	1.34	(1.20–1.50)
Dietary cholesterol (mg/day)	0.72	(0.65–0.81)	0.77	(0.64–0.94)	0.68	(0.60–0.78)
Dietary cholesterol (mg/1,000 kcal)	0.80	(0.72–0.89)	0.89	(0.73–1.08)	0.76	(0.67–0.86)
Urinary urea nitrogen (g/24-h)	0.67	(0.61–0.74)	0.60	(0.51–0.72)	0.66	(0.59–0.74)
Urinary potassium (mmol/24-h)	0.93	(0.85–1.03)	0.79	(0.65–0.96)	0.94	(0.84–1.05)
Urinary sodium (mmol/24-h)[e]	0.62	(0.55–0.69)	0.55	(0.44–0.68)	0.62	(0.54–0.72)
Urinary Na/K ratio	0.67	(0.59–0.77)	0.64	(0.48–0.84)	0.70	(0.59–0.82)

CVD cardiovascular disease, *OR* odds ratio

[a] Odds ratios are presented for each nutrient higher by 1 sex-specific standard deviation

[b] Low CVD risk defined as having all of the following traits: untreated systolic/diastolic blood pressure (BP) $\leq$120/$\leq$80 mmHg, no current smoking; body mass index (BMI) <25.0 kg/m^2 (US and UK) or <23.0 kg/m^2 (Japan and PRC); no heavy alcohol consumption (<26 g/day for men or <13 g/day for women), and no history or treatment for diabetes or CVD

[c] Adjusted for age, sex, sample, use of a special diet for medical or weight loss purposes (yes/no), dietary supplement use (yes/no), and moderate/heavy physical activity (hours/day)

[d] Adjusted for age, sample, special diet (yes/no), dietary supplement use (yes/no), and moderate/heavy physical activity (hours/day)

[e] Test for heterogeneity by sex significant, $P < 0.05$

with having optimal levels of multiple readily measured metabolic CVD risk factors.

It is a reasonable hypothesis that likelihood of being LR is also influenced by genetic determinants. Recent genome-wide association studies have identified common genetic variants associated with major CVD risk factors, including blood pressure [19–23], serum lipid [24–28] and glucose levels [25, 29, 30], and BMI [19, 25, 31], yet these variants only explain 15–60% of the population variance in these individual traits. Family studies and heritability estimates also provide evidence for genetic contributions to variations in CVD risk factors and disease risk [32–34]. However, data are not yet extant on specific genetic variations related to LR status. It is a reasonable judgment based on our data that favorable lifestyles of LR individuals contribute to LR status beyond the role of genetic traits. Specifically, our data lend support to recommendations for improved nutrition for primordial prevention of CHD. This inference is also consistent with findings from the Boston-based Nurses Health [35] and Health Professionals epidemiologic studies [36]. Those investigations used a low-risk definition different from that in the current investigation; rather than defining LR as we have done based on health behaviors and endogenous metabolic risk factors, they used a set of dietary traits (including intake of cereal fiber, omega-3 fatty acids, folate, vegetable protein, fruits and vegetables, and high PUFA/SFA ratio), plus smoking, moderate alcohol consumption, and physical activity status to characterize LR. Only a small percentage of participants from these previous investigations met the criteria and LR so defined was associated prospectively with low CHD/CVD rates. Each nutrient used to define LR in the Nurses' Health Study and the Health Professionals Studies was at a favorable level in LR participants in INTERMAP compared to those not LR. Other investigations have also reported that nutrient intakes comparable to those observed in INTERMAP LR individuals contribute to much lower incidence and prevalence of CHD [7, 36–38]. Such findings provide further evidence that dietary factors contribute to the prevention or delay in onset of major CVD risk factors and CVD.

Table 3 Odds ratios[a] for relation of total energy intake and individual macronutrient intakes to low cardiovascular risk status[b], by sex and for all participants, 1996–1999: The INTERMAP Study ($N = 4{,}680$)

Variable	All participants		Men		Women	
	OR[c]	95% CI	OR[d]	95% CI	OR[d]	95% CI
Energy (kcal/day)	0.77	(0.70–0.84)	0.76	(0.65–0.90)	0.75	(0.67–0.84)
Dietary fiber (g/1,000 kcal)	1.51	(1.37–1.67)	1.71	(1.45–2.02)	1.34	(1.18–1.52)
Total protein (% kcal)	0.94	(0.85–1.04)	0.94	(0.79–1.11)	0.92	(0.81–1.04)
Animal (% kcal)	0.58	(0.64–0.83)	0.66	(0.53–0.82)	0.75	(0.64–0.88)
Vegetable (% kcal)	1.79	(1.51–1.97)	2.12	(1.69–2.65)	1.50	(1.27–1.78)
Glutamic acid (% total protein)	1.06	(0.97–1.16)	1.05	(0.89–1.24)	1.04	(0.93–1.16)
Glycine (% total protein)	0.84	(0.76–0.92)	0.76	(0.69–0.98)	0.88	(0.73–0.93)
Total Fat (% kcal)	0.89	(0.79–0.99)	0.78	(0.63–0.95)	0.90	(0.78–1.03)
SFA (% kcal)	0.83	(0.73–0.94)	0.67	(0.53–0.85)	0.87	(0.75–1.01)
MUFA (% kcal)	0.87	(0.79–0.97)	0.93	(0.66–0.96)	0.96	(0.77–0.99)
PUFA (% kcal)	1.03	(0.95–1.13)	1.00	(0.86–1.16)	1.04	(0.93–1.16)
PUFA/SFA ratio	1.14	(1.02–1.27)	1.24	(1.02–1.51)	1.13	(0.99–1.29)
TFA (% kcal)	0.91	(0.79–1.06)	0.71	(0.55–0.92)	1.01	(0.85–1.20)
Omega 3 PUFA (% kcal)	1.06	(0.95–1.19)	1.05	(0.84–1.32)	1.09	(0.95–1.25)
Omega 6 PUFA (% kcal)	1.03	(0.94–1.13)	1.00	(0.85–1.17)	1.03	(0.93–1.15)
Linoleic acid (% kcal)	1.04	(0.95–1.13)	1.00	(0.85–1.17)	1.02	(0.93–1.16)
Linolenic acid (% kcal)	1.07	(0.97–1.17)	1.15	(0.87–1.24)	1.27	(0.96–1.21)
Keys dietary lipid Score[e]	0.78	(0.70–0.87)	0.73	(0.60–0.89)	0.78	(0.68–0.90)
Total carbohydrates (% kcal)	1.57	(1.39–1.76)	1.87	(1.54–2.28)	1.37	(1.18–1.59)
Starch (% kcal)	1.66	(1.39–2.00)	2.11	(1.56–2.85)	1.46	(1.15–1.86)
Sugar (% kcal)	1.20	(1.06–1.35)	1.31	(1.07–1.60)	1.12	(0.97–1.30)
Alcohol (g/day)	0.47	(0.94–0.96)	0.32	(0.95–0.97)	0.58	(0.93–0.97)
Alcohol (% kcal)	0.87	(0.84–0.90)	.88	(0.84–0.92)	.88	(0.84–0.93)

CVD cardiovascular disease, *MUFA* monounsaturated fatty acid, *OR* Odds Ratio, *PUFA* polyunsaturated fatty acid, *SFA* saturated fatty acid, *TFA* trans fatty acid

[a] Odds ratios are presented for each nutrient higher by 1 sex-specific standard deviation

[b] Low CVD risk defined as having all of the following traits: untreated systolic/diastolic blood pressure (BP) $\leq$120/$\leq$80 mmHg, no drug treatment for high blood pressure (BP) or CVD; no current smoking; body mass index (BMI) <25.0 kg/m^2 (US and UK) or <23.0 kg/m^2 (Japan and PRC); no heavy alcohol consumption (<26 g/day for men or <13 g/day for women), and no history of or treatment for diabetes or CVD

[c] Adjusted for age, sex, sample, use of a special diet for medical or weight loss purposes (yes/no), dietary supplement use (yes/no), and moderate/heavy physical activity (hours/day)

[d] Adjusted for age, sample, use of a special diet for medical or weight loss purposes (yes/no), dietary supplement use (yes/no), and moderate/heavy physical activity (hours/day)

[e] Keys Dietary Lipid Score calculated as $1.35 \times (2 \times$ % energy from saturated fat $-$ % energy from polyunsaturated fat$) + 1.5 \times \sqrt{}$(mg cholesterol/1,000 kcal)

In addition to nutrient intakes, food intakes of LR and not LR individuals was a main focus of this investigation. LR individuals consume a diet higher in nutrient and fiber-rich foods, such as fruits, vegetables, fish, and grains, and lower in energy dense foods (e.g., meat, poultry, eggs, high-calorie snacks and sweets, alcoholic/non-alcoholic beverages, fats) and also lower in sodium. Both the nutrient and food intake patterns of LR individuals from the INTERMAP cohort are consistent with dietary recommendations for the reduction in CVD risk. The low-sodium DASH diet [39–41], the OMNIHEART Trial diets [42, 43], and the heart-healthy diet recommended by the American Heart Association [44] are all based on lower intake of saturated fatty acids (SFA), dietary cholesterol, and sodium, and higher intake of vegetable protein, PUFA, potassium, minerals, vitamins, and fiber from higher intake of fruits, vegetables, fat-free/low-fat dairy products, whole grain products, legumes, nuts, fish, and poultry. Such fare has been shown to decrease blood pressure, serum cholesterol, and overall CVD risk [10, 38, 45, 46]. The lower intakes of poultry by LR than not LR persons—a finding inconsistent with many dietary recommendations for the reduction in CVD risk—are an aspect of their lower total and animal protein intakes and lower intakes of energy

Table 4 Food and food subgroup intake (g/1,000 kcal) by low cardiovascular disease (CVD) risk status[a], all participants (Japan, People's Republic of China, United Kingdom, United States), 1996–1999 the INTERMAP Study ($n = 4,680$)

Food subgroup[b]	Not low CVD risk ($n = 3,923$)	Low CVD risk ($n = 757$)	P value[c]
Total fruits	76.6 (28.0–145.5)	99.1 (48.9–168.6)	<0.001
Total vegetables	152.2 (104.4–212.1)	177.0 (124.0–244.0)	<0.001
Total grains	147.4 (91.2–283.9)	209.6 (120.4–332.7)	0.085
Pasta, rice, including recipes	54.7 (14.7–191.0)	128.8 (34.2–247.8)	<0.001
Nuts and legumes	3.9 (0.2–15.2)	3.0 (0.1–11.4)	0.024
Non-high-fat dairy (milk, yogurt, frozen yogurt, etc.)	40.5 (2.8–105.9)	49.5 (0.7v118.1)	0.020
High-fat dairy (cream, cheese, ice cream, milk, cheese, recipes, etc.)	5.4 (0.0–18.9)	3.3 (0.0–15.0)	<0.001
Fish, fish roe, shellfish	6.6 (0.0–30.6)	12.3 (0.0–35.4)	0.002
Poultry	9.0 (0.0–22.5)	6.9 (0.0–18.0)	<0.001
Beef, pork, veal, game meats	18.5 (7.4–34.6)	14.8 (4.9–27.9)	<0.001
Eggs	9.2 (2.3–19.0)	8.4 (2.0–17.5)	0.031
Processed meats	3.3 (0.0–10.9)	0.0 (0.0–7.4)	<0.001
Total visible fats (animal fats, margarines, table spreads, oils, shortenings, dressings)	13.1 (8.4–19.1)	13.3 (8.5–18.9)	0.874
Snacks, sweets	16.8 (5.6–30.7)	17.70 (6.2–33.4)	0.074
Alcoholic beverages	0.9 (0.0–86.5)	0.3 (0.0–18.4)	<0.001
Non-alcoholic beverages (excluding tea, coffee)	226.0 (0.0–576.0)	41.00 (0.0–485.7)	<0.001
Sugar-sweetened beverages[d] (UK and US samples only)	62.7 (0.0–188.7)	49.6 (0.0–142.8)	0.007
Total energy intake (kcal/day), mean (SD)	2,194.2 (633.2)	1,908.5 (514.7)	<0.001

CVD cardiovascular disease

[a] Low CVD risk defined as having all of the following traits: systolic/diastolic blood pressure (BP) ≤120/≤80 mmHg, no drug treatment for high blood pressure (BP) or CVD; no current smoking; body mass index (BMI) <25.0 kg/m^2 (US and UK) or <23.0 kg/m^2 (Japan and PRC); no heavy alcohol consumption (<26 g/day for men or <13 g/day for women), and no history of diabetes or CVD

[b] All food groups ranked prior to statistical testing to approximate normality

[c] P values adjusted for age, sex and country

[d] Due to low sugar-sweetened beverage consumption in Japan and China, analyses were limited to participants from the UK and US

dense foods. The pattern of lower energy density of foods consumed by LR individuals is particularly evident in their significantly lower intake of non-alcoholic and sugar-sweetened beverages. Although the mix of calorically sweetened and non-calorically sweetened beverages in the non-alcoholic beverages food group could not be determined in all countries, it is reasonable to assume that a large proportion of non-alcoholic beverages were calorically sweetened, so that the lower LR intake contributed to the lower energy density observed in the LR group. INTERMAP LR participants also exhibited a lower Keys dietary lipid score due to lower intake of SFA and dietary cholesterol and higher intake of PUFA, i.e., a dietary pattern consistent with Mediterranean [47] and East Asian [48] traditional fare. The dietary pattern during the early post World War II decades in the olive-growing regions of the Mediterranean (e.g., Greece, Italy) was similar to the recently studied DASH and OMNIHEART diets. In addition to its multiple favorable aspects, it included high calorie intake from olive/seed oils, high salt intake, and (for men especially) moderate to high wine consumption, i.e., unfavorable aspects [49, 50]. Modified to avoid these latter few adverse aspects, these eating styles—adopted across populations—can contribute decisively to the prevention of CHD/CVD (primordial/primary/secondary).

Primordial prevention deals with societal, familial, and personal conditions leading to exposure to causative factors and the major CHD/CVD risk factors they engender. Its aim is prevention of the major risk factors in the first place, by modifying—especially in target or selected populations—conditions that generate and structure health damaging exposures (e.g., sodium content of the food supply at the population level). Primary prevention focuses on prevention of first CHD/CVD events especially by controlling causes and risk factors. Primary prevention can have both a population-wide and high-risk focus; the latter focus is for high-risk individuals. Given the key role of dietary factors in the etiology of epidemic CHD/CVD, improved nutrition is a central emphasis of primordial and primary prevention as well as secondary prevention (along with prevention/cessation of smoking and frequent regular physical activity). Regardless of the level of CHD/CVD prevention being

targeted, utilization of dietary intake consistent with that of LR individuals (i.e., dietary intake consistent with dietary recommendations for the reduction of CVD risk) is an effective approach.

A major strength of this study is that dietary intake was examined using INTERMAP high-quality, standardized, extensive macro-/micronutrient data from 17 diverse population samples in four countries (East Asian and Western). These data were derived from state-of-the-art nutritional assessment methods involving four in-depth multi-pass 24-h dietary recalls per person collected by trained standardized certified dieticians using comprehensive high-quality comparable databases on the nutrient composition of all reported foods from the four countries [13, 14]. Limitations of this study are the following: First, its design was cross-sectional; hence, no data are available over time to test whether the nutrient intakes prospectively predict the endogenous metabolic risk factors. Second, since the definition of LR for this investigation was based on available INTERMAP measurements not including blood samples, biological markers commonly used to define low CVD risk (serum total cholesterol, LDL-C, HDL-C, triglycerides) were not incorporated. Sensitivity analyses based on a subsample indicated that approximately 53% of LR individuals would be reclassified as not LR if both serum total cholesterol <200 mg/dL and HDL-C >40 mg/dL (men) or >50 mg/dL (women) were added to the LR criteria, i.e., LR prevalence would decrease to approximately 10% (consistent with recent reports on LR prevalence) [5]. With serum total cholesterol and HDL-C added to the LR criteria, associations of nutrient and food intake with LR were similar to those for all 4,680 participants.

In summary, intake of multiple specific foods and nutrients—consistent with current dietary recommendations for the reduction and prevention of CVD—is associated with low levels of CVD risk in middle-aged adults. LR individuals exhibit higher intake of non-heme iron, dietary fiber, calcium, phosphorus, potassium, magnesium, vegetable protein, along with lower intake of energy, total and animal protein, glycine, and sodium. Correspondingly, higher consumption of nutrient-rich, low-fat, low-sodium foods, such as fruits, vegetables, fish, and grains, was also observed in LR individuals. These dietary patterns—through their influence on BP, serum cholesterol, and body weight—may be responsible in part for the greatly reduced cardiovascular morbidity and mortality previously reported in LR populations [1–4]. Identification of these specific dietary patterns associated with low CVD risk should be useful for further development of public health efforts aimed to increase population prevalence of low CVD risk for the prevention and reduction of CVD.

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Conflict of interest The authors declare that they have no conflicts of interest.

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