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# Differences in cardiovascular disease risk factors between Japanese in Japan and Japanese-Americans in Hawaii: the INTERLIPID study

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#### **Abstract**

Despite increase in serum total cholesterol, high smoking rate, and frequency of adverse blood pressure levels in Japan, coronary heart disease (CHD) incidence and mortality apparently remain substantially lower at all ages in Japan than in the US and other Western societies. To better understand these differences, we compared CHD biomedical risk factors and dietary variables in Japanese living in Japan and 3rd and 4th generation Japanese emigrants living a primarily Western lifestyle in Hawaii, in an ancillary study of the INTERMAP. Men and women aged 40-59 years were examined by common standardized methods—four samples in Japan (574 men, 571 women) and a Japanese-American sample in Hawaii (136 men, 131 women). Average systolic (SBP) and diastolic (DBP) blood pressures were significantly higher in men in Japan than in Hawaii; there were no significant differences in women. The treatment rate of hypertension was much lower in Japan than Hawaii. Smoking prevalence was higher, markedly so for men, in Japan than Hawaii. Body mass index, serum total and low-density lipoprotein cholesterol, HbA1c, and fibrinogen were significantly lower in Japan than in Hawaii; high-density lipoprotein cholesterol was higher in Japan. Total fat, saturated fatty acid intake, and Keys dietary lipid score were lower in Japan than in Hawaii. Polyunsaturated/saturated fatty acid ratio and omega-3 fatty acid intake were higher in Japan than in Hawaii. In conclusion, levels of several, especially lipid, CHD risk factors were generally lower in Japanese in Japan than in Japanese in Hawaii. These differences were smaller for women than men between Japan and Hawaii. They may partly explain lower CHD incidence and mortality in Japan than Western industrialized countries.

#### **Keywords**

blood pressure; coronary heart disease; diet; serum lipids; smoking; population study; Japanese; Japanese-Americans

#### Introduction

Dietary saturated fat and cholesterol have been demonstrated to cause increases in serum total cholesterol. The intake of these lipids has increased dramatically in Japan in recent decades, especially in the young. 2,3 Thus, the mean serum total cholesterol of young and middle-aged Japanese in Japan appears to have reached levels similar to those of Americans. 2,3 Throughout this period, average blood pressures and rates of hypertension have been at least as high in Japanese adults as among white Americans. In addition, although the smoking rate is declining steadily, Japanese men in Japan still have much higher smoking rates than men in Western societies. Nevertheless, coronary heart disease (CHD) incidence and mortality rates apparently remain substantially lower at all ages in Japan than in the US and other Western societies. 2,3,5 It is important to elucidate reasons for this phenomenon. 4-9 It is also of interest that differences in CHD morbidity and mortality are far smaller between women in Japan and in Western societies than those seen for men. 2,3,5,9

To date, many comparisons of risk factor levels and rates of cardiovascular diseases between the Japanese in Japan and Western populations have been based on nonstandardized data. Differences in traditional as well as more recently described risk factors between the populations are often not well documented. To understand these differences better, we made standardized comparisons of CHD biomedical risk factors and dietary variables in Japanese living in Japan and 3rd and 4th generation Japanese emigrants living a primarily Western lifestyle in Hawaii.

## Population samples and methods

In the INTERLIPID study, an ancillary study to the 17-sample 4-country INTERMAP study,  $^{10}$  574 men and 571 women aged 40–59 years in four centres in Japan, and 136 Japanese-American men and 131 Japanese-American women in the US sample in Honolulu, Hawaii were examined based on a standardized common protocol (Table 1). Methods of the INTERMAP study are reported elsewhere;  $^{10,11}$  a brief description is given here. Blood pressure measurements were made on four different days; medical and lifestyle information, four 24-h dietary recalls, and two 24-h urine collections were obtained per participant. For the INTERLIPID study, nonfasting 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  $-70^{\circ}$ C. Serum lipids, fibrinogen, HbA1c, and other variables were measured in a central laboratory approximately 6–12 months later. For these analyses, samples from Hawaii and the Japanese centres were shipped to the central laboratory in Japan on dry ice. Individual samples from the five centres were allocated for analyses randomly to avoid systematic measurement bias.

The central laboratory was standardized using the Lipid Standardization Program, Centers for Disease Control and Prevention, Atlanta, USA, and successfully met the criteria of precision and accuracy for control measurements. <sup>12</sup> The laboratory is currently a member of the Cholesterol Reference Method Laboratory Network (CRMLN). <sup>13</sup> Except for measurement of fibrinogen and HbA1c, serum was used and analysed by an autoanalyzer (Hitachi 7107). For fibrinogen concentration, the thrombin coagulation time method was used. <sup>14</sup> HbA1c was measured by a high-perfusion liquid chromatography method standardized by the Japanese Diabetes Society. <sup>15</sup>

#### Results

#### **Blood pressure**

Both average systolic (SBP) and diastolic (DBP) blood pressures were significantly higher in men in Japan than in Hawaii (Table 2). No significant SBP or DBP differences were seen in women. The rate of hypertension treatment (defined as taking antihy-pertensive medication) was considerably lower for both men and women in Japan than Hawaii (P < 0.01).

#### **Smoking and drinking**

Japanese men in Japan had far higher smoking rates than Japanese-American men in Hawaii (P<0.01) (Table 2). While smoking rates were higher for women in Japan than Hawaii, differences were not as dramatic. Drinking rates for both men and women in Japan were also significantly higher than those in Hawaii.

#### Dietary and serum lipids, HbA1c, fibrinogen, dietary electrolytes

Body mass index (BMI) (kg/m²), total fat intake, intake of saturated, mono- and polyunsaturated fatty acids (% total kcal), serum total and low-density lipoprotein cholesterol (LDL-C), triglycerides (TG), HbA1c, and fibrinogen were significantly lower in both men and women in Japan than in Hawaii (Tables 2–4). Omega-3 polyunsaturated fatty acid intake and the ratio of dietary polyunsaturated to saturated fatty acid intake (P/S) were significantly higher in Japan than in Hawaii (Table 4). However, cholesterol intakes were significantly higher in both men and women in Japan than in Hawaii (Table 4). Nevertheless, Keys dietary lipid score was significantly lower in men in Japan than in Hawaii. Mean levels of serum high-density lipoprotein cholesterol (HDL-C) were significantly higher in both men and women in Japan than in Hawaii (Table 3). Lp(a) concentration was not different between Japan and Hawaii. Sodium intakes were significantly higher in Japan than Hawaii for both men and women (Table 4). Vitamin A,  $\beta$ -carotene, calcium, magnesium, selenium, and iron intakes were significantly lower in both men and women in Japan than in Hawaii (Table 4).

#### **Discussion**

The main findings from this end-of-century survey of population samples of Japanese in Japan and Japanese-Americans in Honolulu, Hawaii aged 40–59 years are: for both men and women, more favourable levels of several dietary and blood lipid variables were observed in

Japan than in Hawaii, that is, lower intake levels for total fat, SFAs, PFAs/SFAs, and lower serum total cholesterol, LDL-C, triglycerides; higher intake of omega-3 fatty acids, higher serum HDL-C, and lower BMI. HbA1c and fibrinogen levels were also more favourable (ie, lower) for both men and women in Japan than in Hawaii. In contrast, cigarette smoking rates were higher for Japanese than Japanese-Americans, as were average levels of SBP, DBP, and rates of hypertension for Japanese men than Japanese-American men. Rates of hypertension treatment were lower for Japanese than Japanese-Americans.

This pattern of contrasting findings for the traditional readily measured major CHD–CVD risk factors (serum cholesterol, SBP/DBP, cigarette smoking) and dietary neutral fats in middle-aged Japanese compared to Japanese-Americans (also, Americans generally) at the end of the 20th century is consistent with the results repeatedly reported during the latter half of the century, for example, by the Seven Countries and Ni-Hon-San studies. <sup>16–18</sup> Given the extensive data showing that CHD rates have been much lower for Japan than the USA throughout this period, with the contrast especially marked for men (present but quantitatively less for women), and that this contrast remains conspicuous in the latest data, key theoretical inferences are self-evident. Among the established major risk factors, dietary lipids and the serum lipids they influence are critically important for the occurrence of epidemic CHD. <sup>19–21</sup> When these are favourable in the whole population, the impact of other major risk factors (adverse SBP/DBP, cigarette smoking) on CHD risk is of limited expression. When these are adverse, the impact of each major risk factor is massive, especially in combination, producing full-blown epidemic CHD. <sup>2,5,16–21</sup>

In the present study, these differences in CHD risk factors were larger in men than in women. Thus, gender differences in CHD risk factors between the populations may contribute to apparent differences in CHD and stroke morbidity and mortality patterns on a population basis. <sup>2,3,5</sup>

BMI for Japanese men and women was lower than for Japanese-Americans. There was no difference in height for men or women between Japan and Hawaii. Among Japanese, obesity was much less common than among Japanese-Americans, especially among men. Thus in Japan, lean body mass, especially in men, may have contributed to lower CHD risk, that is, lower serum total cholesterol, LDL-C, triglycerides, HbA1c, and fibrinogen levels and higher HDL-C levels (despite much higher smoking rates) than those of Japanese-Americans in Hawaii. Lower serum total cholesterol and LDL-C levels in Japan are correlated with lower saturated fat and PFA/SFA intakes and Keys lipid score than those in Hawaii, and prevail despite higher dietary cholesterol intake in Japan, a development in recent decades, reflecting the encouragement of whole egg intake to improve protein nutrition. Preliminary data from INTERMAP indicate that the higher omega-3 fatty acid intake in Japanese is apparently related to higher fish intake.<sup>22</sup> In Japan, those aged 40 years and older consume more than 100 g of fish daily,<sup>23</sup> a general finding nationwide, also recorded in INTERMAP. <sup>22</sup> The higher fish consumption in Japan may also relate to the lower serum total cholesterol, LDL-C, and triglycerides. In addition, data from Japanese participants in the Honolulu Heart Program—the fathers of the Hawaii population in the present study—indicate that fish consumption may be a protective factor against heart disease in smokers.<sup>24</sup>

Despite the higher per cent of calories from carbohydrate, and despite higher smoking rates for Japanese compared to Japanese-Americans, most conspicuously in men, HDL-C levels were higher in Japanese than in Japanese-Americans. This finding is related to the lower BMI of the Japanese, although there may be other factors involved as well, including a higher per cent of total calories from alcohol for the Japanese compared to the Japanese-Americans. Be all that as it may, these data refute the notion about a presumed problem with lower intake of per cent total calories from fat, and higher intake of per cent total calories from carbohydrate instead, that is, the claim that this dietary pattern is responsible for lower HDL-C. Chinese data from the PRC-USA co-operative study are consistent with our INTERLIPID findings.<sup>25</sup>

Blood pressure levels in Japanese men were higher than those in Japanese in Hawaii, despite lower body weight in Japan. This appears to be due principally to the large difference in the treatment rate of hypertension, which was much lower in Japan than in Hawaii. It may also relate to higher salt (NaCl) intake and higher dietary Na/K in Japanese than Japanese-Americans. We found similar phenomena in INTERSALT study samples in the late 1980s).

In conclusion, levels of diet and blood lipid CHD risk factors (as well as BMI, HbA1c, fibrinogen) were generally lower in Japanese in Japan than in Japanese-Americans in Hawaii. In contrast, the smoking rate in Japan was much higher. In addition, there was a tendency for SBP/DBP and hypertension rates to be higher in Japan. All differences in CHD risk factors were larger in men than in women. Gender differences in CHD risk factors between the populations may help to explain known cross-population patterns of CHD and stroke morbidity and mortality. A better understanding of these differences in risk factor levels and their relationships to cardiovascular diseases in these societies can enhance the ability to cope more effectively with evolving lifestyles and lifestyle-related risk factor patterns, hence achieve greater success in preventing cardiovascular diseases in the 21st century.

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Table 1

Number of participants: four samples in Japan and Hawaii sample, INTERLIPID/INTERMAP 1997–1998, by gender and age

Centre		40-49 years (n)	50-59 years (n)	Total (n)
Men				
Japan	Hokkaido	75	74	149
	Toyama	72	77	149
	Shiga	68	62	130
	Wakayama	73	73	146
	Total	288	286	574
Hawaii		67	69	136
Women				
Japan	Hokkaido	74	74	148
	Toyama	76	74	150
	Shiga	66	63	129
	Wakayama	75	69	144
	Total	291	280	571
Hawaii		66	65	131

Table 2

Height, weight, and body mass index (BMI), systolic and diastolic blood pressures, treatment rate of hypertension, smoking and drinking rates, and sodium and potassium excretion in timed 24-h urine, in Japan and Hawaii, INTERLIPID, 1997-1998, by gender and age

	4	40-49 years		5(	50–59 years		4	40–59 years	
	4 samples in Japan (288) Mean (s.d.)	Hawaii (67) Mean (s.d.)		4 samples in Japan (286) Mean (s.d.)	Hawaii (69) Mean (s.d.)		4 samples in Japan (574) Mean (s.d.)	Hawaii (136) Mean (s.d.)	
Men									
Body weight (kg)	(6.9 (9.0)	78.2 (14.8)	P < 0.001	(8.8)	79.2 (15.1)	P < 0.001	(8.8)	78.7 (14.9)	P<0.001
Height (cm)	168.8 (5.8)	167.3 (11.0)	P=0.059	167.1 (5.8)	167.0 (5.9)	P=0.907	167.9 (5.8)	167.1 (5.7)	P=0.156
Body mass index (kg/m <sup>2</sup> )	23.5 (2.7)	27.9 (4.9)	P < 0.001	23.9 (2.7)	28.3 (4.6)	P<0.001	23.7 (2.7)	28.1 (4.7)	P<0.001
Systolic blood pressure (mmHg)	119.5 (13.0)	117.2 (11.0)	P=0.177	121.3 (13.1)	118.7 (12.1)	P=0.134	120.4 (12.9)	117.9 (11.6)	P=0.045
Diastolic blood pressure (mmHg)	76.6 (10.3)	74.2 (8.7)	P=0.076	77.0 (9.7)	73.6 (8.2)	P=0.007	76.8 (10.0)	73.9 (8.5)	P=0.002
Treatment rate of hypertension (%)	2.8	17.9	P<0.01	9.1	36.2	P<0.01	5.9	27.2	P<0.01
Smoking rate (%)	56.6	16.4	P < 0.01	46.9	10.1	P < 0.01	51.7	13.2	P<0.01
Drinking rate (%)	97.2	65.7	P < 0.01	96.5	7.67	P < 0.01	6.96	72.8	P<0.01
Sodium (mmol/day) in 24-h urine	204.7 (53.9)	174.5 (61.4)	P < 0.001	216.5 (58.6)	177.7 (55.5)	P < 0.001	210.5 (56.6)	176.1 (58.5)	P < 0.001
Potassium (mmol/day) in 24-h urine	48.4 (12.6)	53.1 (17.1)	P=0.012	50.1 (13.9)	52.9 (14.0)	P=0.128	49.2 (13.3)	53.0 (15.6)	P=0.004
Sodium/potassium ratio in 24-h urine	4.4 (1.2)	3.5 (1.3)	P<0.001	4.5 (1.3)	3.6 (1.4)	P<0.001	4.5 (1.3)	3.6 (1.3)	P<0.001
	4	40–49 years		5(	50–59 years		4	40–59 years	
	4 samples in Japan (291) Mean (s.d.)	Hawaii (66) Mean (s.d.)		4 samples in Japan (280) Mean (s.d.)	Hawaii (65) Mean (s.d.)		4 samples in Japan (571) Mean (s.d.)	Hawaii (131) Mean (s.d.)	
Women									
Body weight (kg)	56.2 (8.4)	59.3 (10.1)	P=0.022	54.8 (7.6)	62.7 (13.9)	P<0.001	55.5 (8.0)	61.0 (12.2)	P<0.001
Height (cm)	156.2 (5.6)	152.8 (5.0)	P < 0.001	153.3 (5.3)	154.2 (4.5)	P=0.241	154.8 (5.6)	153.5 (4.8)	P=0.007
Body mass index (kg/m <sup>2</sup> )	23.0 (3.1)	25.5 (4.8)	P < 0.001	23.3 (3.0)	26.4 (5.9)	P < 0.001	23.2 (3.1)	25.9 (5.4)	P < 0.001
Systolic blood pressure (mmHg)	112.0 (12.8)	113.1 (12.4)	P=0.449	116.3 (14.7)	118.2 (15.4)	P=0.358	114.1 (13.9)	115.6 (14.1)	P=0.252
Diastolic blood pressure (mmHg)	(6.5 (9.5)	69.7 (8.1)	P=0.899	71.5 (9.7)	70.3 (8.9)	P=0.384	70.5 (9.6)	70.0 (8.5)	$P\!\!=\!\!0.602$
Treatment rate of hypertension (%)	2.4	15.2	P<0.01	9.6	33.8	P<0.01	6.5	24.4	P<0.01

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Smoking rate (%)	11.7	9.1	P<0.01	5.4	0.0	P<0.01	8.6	4.6	P<0.01
Drinking rate (%)	82.1	40.9	P<0.01	82.5	41.5	P < 0.01	82.3	41.2	P<0.01
Sodium (mmol/day) in 24-h urine	185.5 (54.9)	128.6 (35.6)	P < 0.001	186.6 (51.0)	134.0 (48.6)	P < 0.001	186.0 (53.1)	131.3 (42.7)	
Potassium (mmol/day) in 24-h urine	47.2 (13.1)	39.8 (9.8)	P<0.001	49.9 (14.5)	44.1 (15.0)	P=0.004	48.5 (13.9)	41.9 (12.9)	
Sodium/potassium ratio in 24-h	4.1 (1.18)	3.4 (1.1)	P<0.001	4.0 (1.3)	3.2 (1.0)	P<0.001	4.1 (1.2)	3.3 (1.1)	P<0.001

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Serum lipids, uric acid, fibrinogen, and HbA1c in Japan and Hawaii, INTERLIPID 1997-1998, by gender and age

	4	40–49 years		5(	50–59 years		40	40–59 years	
	4 samples in Japan (287) Mean (s.d.)	Hawaii (47) Mean (s.d.)		4 samples in Japan (285) Mean (s.d.)	Hawaii (53) Mean (s.d.)		4 samples in Japan (572) Mean (s.d.)	Hawaii (100) Mean (s.d.)	
Men									
Serum total cholesterol (mg/dl)	200.1 (28.6)	206.0 (30.5)	P=0.191	198.5 (29.0)	213.1 (27.4)	P < 0.001	199.3 (28.8)	209.8 (29.0)	P < 0.001
HDL-cholesterol (mg/dl)	53.6 (13.1)	49.1 (10.6)	P=0.025	53.7 (14.2)	51.2 (9.9)	P=0.1111	53.7 (13.7)	50.2 (10.2)	P=0.003
LDL-cholesterol (mg/dl)	122.0 (28.3)	130.9 (28.9)	P=0.047	119.0 (28.7)	136.9 (27.5)	P<0.001	120.5 (28.5)	134.1 (28.2)	P < 0.001
HDL-cholesterol/LDL-cholesterol	0.471 (0.198)	0.390 (0.110)	P < 0.001	0.486 (0.216)	0.389 (0.104)	P < 0.001	0.479 (0.207)	0.389 (0.106)	P < 0.001
Triglyceride (geometric mean, mg/dl)	135.9 (1.8)	194.8 (1.8)	P < 0.001	133.6 (1.8)	198.3 (1.9)	P < 0.001	134.8 (1.8)	196.6 (1.8)	P < 0.001
Lp (a) (geometric mean, mg/dl)	8.5 (2.2)	8.6 (2.7)	P=0.941	9.6 (2.3)	8.7 (2.5)	P=0.410	9.0 (2.3)	8.6 (2.6)	P=0.648
$\gamma$ -GTP (geometric mean, U/I)	42.8 (2.2)	35.8 (1.8)	P=0.077	43.6 (2.2)	38.4 (1.7)	P=0.155	43.2 (2.2)	37.2 (1.8)	P=0.024
Uric acid (mg/dl)	5.80 (1.18)	5.99 (1.14)	$P\!\!=\!\!0.316$	5.83 (1.20)	6.59 (1.17)	P < 0.001	5.80 (1.20)	6.30 (1.20)	P < 0.001
HbA1c (%)	4.72 (0.50)	4.92 (0.85)	P=0.132	4.82 (0.60)	5.08 (0.73)	P=0.006	4.80 (0.60)	5.00 (0.80)	P=0.006
Fibrinogen (mg/dl)	248.3 (71.6)	288.9 (55.2)	P < 0.001	259.0 (66.1)	286.9 (60.4)	P=0.004	253.7 (69.0)	287.8 (57.8)	P < 0.001
	4	40-49 years		5(	50–59 years		40	40–59 years	
	4 samples in Japan (290) Mean (s.d.)	Hawaii (52) Mean (s.d.)		4 samples in Japan (280) Mean (s.d.)	Hawaii (54) Mean (s.d.)		4 samples in Japan (570) Mean (s.d.)	Hawaii (106) Mean (s.d.)	
Women									
Serum total cholesterol (mg/dl)	194.7 (29.3)	204.5 (30.6)	P=0.028	210.2 (30.6)	218.2 (32.5)	P=0.082	202.3 (30.9)	211.5 (32.2)	P=0.005
HDL-cholesterol (mg/dl)	61.1 (14.7)	57.0 (10.8)	$P\!\!=\!\!0.056$	58.9 (13.7)	62.3 (14.8)	$P\!\!=\!\!0.109$	60.0 (14.2)	59.7 (13.2)	P=0.810
LDL-cholesterol (mg/dl)	117.2 (27.4)	132.6 (30.3)	P < 0.001	130.7 (30.9)	141.3 (36.0)	P=0.048	123.8 (29.9)	137.0 (33.5)	$P \!\!<\!\! 0.001$
HDL-cholesterol/LDL-cholesterol	0.560 (0.251)	0.460 (0.170)	$P \!\!<\!\! 0.001$	0.485 (0.204)	0.492 (0.255)	P=0.845	0.523 (0.232)	0.476 (0.217)	P=0.052
Triglyceride (geometric mean, mg/dl)	89.2 (1.6)	125.5 (1.7)	P < 0.001	107.5 (1.6)	151.2 (1.7)	P < 0.001	97.8 (1.6)	138.0 (1.7)	P < 0.001
Lp (a) (geometric mean, mg/dl)	9.5 (2.3)	12.2 (2.3)	P=0.051	11.7 (2.4)	12.4 (2.5)	P=0.644	10.5 (2.4)	12.3 (2.4)	P=0.087
$\gamma$ -GTP (geometric mean, U/I)	16.9 (2.2)	21.5 (1.8)	P=0.003	43.6 (2.2)	38.4 (1.7)	P=0.002	43.2 (2.2)	37.2 (1.8)	P < 0.001
Uric acid (mg/dl)	3.95 (0.90)	4.43 (0.95)	P < 0.001	4.38 (0.85)	4.85 (1.38)	$P\!\!=\!\!0.019$	4.20 (0.90)	4.60 (1.20)	P < 0.001
HbA1c (%)	4.52 (0.41)	4.62 (0.44)	$P\!\!=\!\!0.109$	4.67 (0.46)	4.87 (0.80)	$P\!\!=\!\!0.078$	4.60 (0.40)	4.70 (0.70)	P=0.021
Fibrinogen (mg/dl)	250.5 (63.6)	308.8 (63.0)	P<0.001	267.0 (66.1)	312.3 (58.7)	P<0.001	258.6 (65.3)	310.6 (60.6)	P < 0.001

Table 4

Nutrient intake in Japan and Hawaii, average of 4 days of 24-h dietary recalls, INTERLIPID 1997-1998, by gender and age

		40–49 years		41	50–59 years			40–59 years	
	4 samples in Japan (288) Mean (s.d.)	Hawaii (67) Mean (s.d.)		4 samples in Japan (286) Mean (s.d.)	Hawaii (69) Mean (s.d.)		4 samples in Japan (574) Mean (s.d.)	Hawaii (136) Mean (s.d)	
Men									
Energy (kcal/day)	2,295.2 (462.1)	2,516.2 (651.2)	$P\!=\!0.010$	2,260.0 (389.9)	2,345.4 (588.0)	P=0.254	2,277.6 (427.7)	2,429.6 (623.5)	P=0.008
Protein (g/day)	88.4 (20.8)	106.2 (33.2)	P < 0.001	90.3 (19.3)	99.7 (27.4)	$P\!=\!0.008$	89.3 (20.1)	102.9 (30.4)	P < 0.001
Fat (g/day)	62.9 (18.8)	92.0 (31.0)	P < 0.001	58.2 (15.9)	85.6 (29.8)	P < 0.001	60.6 (17.5)	88.8 (30.4)	P < 0.001
Saturated fatty acids (g/day)	16.3 (5.7)	27.8 (10.4)	P<0.001	14.8 (4.7)	25.0 (9.5)	P<0.001	15.6 (5.3)	26.4 (10.0)	P<0.001
Monounsaturated fatty acids (g/day)	23.2 (7.6)	35.2 (13.1)	P<0.001	20.8 (6.4)	32.8 (12.5)	P<0.001	22.0 (7.1)	34.0 (12.8)	P<0.001
Polyunsaturated fatty acids (g/day)	16.0 (5.1)	21.5 (7.2)	P<0.001	15.5 (4.8)	20.7 (7.8)	P<0.001	15.8 (5.0)	21.1 (7.5)	P<0.001
$\omega$ -3 fatty acids (g/day)	3.4 (1.2)	2.4 (0.9)	P < 0.001	3.4 (1.2)	2.3 (0.9)	P < 0.001	3.4 (1.2)	2.3 (0.9)	P < 0.001
$\omega$ -6 fatty acids (g/day)	12.6 (4.3)	19.0 (6.5)	P < 0.001	12.0 (4.0)	18.3 (7.1)	P < 0.001	12.3 (4.2)	18.6 (6.8)	P < 0.001
P/S ratio	1.0 (0.3)	0.8 (0.3)	P < 0.001	1.1 (0.3)	0.9 (0.3)	$P \!\!<\!\! 0.001$	1.1 (0.3)	0.8 (0.3)	$P \!\!<\!\! 0.001$
Cholesterol (mg/day)	455.6 (178.2)	324.5 (147.2)	P < 0.001	436.0 (171.6)	324.7 (145.9)	$P \!\!<\!\! 0.001$	445.8 (175.1)	324.6 (146.0)	$P \!\!<\!\! 0.001$
Keys lipid score	29.4 (5.8)	32.4 (8.2)	$P\!\!=\!\!0.006$	28.0 (6.0)	31.3 (7.7)	$P\!\!=\!\!0.001$	28.7 (5.9)	31.8 (8.0)	$P \!\!<\!\! 0.001$
Carbohydrate (g/day)	296.9 (67.7)	300.0 (80.7)	P=0.743	292.3 (65.4)	273.9 (75.2)	P=0.042	294.6 (66.5)	286.7 (78.8)	$P\!\!=\!\!0.282$
Dietary fibre (g/day)	14.8 (4.7)	19.4 (5.9)	P < 0.001	16.1 (4.8)	19.1 (7.5)	P=0.002	15.5 (4.8)	19.3 (6.8)	$P \!\!<\!\! 0.001$
Na (mg/day)	4,992.1 (1,230.2)	4,617.6 (1,444.9)	$P\!\!=\!\!0.053$	5,206.9 (1,398.9)	4,300.0 (1,328.4)	P < 0.001	5,099.1 (1,320.2)	4,456.4 (1,391.0)	P < 0.001
K (mg/day)	2,813.0 (723.3)	3,062.7 (956.3)	$P\!\!=\!\!0.048$	2,978.1 (713.1)	3,073.3 (951.7)	P=0.438	2,895.3 (722.4)	3,068.1 (950.4)	$P\!\!=\!\!0.048$
Ca (mg/day)	573.9 (209.2)	705.8 (362.7)	$P\!\!=\!\!0.005$	637.1 (233.7)	603.8 (237.7)	P=0.290	605.4 (223.8)	654.1 (308.9)	$P\!\!=\!\!0.085$
Mg (mg/day)	283.1 (69.3)	395.6 (146.9)	P < 0.001	292.7 (67.2)	383.7 (126.6)	P < 0.001	287.9 (68.4)	389.6 (136.6)	$P \!\!<\!\! 0.001$
Se (µg/day)	180.8 (70.4)	177.0 (52.8)	$P\!\!=\!\!0.684$	201.0 (86.7)	177.3 (61.0)	P=0.033	190.8 (79.5)	177.2 (56.9)	$P\!\!=\!\!0.021$
Fe (mg/day)	11.0 (2.9)	20.5 (6.8)	P < 0.001	11.8 (3.0)	19.5 (5.7)	P < 0.001	11.4 (3.0)	20.0 (6.3)	P < 0.001
P (mg/day)	1,217.1 (292.9)	1,437.3 (441.5)	P < 0.001	1,246.6 (276.6)	1,345.9 (384.6)	$P\!\!=\!\!0.046$	1,231.8 (285.0)	1,390.9 (414.6)	$P \!\!<\!\! 0.001$
Vitamin C (mg/day)	120.1 (84.5)	128.1 (83.2)	P=0.485	131.0 (76.1)	130.6 (86.3)	P=0.969	125.6 (80.5)	129.4 (84.5)	$P\!\!=\!\!0.621$
Vitamin A (IU/day)	5,882.2 (3,810.1)	9,690.0 (6,892.7)	P < 0.001	6,494.9 (4,700.1)	9,299.5 (5,751.8)	P < 0.001	6,187.5 (4,284.0)	9,491.9 (6,319.0)	$P \!\!<\!\! 0.001$
Retinol (µg/day)	415.8 (665.7)	355.8 (379.1)	P=0.325	438.3 (1,084.9)	315.2 (284.2)	P=0.351	427.0 (898.6)	335.2 (333.7)	P=0.052
$eta$ -carotene ( $\mu$ g/day)	2,697.8 (1,894.3)	5,093.2 (4,014.5)	P<0.001	3,020.4 (1,931.0)	4,940.7 (3,316.8)	P<0.001	2,858.6 (1,917.8)	5,015.8 (3,664.2)	P<0.001

		40-49 years			50–59 years			40–59 years	
	4 samples in Japan (291) Mean (s.d.)	Hawaii (66) Mean (s.d.)		4 samples in Japan (280) Mean (s.d.)	Hawaii (65) Mean (s.d.)		4 samples in Japan (571) Mean (s.d.)	Hawaii (131) Mean (s.d)	
Women									
Energy (kcal/day)	1,844.6 (323.8)	1,836.1 (418.5)	P=0.877	1,750.3 (319.4)	1,745.3 (412.7)	P=0.927	1,798.4 (324.8)	1,791.0 (416.6)	P=0.850
Protein (g/day)	72.9 (15.3)	73.2 (18.9)	P=0.902	71.1 (15.5)	71.8 (20.0)	P=0.792	72.0 (15.4)	72.5 (19.4)	P=0.786
Fat (g/day)	56.8 (15.1)	68.4 (23.8)	P < 0.001	49.1 (13.4)	63.6 (24.4)	P < 0.001	53.0 (14.8)	66.0 (24.1)	P<0.001
Saturated fatty acids (g/day)	15.5 (5.1)	20.9 (7.8)	P<0.001	13.2 (4.3)	18.6 (7.1)	P<0.001	14.4 (4.9)	19.7 (7.5)	P<0.001
Monounsaturated fatty acids (g/day)	20.9 (6.1)	26.0 (9.9)	P<0.001	17.4 (5.4)	23.9 (11.1)	P<0.001	19.2 (6.0)	25.0 (10.5)	P<0.001
Polyunsaturated fatty acids (g/day)	14.0 (4.0)	16.0 (6.1)	P=0.014	12.7 (3.6)	15.9 (6.8)	P=0.001	13.4 (3.9)	16.0 (6.4)	P<0.001
$\omega$ -3 fatty acids (g/day)	2.8 (0.9)	1.8 (0.7)	P < 0.001	2.7 (0.9)	1.9 (0.9)	P < 0.001	2.7 (0.9)	1.8 (0.8)	P<0.001
$\omega$ -6 fatty acids (g/day)	11.2 (3.4)	14.1 (5.5)	P < 0.001	9.9 (3.1)	14.0 (6.1)	P < 0.001	10.6 (3.4)	14.0 (5.8)	P < 0.001
P/S ratio	1.0 (0.3)	0.8 (0.3)	P < 0.001	1.0 (0.3)	0.9 (0.4)	P=0.022	1.0 (0.3)	0.9 (0.3)	P < 0.001
Cholesterol (mg/day)	383.3 (138.8)	242.9 (105.4)	P < 0.001	333.6 (134.3)	242.6 (130.7)	P < 0.001	358.9 (138.7)	242.8 (118.2)	P < 0.001
Keys lipid score	32.3 (6.6)	33.1 (8.4)	P=0.467	29.8 (6.2)	31.1 (10.2)	P=0.296	31.1 (6.5)	32.1 (9.4)	P=0.212
Carbohydrate (g/day)	252.2 (50.5)	229.1 (57.0)	$P\!\!=\!\!0.001$	249.9 (53.6)	217.8 (59.2)	P < 0.001	251.0 (52.0)	223.5 (58.2)	P < 0.001
Dietary fibre (g/day)	15.3 (4.5)	15.2 (5.8)	P=0.866	16.3 (5.0)	16.2 (6.0)	P=0.857	15.8 (4.8)	15.7 (5.9)	P=0.838
Na (mg/day)	4,222.5 (1,095.2)	3,299.2 (1,142.6)	P < 0.001	4,177.3 (1,027.9)	3,207.5 (1,022.5)	P < 0.001	4,200.3 (1,062.0)	3,253.7 (1,081.5)	P < 0.001
K (mg/day)	2,623.0 (637.4)	2,325.0 (727.1)	$P\!\!=\!\!0.001$	2,734.9 (682.0)	2,367.9 (637.3)	P < 0.001	2,677.9 (661.5)	2,346.3 (681.7)	P < 0.001
Ca (mg/day)	586.4 (210.2)	545.9 (209.0)	$P\!\!=\!\!0.158$	628.1 (225.9)	511.3 (176.6)	P < 0.001	606.9 (218.8)	528.8 (193.6)	P < 0.001
Mg (mg/day)	248.9 (56.0)	278.2 (88.4)	P=0.012	251.1 (59.3)	283.6 (88.4)	$P\!\!=\!\!0.006$	249.9 (57.6)	280.9 (88.1)	P < 0.001
Se (µg/day)	150.1 (61.3)	128.2 (42.0)	$P\!\!=\!\!0.001$	152.2 (65.8)	123.3 (33.3)	P < 0.001	151.2 (63.5)	125.7 (37.8)	P < 0.001
Fe (mg/day)	9.9 (2.4)	15.3 (4.7)	P < 0.001	10.0 (2.6)	15.1 (4.5)	P < 0.001	9.9 (2.5)	15.2 (4.6)	P < 0.001
P (mg/day)	1,040.8 (243.2)	1,025.0 (248.6)	P=0.636	1,032.1 (243.7)	994.0 (233.3)	P=0.253	1,036.5 (243.2)	1,009.6 (240.7)	P=0.253
Vitamin C (mg/day)	126.5 (72.1)	101.7 (70.2)	P=0.012	137.1 (70.5)	118.1 (72.7)	$P\!\!=\!\!0.053$	131.7 (71.4)	109.9 (71.7)	P=0.002
Vitamin A (IU/day)	5,901.6 (3,420.3)	7,864.6 (5,206.6)	P=0.005	6,570.1 (3,986.0)	9,419.6 (8,039.1)	$P\!\!=\!\!0.007$	6,229.4 (3,720.3)	8,636.2 (6,780.9)	P < 0.001
Retinol (µg/day)	369.8 (501.0)	275.9 (164.4)	P=0.009	266.0 (327.4)	300.5 (403.3)	P=0.465	318.9 (427.6)	288.1 (306.2)	P=0.339
$\beta$ -carotene (mg/day)	2,801.4 (1,839.0)	4,159.6 (3,084.5)	$P\!\!=\!\!0.001$	3,410.1 (2,315.3)	5,041.8 (4,871.9)	$P\!\!=\!\!0.010$	3,099.9 (2,106.5)	4,597.4 (4,079.0)	P < 0.001

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P/S ratio: polyunsaturated/saturated fatty acids ratio.