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Biological and Lifestyle Factors, and Lipid and Lipoprotein Levels among Japanese Americans in Seattle and Japanese Men in Japan

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Background. It has been previously shown that Japanese Americans in Seattle have significantly higher cholesterol levels than native Japanese. The present study examines the association of biological and lifestyle factors with plasma lipid and lipoprotein levels among Japanese Americans (JA) and native Japanese (NJ) to determine if these associations are consistent between these high and low cholesterol populations.

Methods. Study samples consisted of 710 JA male and 728 JA female volunteers living in the Seattle area and a random sample of 3833 NJ male urban workers who participated in parallel cardiovascular disease screening and lifestyle surveys for 1989–1994. Multiple regression analysis was conducted to examine the association of lifestyle and biological factors with lipid and lipoprotein levels.

Results. Alcohol consumption was positively and linearly associated with high density lipoprotein cholesterol (HDL-C) levels and negatively associated with both low density lipoprotein cholesterol (LDL-C) levels and the ratio of total cholesterol (TC)/HDL-C ($P < 0.05$ to $P < 0.001$) among JA males and JA females and NJ males. Current smoking habit was observed to be negatively associated with HDL-C levels and positively with TC/HDL-C ratio and log TG levels (logarithmic transformation of triglyceride values) ($P < 0.05$ to $P < 0.001$) among all three groups. Body mass index (BMI) was negatively associated with HDL-C levels and positively associated with log TG and TC/HDL-C ratio among all three groups ($P < 0.05$ to $P < 0.001$). Moderate alcohol consumption was negatively associated with log TG levels among JA males and females ($P < 0.05$), whereas heavy alcohol consumption was positively associated with log TG levels in NJ males ($P < 0.001$). Smoking was positively associated with TC and LDL-C levels ($P < 0.05$) among JA males, whereas a negative association ($P < 0.05$) was observed in NJ males.

Conclusion. Overall, the fitted models were consistent between JA males and females and NJ males with the exception of smoking on TC and LDL-C. The results suggest that moderate alcohol consumption favourably influences lipid profiles in both high and low cholesterol populations. The results also indicate that light alcohol consumption is associated with decreased triglyceride levels, whereas heavy alcohol consumption is associated with increased triglyceride levels.

Keywords: alcohol, Japanese, Japanese Americans, lipids, lipoproteins, smoking

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It is well known that high serum total cholesterol (TC) and low density lipoprotein cholesterol (LDL-C) levels are primary risk factors for coronary heart disease (CHD), and high serum levels of high density lipoprotein cholesterol (HDL-C) confer a protective benefit against its development.[1–3] Reducing TC levels has been shown to decrease the risk of CHD[4–6] and the National Cholesterol Education Program (NCEP) has identified LDL-C as the major atherogenic lipoprotein and the primary target of cholesterol lowering therapy.[7] Elevated triglyceride (TG) levels are also considered to increase the risk for CHD, partly because high TG levels are correlated with high levels of LDL-C[8] and low levels of

HDL-C.[9] In addition to constitutional determinants such as age, sex, ethnicity and genetic factors, other variables such as dietary fat and lifestyle factors including physical activity, alcohol consumption and smoking habit are known to affect serum lipid and lipoprotein levels.[10,11]

Compared with other industrialized nations, Japanese are known to be at a lower risk for CHD.[12] Annual CHD mortality rates per 100 000 population were 41.8 in Japan (1991),[13] 86.9 in France (1990),[14] 192.5 in the US (1991),[15] and 294.6 in England and Wales.[14] Cross-cultural epidemiological studies conducted more than two decades ago have shown that lipid levels and the prevalence of CHD was lowest among native Japanese in Japan, higher in Japanese Americans living in Hawaii and highest in Japanese Americans living in California.[16]

Over the past 25 years since the initiation of the Ni-Hon-San Study[16] there have been dramatic changes in health behaviours among Americans, including a decrease in the number of smokers, a decrease in the level of alcohol consumption and an increase in physical activity level.[17–19] Among native Japanese, there has been an increase in fat intake and alcohol consumption and a decline in smoking.[20] Despite these changes, current studies have shown that Seattle Japanese Americans have significantly higher TC levels and TG levels and lower HDL-C levels than native Japanese urban workers.[21] The present study examines the association between biological and lifestyle factors among Japanese Americans (JA) in Seattle and native Japanese (NJ) in Japan to examine if the associations are consistent between these low and high cholesterol groups. Such cross-cultural comparisons allow for minimization of the genetic components influencing lipid levels, and thus provide a better understanding of the impact of environmental factors including changes in lifestyle and constitutional factors on lipid and lipoprotein levels.

MATERIALS AND METHODS

Parallel cardiovascular disease screening was conducted by the Nikkei Disease Prevention Center in Seattle, Washington from 1989 to 1994 and the Epidemiological Arteriosclerosis Research Institute (EARI) in major cities in Japan in 1994. The study sample consisted of male and female JA residing in the greater Seattle area (King County) and NJ males from major metropolitan areas in Japan who participated in screening at EARI. Japanese American screening participants were respondents from a media and family registration campaign conducted by mail. A total of 1438 individuals (710 men and 728 females) who are of full Japanese ancestry aged 30–79 years participated in the study with complete clinical and lifestyle information. The composition of the study sample with respect to generation was as follows: 12.3% Issei (first generation), 49.4% Nisei (second generation), 37.0% Sansei (third generation) and 1.3% Yonsei (fourth generation). The study sample represented 12.7% of the JA men and 10.3% of JA women in the Seattle area according to an estimation of the JA population based on the 1990 US Census.[22]

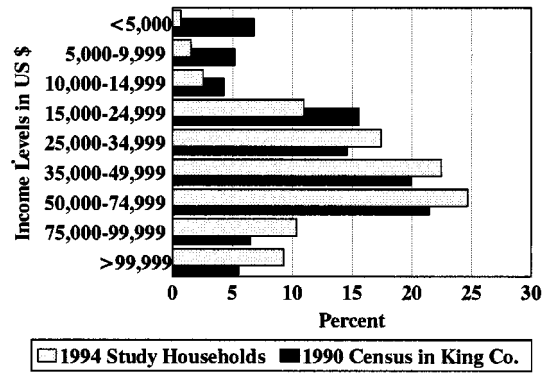

FIGURE 1 *Income distribution of 1175 study participants' households and the Japanese American households of the 1990 US census in King County*

Due to the fact that the study subjects in Seattle were voluntary participants, we conducted an additional survey on 1994 household income levels to better define our study sample characteristics and examine whether they were representative of the JA population in Seattle. We compared the household incomes from study participants with that of JA households in the 1990 census for King County.[23] Figure 1 shows that the income distribution of the screening participants is slightly higher than that reported for the JA population in King County for the 1990 census. We will later discuss possible response bias observed in the study results.

Native Japanese study subjects consisted of mostly urban white collar employees from major cities in Japan, including Tokyo, Chiba, Osaka, Sapporo, and Kitakyushu. A total of 3833 study subjects were randomly drawn from a pool of 28 635 male employees of various companies in Japan who had participated in cardiovascular disease screening conducted by EARI in 1994. Their occupations were classified as follows: 50.8% professionals, researchers, engineers and highly trained technicians, 35.7% administrators, accountants, salesmen and survey staff, and 13.5% others. In general, annual health screening is offered by the respective company as part of the employee's health benefits and participation is almost mandatory.

Venous blood samples were obtained after a 12-hour fast from JA study participants. Lipid analyses were conducted at the University of Washington Northwest Lipid Research Laboratories which participates in the Centers for Disease Control and Prevention/National Heart, Lung and Blood Institute's lipid standardization programme. Total cholesterol and TG levels were measured enzymatically on the Abbott Spectrum analyser using methods standardized to in-house reference methods and to the CDC's reference methods and in-house prepared reagent.[24] The HDL-C levels were measured by dextran sulphate magnesium precipitation method.[25] The LDL cholesterol was determined by the Friedewald algorithm: LDL-C = TC minus HDL-C minus TG/5.[26] Because LDL-C estimation becomes less accurate if the TG value >400 mg/dl, we excluded these few cases from statistical analysis involving LDL-C.[27]

Among the NJ screening participants, non-fasting venous blood samples were analysed by EARI's laboratory in Japan. Total cholesterol was measured by an enzymatic method which was described by Allain *et al.*[28] Serum TG levels were determined by a colorimetric method with lipoprotein lipase and glycerol dehydrogenase.[29] The HDL-C measurement was done by using the dextran sulphate magnesium method.[30] The LDL-C was determined by the Friedewald algorithm.[26]

Quality control (QC) examinations for EARI's laboratory were conducted by shipping frozen serum samples twice from Seattle to EARI prior to the screening. For each QC examination, nine standardized samples were used for TC measurements and six standardized samples were used for TG, LDL-C and HDL-C. After adjustments were made at EARI's laboratory based on the values obtained from the first measurements, all measured values in the second QC examination fell within 5% of the true value (10% range criteria was established for HDL-C), with the exception of a few samples. High correlation coefficients were obtained between true values and the second measurement values: r = 0.999 ($P < 0.01$) for TC, r = 0.969 ($P < 0.01$) for HDL-C, r = 0.910 ($P < 0.05$) for LDL-C and r = 0.999 ($P < 0.01$) for triglycerides.

Height and weight were measured with participants clothed in a hospital gown. Body mass index (BMI) was obtained by dividing weight in kilograms by the square of height in metres. Similar questionnaires were self-administered at the time of screening, which contained questions on personal and demographic background, disease history and lifestyle factors; one written in Japanese for NJ participants, and one in English for JA. Only those questions which could be considered comparable were used in our analysis. Average daily alcohol consumption was estimated based on responses to specific questions regarding frequency of drinking, size of serving and type of alcoholic beverage consumed. The estimated average amount of alcohol consumed was converted to pure alcohol equivalents. Then, one drink was defined as an equivalence of 10 g of pure alcohol. The study samples were stratified into six groups: non-drinkers, <1 drink/week, 1–6 drinks/week, 1–2 drinks/day, 3–5 drinks/day and >5 drinks/day and treated as dummy variables. Participants who had quit drinking less than one year ago were considered to be current drinkers.

Multiple regression models were constructed to explain differences in levels of lipids and lipoproteins by age, BMI, hypertensive medication, alcohol consumption and smoking status. Because TG values were highly skewed, logarithmic transformation of TG values was performed for normalization for regression analysis. All analyses were conducted separately by sex using IBM AT with SPSSPC + V3.0.[31]

RESULTS

Characteristics of the JA and NJ study samples are presented in Table 1. The average age for each of the three groups fell between 55 and 56 years. Higher averages of BMI, TC, LDL-C, TG and TC/HDL ratio were observed in JA males and females as compared to NJ males. The HDL-C average values were highest in JA females (63.2 mg/dl), lowest in JA males (51.0 mg/dl) and the average value for NJ males fell in the middle (55.4 mg/dl). There was a great difference in the amount of alcohol consumed between JA males and NJ males: NJ men consumed more than four times the amount consumed by JA men (27.3 versus 5.8 g/day). The percentage of current smokers was three times higher in NJ males than in JA males (46.0% versus 15.4%), while only 9% of JA women smoked. Current use of anti-hypertensive medication was more prevalent in both JA men and women than in NJ men. Overall, the lipid profiles of JA men and perhaps JA women (with the exception of high HDL-C averages) were worse than in NJ men despite less smoking and alcohol consumption among JA participants.

Table 2 summarizes the results of multiple regression analysis to explain differences in lipoprotein and lipid levels in JA and NJ male participants and JA female participants with age, BMI, level of alcohol consumption, smoking status and hypertensive medication as explanatory variables. The strength of the association, indicated by R^2, of lipids and lipoproteins with lifestyle and biological factors varied from 4.6% in the TC model to 19.7% in the HDL-C model among JA

TABLE 1 *Characteristics of Japanese Americans in Seattle, Washington, USA and native urban Japanese in Japan who participated in screening*

	Japanese American males n = 710		Japanese American females n = 728		Native Japanese males n = 3833	
	Mean	SD[a]	Mean	SD	Mean	SD
Age	56.4	13.7	55.9	13.6	55.6	7.7
BMI	25.7	3.2	24.0	3.8	23.8	2.7
TC[b] (mg/dl)	224.1	37.8	227.3	41.6	191.1	32.4
LDL-C[c] (mg/dl)	139.1	35.3	135.0	38.0	108.6	31.1
HDL-C[d] (mg/dl)	51.0	14.0	63.2	16.7	55.4	14.3
Triglycerides (mg/dl)	169.8	158.6	143.9	120.5	135.6	101.3
Log TG[e]	4.9	0.6	4.8	0.6	4.7	0.6
TC/HDL ratio	4.7	1.4	3.9	1.3	3.7	1.1
Alcohol (g/day)	5.8	11.9	1.3	4.6	27.3	22.2
	No.	%	No.	%	No.	%
Drinking habit						
Nondrinkers	257	36.2	389	53.4	686	17.9
<1 drink/week	157	22.1	212	29.1	378	9.9
1–6 drinks/week	157	22.1	98	13.5	621	16.2
1–2 drinks/day	89	12.5	24	3.3	516	13.5
3–5 drinks/day	44	6.2	4	0.5	1015	26.5
>5 drinks/day	6	0.8	1	0.1	617	16.1
Smoking						
Nonsmokers	265	37.3	512	70.3	1355	35.4
Current smokers	109	15.4	66	9.1	1762	46.0
Ex-smokers	336	47.3	150	20.6	716	18.7
Hypertensive medication	102	14.4	112	15.4	413	10.3

[a] SD = standard deviation.
[b] Total cholesterol.
[c] Low density lipoprotein cholesterol.
[d] High density lipoprotein cholesterol.
[e] Triglycerides.

males with the strongest association found in HDL-C. Among NJ males the strength of the association, R^2, varied from 4.2 in the TC model to 16.4 in the TC/HDL model. The R^2 in the regression models for JA females were high overall: from 15.4% in the HDL-C model to 26.9% in the log TG model. The appearance of significant regression coefficients varied somewhat between the three groups and between models. In the models predicting TC levels, there was a positive association with age in all three groups ($P < 0.001$) and BMI appeared positively significant in both JA females and NJ males ($P < 0.001$). Current smoking habit was observed to be positively associated with TC levels in JA males ($P < 0.05$), whereas in NJ males, a negative association was observed ($P < 0.05$).

Similar relationships were found for LDL-C levels as well; age was positively associated with LDL-C levels among all three groups ($P < 0.001$), and BMI was positively associated among NJ males and JA females ($P < 0.001$). Hypertensive medication was negatively associated with LDL-C in JA females ($P < 0.05$) and NJ males ($P < 0.01$). Among NJ males, LDL-C levels showed a negative association to levels of alcohol consumption in a dose dependant manner ($P < 0.01$ to $P < 0.001$). Alcohol consumption significantly reduced levels of LDL-C in JA males and females at one to two drinks per day ($P < 0.05$). Opposite associations were seen with current smoking status; a positive association was observed among JA males ($P < 0.05$), whereas in NJ males, smoking was negatively associated with LDL-C levels ($P < 0.05$).

The relationships observed between HDL-C and the explanatory variables were consistent between all three study groups. Overall, HDL-C was positively associated with alcohol consumption in a dose dependant manner ($P < 0.001$) and negatively associated with BMI ($P < 0.001$) and smoking ($P < 0.05$ to $P < 0.001$) in all three groups.

TABLE 2 *Multiple regression coefficients for examining the association between lipid and lipoprotein levels and biological and lifestyle factors*

Explanatory variables	Total cholesterol (mg/dl)			Low density lipoprotein cholesterol (mg/dl)			High density lipoprotein cholesterol (mg/dl)		
	JA[a] males	JA females	NJ[b] males	JA males	JA females	NJ males	JA males	JA females	NJ males
Age	0.419***	1.372***	0.243***	0.342**	0.956***	0.186**	0.029	0.048	0.057*
	(0.117)[c]	(0.112)	(0.069)	(0.104)	(0.104)	(0.065)	(0.040)	(0.047)	(0.028)
BMI	0.629	1.279***	2.166***	0.693	1.565***	1.966***	–1.203***	–1.387***	–1.567***
	(0.443)	(0.368)	(0.195)	(0.395)	(0.347)	(0.184)	(0.151)	(0.157)	(0.081)
Hypertensive	5.730	–4.355	–1.997	2.882	–8.536*	–4.476**	1.637	–0.314	0.099
medication	(4.120)	(4.045)	(1.709)	(3.797)	(3.813)	(1.616)	(1.428)	(1.677)	(0.705)
Drinking habit									
Nondrinkers (ref)									
<1 drink/week	–0.096	1.020	2.142	1.647	0.796	–0.097	–1.162	1.551	2.730**
	(3.860)	(3.291)	(2.048)	(3.432)	(3.078)	(1.936)	(1.311)	(1.364)	(0.845)
1–6 drinks/week	2.348	–1.498	0.227	2.946	–6.844	–4.713**	1.103	6.600***	4.632***
	(3.830)	(4.483)	(1.773)	(3.436)	(4.183)	(1.676)	(1.302)	(1.858)	(0.731)
1–2 drinks/day	–7.710	–3.902	–1.622	–10.179*	–16.367*	–5.568**	7.927***	12.682***	4.858***
	(4.650)	(7.922)	(1.858)	(4.109)	(7.287)	(1.757)	(1.581)	(3.284)	(0.767)
3–5 drinks/day	10.307	–3.859	0.494	–7.895	–20.436	–8.518***	15.348***	26.940***	9.565***
	(6.120)	(18.910)	(1.584)	(5.570)	(17.377)	(1.497)	(2.081)	(7.839)	(0.653)
>5 drinks/day[d]	6.333		1.451	–9.744		–16.244***	15.988**		11.051***
	(15.402)		(1.797)	(13.434)		(1.699)	(5.237)		(0.741)
Smoking habit									
Nonsmokers (ref)									
Smokers	8.648*	2.879	–2.495*	8.048*	6.615	–2.393*	–2.951*	–6.411**	–5.406***
	(4.358)	(5.104)	(1.173)	(3.957)	(4.650)	(1.109)	(1.482)	(2.079)	(0.484)
Ex-smokers	–1.571	–2.812	2.951	–0.586	0.550	1.476	–1.433	–2.226	–1.171
	(3.398)	(3.502)	(1.478)	(3.044)	(3.258)	(1.397)	(1.155)	(1.452)	(0.609)
Intercept	182.8	120.8	127.7	103.9	47.3	60.1	79.1	93.0	86.6
R^2(%)	4.6	21.1	4.2	4.7	16.3	6.5	19.7	15.4	16.0
F value	3.35***	19.15***	16.61***	3.30***	13.58***	26.53***	17.20***	13.10***	72.91***

continued overleaf

For TC/HDL-C ratio, consistent relationships were observed among all three groups as well; TC/HDL-C ratio was negatively associated with alcohol consumption in a dose-dependant manner ($P < 0.05$ to $P < 0.001$) and positively associated with BMI ($P < 0.001$) and current smoking habit ($P < 0.05$ to $P < 0.001$).

Triglyceride levels (log TG) appeared to be more strongly correlated with lifestyle and biological factors in JA females than in JA males. For JA females, all explanatory variables with the exception of two categories (ex-smokers and >5 drinks/day) showed a significant relationship to log TG; age ($P < 0.001$), BMI ($P < 0.001$) and medication for hypertension ($P < 0.05$) were positively associated and alcohol consumption was negatively associated ($P < 0.05$). Among JA males, log TG was positively associated with BMI ($P < 0.001$) and smoking status ($P < 0.05$) and negatively associated with a level of alcohol consumption of 1–2 drinks/day ($P < 0.05$). Among NJ males, log TG levels were positively associated with BMI ($P < 0.001$), hypertensive medication ($P < 0.05$), a level of alcohol consumption of ⩾5 drinks/day ($P < 0.001$), current smoking habit and ex-smoking habit ($P < 0.001$).

DISCUSSION

The observed relationships in the present study were fairly consistent between JA and NJ study participants for models predicting TC and HDL-C levels. Some differences were observed in the models predicting LDL-C and log TG levels. The analysis for each lipid component examined will be discussed separately.

Age and BMI were associated with a significant increase in TC levels among JA females and NJ males. Among JA males, age but not BMI was a significant predictor of TC levels. Other studies have shown that the association between TC and lifestyle factors was not strong.[32] The Honolulu Heart Study[11] showed no

TABLE 2 *Continued*

Explanatory variables	log Triglycerides (mg/dl)			Total cholesterol/High density lipoprotein cholesterol		
	JA males	JA females	NJ males	JA males	JA females	NJ males
Age	0.002	0.016***	0.001	0.006	0.020***	0.002
	(0.002)	(0.002)	(0.001)	(0.004)	(0.004)	(0.002)
BMI	0.050***	0.048***	0.068***	0.112***	0.104***	0.138***
	(0.007)	(0.005)	(0.003)	(0.016)	(0.012)	(0.006)
Hypertensive	0.054	0.120*	0.064*	0.022	0.012	–0.043
medication	(0.066)	(0.059)	(0.028)	(0.149)	(0.129)	(0.054)
Drinking habit						
Nondrinkers (ref)						
<1 drink/week	–0.008	–0.102*	–0.041	0.091	–0.128	–0.171**
	(0.061)	(0.048)	(0.038)	(0.137)	(0.104)	(0.065)
1–6 drinks/week	–0.042	–0.145*	0.008	–0.050	–0.382**	–0.353***
	(0.061)	(0.065)	(0.029)	(0.136)	(0.143)	(0.056)
1–2 drinks/day	–0.172*	–0.059*	–0.052	–0.837***	–0.721**	–0.397***
	(0.074)	(0.115)	(0.031)	(0.165)	(0.253)	(0.059)
3–5 drinks/day	0.099	–0.611*	–0.036	–0.986***	–1.356*	–0.645***
	(0.097)	(0.275)	(0.026)	(0.218)	(0.603)	(0.050)
>5 drinks/day[‡]	0.048		0.137***	–1.089*		–0.677***
	(0.244)		(0.030)	(0.548)		(0.057)
Smoking habit						
Nonsmokers (ref)						
Smokers	0.136*	0.168*	0.173***	0.512**	0.397*	0.341***
	(0.069)	(0.073)	(0.019)	(0.155)	(0.160)	(0.037)
Ex-smokers	–0.007	–0.043	0.096***	0.057	0.131	0.140***
	(0.054)	(0.051)	(0.024)	(0.121)	(0.112)	(0.047)
Intercept	3.5	2.8	3.0	1.5	0.3	0.5
R^2(%)	8.5	26.9	14.0	14.5	18.5	16.4
F value	6.49***	26.33***	62.20***	11.86***	16.32***	74.71***

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.
[a] Japanese American.
[b] Native Japanese.
[c] Standard error.
[d] No meaningful result for JA females could be obtained because only one person fell in this category.

strong association between lifestyle factors and TC in Japanese American men. Similarly, in the study examining Japanese white collar male workers,[33] age and BMI were significantly related to TC, but alcohol consumption was not. Total cholesterol is considered a crude indicator of lipid profile status, and factors such as alcohol may have opposite effects on TC components, LDL-C (negative) and HDL-C (positive), resulting in nonsignificant or spurious associations between lifestyle factors and TC.

Low density lipoprotein cholesterol has been labelled as the major atherogenic lipoprotein and has become the primary focus for cholesterol lowering therapy.[7] As observed in the model for TC, BMI was a significant predictor of LDL-C in JA females and for NJ males, but not among JA males. Similar to the Honolulu Heart Study[11] and other studies with native Japanese males[33] and American females,[34] alcohol consumption was significantly associated with reduced LDL-C levels in all three groups of our study. This effect was significant only at a consumption level of 1–2 drinks/day among JA subjects whereas among NJ it was significant for all levels of regular alcohol consumption. Sample size between study populations may account for such observed differences, in that the majority of JA study subjects were found to be non- or light to moderate drinkers with only a small percentage consuming ⩾3 drinks/day.

In accordance with numerous other epidemiological studies,[10,11,33,35,36] HDL-C levels were positively associated with alcohol consumption and inversely associated with BMI and smoking in both JA and NJ screening participants. Table 3 presents regression models for

TABLE 3 *Comparison of regression models for high density lipoprotein cholesterol among epidemiological studies*

Explanatory variables	Seattle Japanese Americans Seattle Nikkei Health Study		Native Japanese urban workers Seattle Nikkei Health Study	Hawaiian Japanese Americans Yano *et al.*[11]	US & Japan telephone company executives Ohara *et al.*[36]	Native Japanese white collar employees Choudhury *et al.*[33]
	Females	Males	Males	Males	Males	Males
Race (American versus Japanese)					–4.157***	
Age	NS[a]	NS	0.057*	NS	NS	0.132*
BMI	–1.387***	–1.203***	–1.567***	–1.351***	–0.726***	–1.408***
Medication for hypertension	NS	NS	NS	–1.589*		
Drinking habit						
Nondrinkers versus current drinker				0.544***		
<1 drink/week	NS	NS	2.730**			
1–6 drinks/week	6.600***	NS	4.632***			
1–2 drinks/day	12.682***	7.927***	4.858***			
3–5 drinks/day	26.940***	15.348***	9.565***			
>5 drinks/day		15.988***	11.051***			
<once/day					5.257***	
<30 cc/day					6.457***	
>30 cc/day					9.104***	
Alcohol (ml/day)						0.102***
Smoking habit						
Nonsmokers versus current smokers	–6.411**	–2.951*	–5.406***	NS	–4.004***	
ex-Smokers	NS	NS	NS			
no. of cigarettes/day						–0.164***
Physical activity				0.209*	1.806**	
Walking				NS		
Diastolic blood pressure				NS		
Haematocrit (%)				NS		
Serum uric acid (mg/dl)					–1.633***	
Intercept	92.97	79.11	86.6	65.10	73.60	not available
R^2 (%)	15.4	19.7	16.0	17.5	11.2	21.1
Sample size	728	710	3833	1363	1499	1010
Average age	56	56	56	68	46	47

*$P < 0.05$, ** $P < 0.01$, *** $P < 0.001$.
[a] Not significant.

HDL-C obtained from the present study and other similar studies as follows JA males in the Honolulu Heart Study,[11] Japanese and American caucasian male telephone executives,[36] and NJ white collar workers in Japan.[33] The HDL-C levels were positively associated with alcohol and negatively with BMI in all four studies. A significant positive association between HDL-C levels and age was observed in NJ male subjects and in NJ white collar employees.[33] Smoking was consistently inversely associated with HDL-C levels with the exception of the Honolulu Heart Study. Many other studies have noted an inverse relationship between smoking and HDL-C levels,[10,37–42] which in conjunction to alteration of HDL-C's antiatherogenic properties,[43] is one mechanism proposed whereby smoking increases the risk of coronary atherosclerosis.

Similar to the LRC study[44] and others,[11,33] BMI was found to be positively associated with TG levels in all three groups. Alcohol consumption has also been reported to be positively associated with TG levels.[11,44,45] Among the NJ male study subjects, heavy alcohol consumption (>5 drinks/ day) was associated with a significant increase in TG levels, whereas alcohol consumption was negatively associated with TG levels in JA males who consumed 1–2 drinks/day and in JA women who consumed any amount. The difference in the fitted models for TG between JA males and NJ males might have been influenced by the difference in

alcohol consumption levels: JA male drinkers were predominantly light to moderate drinkers, whereas NJ male drinkers were predominantly moderate to heavy drinkers. A similar relationship was shown in NJ male subjects by Choudhury *et al.*;[33] light drinkers had significantly lower TG levels than heavy drinkers. Similarly, in British men[46] heavy drinking habit has a tendency to raise TG levels. However, log TG levels were significantly and negatively associated with more drinking levels in females than in either JA or NJ males despite the fact that JA females drink much less than JA and NJ males. This implies that even slight intake of alcohol might lower TG levels among females but not among males. In the future, this issue should be investigated in other female populations as well.

Anti-hypertensive medications, e.g. diuretics and selective and non-selective beta-blockers, have been shown to adversely affect blood lipids.[47] In our study, anti-hypertensive medication showed a negative association with LDL-C and a positive association with log TG in JA females and NJ males. The majority of study participants using anti-hypertensive medications were taking either diuretics, calcium channel blockers or adrenergic blockers, and a few of them were taking angiotensin converting enzyme inhibitors and vasodilators. Yano *et al.*[11] reported that anti-hypertensive medication (mainly thiazide diuretics) was associated with reduced HDL-C levels and increased TG levels independent of diastolic blood pressure, BMI and other confounding factors. In our study the sample size was too small to analyse the data by types of hypertensive medication.

Another observed difference between study groups was the effect of smoking on TC and LDL-C levels between JA and NJ males. Among JA males, a positive association between current smoking habit and TC or LDL-C levels was observed. This is consistent with other studies as reviewed by Craig *et al.*[48] In order to determine if the significant effects of smoking on lipid levels (TC, TC/HDL-C, HDL-C, LDL-C and log TG) depend on drinking habits, an effect for the interaction between smoking and drinking was estimated for each regression equation in the samples of Seattle JA. No significant interaction effects were found except for LDL-C among JA males ($F_{4,665} = 2.72$, $P < 0.05$). The results suggest that the effect of smoking on LDL-C is substantially greater for drinkers than for ex-drinkers and nondrinkers among JA males but not among JA females. Among NJ males the association of smoking with TC and LDL-C was found to be significant but negative. Choudhury *et al.* reported negative non-significant associations between the number of cigarettes smoked and TC or LDL-C levels among NJ male white collar male employees.[33] It is quite possible that other factors such as dietary intake might act as a confounding variable or interact with smoking to influence serum lipid levels among NJ men. Interactions between smoking and alcohol consumption with diet are currently under investigation in our study population.

The results of the present study need to be interpreted within the context of some limitations. One potential bias is that the sample was not randomly drawn from the JA population in the Seattle area and nonparticipants may have different characteristics and health status than participants. Other surveys have shown that non-participants have poorer health than participants,[49,50] and if this were the case in our survey, it would be possible that we might have observed a higher percentage of current smokers and drinkers among non-participants. In order to examine this issue further, we conducted an additional survey to determine the 1994 annual household income levels of our study sample and compared their income distribution with that of JA households in King County from the 1990 US census (which includes Seattle and the surrounding metropolitan area) (Figure 1).[23] Although our sample distribution is slightly shifted to higher income levels as compared to the census distribution, it is remarkably similar to that of JA in King County. The 4-year gap between our sample and the census population might have contributed to the slightly higher income levels observed in our study sample because of the rate of inflation in household income. Additionally, lipid levels were compared among JA men and women according to household income levels. No differences were found except for average HDL-C levels: 56.6 mg/dl for $<$ \$25 000, 57.6 mg/dl for \$25 000–\$49 999 and 52.9 mg/dl for $>$\$49 999; and thus, it may be considered that our Seattle JA sample reasonably represents the JA population in the area, although we must be cautious about possible selection bias in a comparison of health outcomes between populations.

Native Japanese screening participants represent urban white collar office workers from several major metropolitan areas in Japan. Overall, workers are considered to be healthier than the general population. In fact, comparison in TC and LDL-C between the two populations shows that urban workers had significantly lower averages than the general Japanese population.[21]

Fasting requirements were not imposed on NJ urban workers, whereas JA were required to fast 12 hours prior to blood drawing. Nonfasting status has been shown to influence TG levels. The National Cardiovascular Disease Examination Survey Report[51] shows an inverse relationship between average TG levels and the number of fasting hours before blood drawing: 141.0 mg/dl among those with $<$3 hours of fasting, 132.1 mg/dl among those

with 3–6 h of fasting and 116.2 mg.dl among those with >6 h of fasting. Despite the nonfasting requirements, NJ men had considerably lower TG values as compared with JA males: 135.6 mg/dl and 169.8 mg/dl, respectively. Also, nonfasting requirements might have influenced LDL-C values among native Japanese because LDL-C values were estimated based on the Friedewald equation, which includes TG. However, if any systematic bias were introduced due to nonfasting status, the deviation from true values of LDL-C would be quite small and almost negligible because TG values are divided by a factor of five in the estimation. Furthermore, the average LDL-C level of NJ males was much lower than that of JA males (108.6 mg/dl versus 139.1 mg/dl).

Nutrient intake was not included in the present analysis and may enhance predictive value of the current models or act as potential confounding factors to BMI, smoking and alcohol consumption. Some investigators have reported that calories from alcohol supplements normal energy intake,[52–54] whereas others have found that calories from alcohol replaces energy intake from other sources, especially in heavy drinkers.[55] Physical activity was also not included in the present analysis which has been shown to increase HDL-C levels.[11,36] In our previous investigation with Seattle JA males,[56] we observed no significant relationship between physical activity and HDL-C levels. This may have been due to the fact that the majority of Seattle JA males were found to be fairly sedentary, thus any associations may not be apparent in this group. We suspect that NJ urban workers are more physically active due to various factors such as limited use of automobiles, more commuting by public transportation, and thus more walking in metropolitan areas in Japan. Effects of dietary habits and physical activity on lipid levels are currently under investigation.

In conclusion, the observed associations between plasma lipid and lipoprotein levels and biological and lifestyle factors among the three study groups (Seattle JA males and females and NJ males) are consistent with findings from other studies. Recently, we have reported that Seattle JA males and females have significantly higher total serum cholesterol levels[21] and others have reported higher prevalence of diabetes[57] among Seattle JA than among NJ or the general American population. Thus, it is apparent that the current campaign by CDC for 'Healthy People 2000'[58] which includes lowering total cholesterol levels to an average of <200 mg/dl before year 2000 and changing lifestyle to promote cardiovascular health is quite relevant to Seattle JA. Although such general guidelines are quite useful, there is a growing appreciation for the interaction between environmental and genetic factors to the contribution of cardiovascular disease, and thus sensitivity to changes in environment and diet may vary significantly between ethnic groups. Current studies conducted with Seattle JA suggest that a westernized lifestyle may be more harmful to people of Japanese ancestry who may have a greater propensity for the development of various metabolic abnormalities such as diabetes[57] and hyperlipidaemia.[21] Further cross-cultural investigations of this nature which reduce the genetic variation between cohorts are important for providing a clearer picture of the mechanisms involved in these complex relationships.

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