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Differences in lipoprotein particle subclass distribution for Japanese Americans in Hawaii and Japanese in Japan: The INTERLIPID Study

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Abstract

BACKGROUND: Current data suggest that low density lipoprotein (LDL) and high density lipoprotein (HDL) subclass concentrations relate directly to the risk of coronary heart disease (CHD). Earlier Studies indicated that Japanese in Japan had lower rates of CHD than Japanese Americans in Hawaii. Rates of CHD appear to continue to be lower in Japan despite increasing cholesterol levels in Japan and decreasing CHD rates in the United States.

OBJECTIVE: To provide insight into CHD rate differences.

METHODS: Nuclear Magnetic Resonance (NMR) measurements of lipoprotein subclasses were used to assess lipoprotein particle concentration and size in samples from these two genetically similar populations in Japan and Hawaii.

RESULTS: Japanese Americans had significantly higher age- and risk factor-adjusted concentrations of lipoprotein particles implicated in atherogenesis, including large very low density lipoprotein (VLDL; $P < 0.001$), small LDL ($P < 0.001$), and small HDL (women, $P < 0.001$; men, $P < 0.01$), and significantly lower concentrations of large LDL ($P < 0.001$) and the putative cardio-protective large HDL ($P < 0.05$) than Japanese in Japan. Average age- and risk factor-adjusted LDL and HDL particle sizes were also significantly ($P < 0.001$) smaller in Japanese Americans. Adjustment for body mass index markedly reduced the differences in some lipoprotein measures, including total LDL and large HDL particle concentrations for both genders, total VLDL particle concentration for women, and large VLDL concentration and average HDL particle size for men.

CONCLUSIONS: Differences in lipoprotein subclass distributions and lifestyle factors such as body weight may contribute to differences in CHD incidence for Japanese in Japan and Japanese Americans.

Keywords

Lipids; Coronary heart disease; Japanese; Japanese-Americans; Lipoprotein particles; Lifestyle; BMI

Since the end of World War II, Japanese in Japan have undergone a process of westernization, involving major changes in diet and other lifestyle factors. However, despite a marked increase in intake of cholesterol and saturated fat, increases in enzymatically determined total serum cholesterol levels, and high rates of smoking and hypertension, the incidence of coronary heart disease (CHD) incidence and rates of mortality remain substantially lower in Japan than the United States.¹⁻⁵ These differences are most striking in comparisons of Japanese and American men.^{2,3,6}

Japanese Americans also appear to have significantly greater mortality rates attributable to CHD than Japanese in Japan,⁷⁻⁹ illustrating the important influences of lifestyle and environment on cardiovascular health. In studies comparing enzymatically determined total cholesterol levels in Japanese Americans and native Japanese, the authors show that the differences between these two populations have decreased greatly from the previous generation but remain significant.^{4,9} However, there have been few standardized comparisons of lipid/lipoprotein levels between these populations in the last decade.

Recent evidence indicates that lipoprotein subclass distributions determined by nuclear magnetic resonance (NMR) spectroscopy may improve the prediction of CHD in individuals beyond risk assessments provided by conventional enzymatically determined lipid levels.^{10–15} The basis for this assessment is that each lipoprotein subclass emits a characteristic NMR signal, which differs in frequency and shape depending on the diameter of the lipoprotein particles. The amplitude of the NMR signal is proportional to the quantity of subclass particles. Concentration and average size of very low-density lipoprotein (VLDL), low-density lipoprotein (LDL), and high-density lipoprotein (HDL) particle subclasses can be calculated from the NMR signals using conversion factors derived from analyses of purified lipoprotein subclass reference standards.¹⁵

On the basis of this technology, high concentrations of large VLDL, small LDL, and small HDL, and smaller LDL particle size have been linked with greater risk for cardiovascular disease (CVD).^{16–18} Larger average LDL and HDL particle sizes have been linked with longevity.¹⁹ Coronary calcium score has been positively associated with small, medium, and large VLDL concentration, small LDL concentration, and smaller LDL particle size and inversely associated with large HDL concentration.²⁰ Progression of coronary artery disease has been positively associated with small and total LDL concentration and small HDL concentration, and inversely associated with large HDL concentration.²¹

In this study, standardized NMR measurements of lipoprotein subclasses were used to assess lipoprotein particle concentration and particle size differences in two genetically similar populations: Japanese Americans in Hawaii and Japanese in Japan from the INTERLIPID Study, ancillary to the INTERMAP Study of diet and blood pressure.⁴

Methods

As part of the 17-sample, 4-country INTERMAP study,^{22,23} 40- to 59-year-old men and women of Japanese ancestry in four population samples in Japan and one in Honolulu, Hawaii were examined based on a standardized common protocol. In the analyses reported here, participants from Hawaii and three of the four Japanese sites were included (198 from Honolulu, Hawaii; 284 from Toyama, Japan; 248 from Aito, Japan; 283 from Wakayama, Japan; participants from the Sapporo, Japan, center were omitted from this analysis because plasma samples thawed during shipment). Parents of all participants in Japan and Hawaii were entirely of Japanese ancestry. Detailed methods of the INTERMAP Study have been reported.^{22,23} In brief, blood pressure measurements were made on four different days and medical and lifestyle information was collected. Hypertension was defined as systolic blood pressure ≥ 140 mm Hg, diastolic blood pressure of ≥ 90 mm Hg, or use of antihypertensive drugs. Four 24-h dietary recalls and two 24-h urine collections were obtained per participant. Alcohol consumption for the previous 7 days was obtained during two of the examinations. Nonfasting blood was drawn and centrifuged within 30 min. Serum and plasma were immediately placed under refrigeration and all specimens were frozen and stored at -70°C within 24 hours. Serum lipids and other serum variables were measured approximately 6 to 12 months later in a Center for Disease Control and Prevention standardized laboratory in Japan. These values have been reported.⁴ Institutional review committees of the Shiga University of Medical Science, the Kanazawa Medical University, the Wakayama Medical

University, the Pacific Health Research Institute, and Northwestern University approved the study protocol. Written informed consent was obtained from all participants.

Laboratory

Plasma samples from Japan were shipped on dry ice to Hawaii shortly after collection, and stored along with the plasma samples from Hawaii for approximately 4 years at -70°C . Samples were then shipped on dry ice to Lipo-Science, Inc. (Raleigh, NC) for NMR spectroscopy lipoprotein analysis. Lipoprotein subclass particle sizes and concentrations were measured by NMR spectroscopy in freshly thawed specimens (0.5 mL) as previously described.^{14,15,24} In brief, signals for each lipoprotein particle subclass were identified in the NMR spectrum by their characteristic frequency and shape. The amplitude of the NMR signal for each particle subclass was converted to concentration (molar levels of lipoprotein particles per liter) by the use of conversion factors derived from studies of a subclass reference library. The following subclass concentrations were analyzed (diameter ranges are approximate): small (27–35 nm), medium (35–60 nm), and large (>60 nm) VLDL; intermediate density lipoprotein (IDL, 23–27 nm); small (18.0–21.2 nm) and large (21.2–23.0 nm) LDL; and small (7.3–8.2 nm), medium (8.2–8.8 nm), and large (8.8–13 nm) HDL. Weighted average VLDL, LDL, and HDL particle sizes (nm diameter) were calculated from the subclass concentrations by summing the diameter of each subclass multiplied by its relative mass percentage, which was estimated from the intensity of the NMR signal.¹⁵

Statistical methods

The mean values of many potential covariates (Table 1) and the distributions of the NMR measurements were different for men and women so sex-specific analyses were performed. Because a large proportion of the NMR measurement distributions were heavily right-skewed, the median and ranges are presented in Tables 2 and 3. The Wilcoxon's rank sum test was first used to compare NMR measurements for participants from Hawaii and Japan. The median regression model, which minimizes the sum of the absolute value of the residuals,²⁵ was then used to compare the lipid subclass measurements with adjustments for conventional CVD risk factors to determine whether the lipoprotein profile differences were independent of these variables. Three models were used in the median regression analyses: 1) adjustment for age alone, 2) adjustment for age and certain CVD risk factors (dietary cholesterol, saturated fat, and alcohol intake, smoking, and menopause for women), and 3) adjustment for age, CVD risk factors, and body mass index (BMI). Additional models adjusted for age, CVD risk factors, carbohydrate intake, total caloric intake, physical activity, and non-fasting triglyceride levels successively (data not shown). In a separate analysis, the bootstrap method was used to estimate the standard errors and p-values of the four median regression models.²⁶ This method yielded similar results. SAS procedures NPAR1WAY (SAS Institute Inc, Cary, NC) and STATA programs QREG (STATA Corp, College Station, TX) were used in the analysis.

Results

Demographic, anthropomorphic, and biochemical characteristics

Japanese-American men and women in Hawaii had significantly greater BMI ($P<.001$), and a significantly greater percentage had hypertension ($P<.001$) when compared with the Japanese men and women in Japan (Table 1). Smoking rates were significantly greater for men in Japan ($P<.001$). Smoking was much less prevalent for women than men in both Hawaii and Japan. Former smokers were more common for both genders in Hawaii. Alcohol intake was significantly lower for men ($P<.001$) and women ($P<.01$) in Hawaii compared with Japan, and alcohol intake was much lower for women than men in both Hawaii and Japan. Saturated fat intake was significantly greater for both genders ($P<.001$) in Hawaii, whereas dietary cholesterol intake was significantly lower for both genders ($P<.001$) in Hawaii. Carbohydrate intake was significantly lower in women but not men in Hawaii.

Enzymatically determined concentrations of serum lipids were also evaluated for the cohorts in Hawaii and Japan (Table 1). Japanese-American men and women in Hawaii had significantly greater levels of total cholesterol (men, $P<.01$; women, $P<.05$) and LDL-C (men, $P<.001$; women, $P<.01$) than the respective genders in Japan, and nonfasting triglyceride levels were significantly greater for both genders ($P<.001$) in Hawaii. HDL-C levels were significantly lower for men ($P<.01$) in Hawaii; differences in HDL-C levels for women in Hawaii and Japan were small and not significant.

Lipoprotein particle subclass concentration analysis

NMR spectroscopy was used to compare lipoprotein particle concentrations for the women (Table 2) and men (Table 3) in the Hawaii and Japan cohorts. Although the differences among samples from the three Japanese centers were not significant for NMR-derived variables (data not shown), many differences were evident between the Hawaii and Japan cohorts with lipoprotein concentrations subdivided by particle size.

Small VLDL particle concentrations were not significantly different for Japanese and Japanese Americans of either gender, and total VLDL particle concentrations were not significantly different for men between the Hawaii and Japan cohorts (Tables 2 and 3). Each gender in Hawaii had significantly higher age-adjusted concentrations of medium VLDL (women, $P<.001$; men, $P<.01$) and large VLDL ($P<.001$), small and total LDL ($P<.001$), and small, medium, and total HDL ($P<.001$) than the respective gender in Japan. Each gender in Hawaii had significantly lower age-adjusted levels of both large LDL and large HDL ($P<.001$) than the respective gender in Japan.

Adjustment for age and certain risk factors for CVD (dietary cholesterol, saturated fat, and alcohol intake, smoking, and menopause for women) reduced the difference between the Hawaii and Japan cohorts for some lipoprotein variables in comparison to the age-adjusted model. For women, concentration differences for total VLDL (–38.5% change), medium VLDL (–28.1% change), and total LDL (–24.4% change) were reduced in magnitude and significance after this adjustment (Table 2). For men, age and CVD risk factor adjustment had a smaller effect on the magnitude of the differences compared to the age-adjusted model; however, concentration differences for total LDL (+14.2% change), total HDL

(−9.2% change), small HDL (−14.9% change), and large HDL (−12.1% change) were reduced in significance with this adjustment, and the concentration difference for medium VLDL (−6.4% change) was no longer significant with this adjustment (Table 3). Additional adjustment for caloric intake or physical activity made little difference in the findings. Adjustment for carbohydrate intake reduced the significance levels in men for small LDL ($P < .01$ to $P < .05$) and small HDL ($P < .05$ to ns) but not in women (data not shown). However, additional adjustment for BMI had a much larger effect. This further reduced the differences between the Hawaii and Japan cohorts for several lipoprotein variables in comparison to the age-adjusted model. For women, the concentration differences for total VLDL (−77.9% change), total LDL (−64.2% change), and large HDL (−77.4% change) were no longer significant after this adjustment (Table 2). For men, the concentration differences for small LDL (−31.0% change) and medium HDL (−43.8% change) had reduced significance, and the differences for large VLDL (−70.0% change), total LDL (−69.8% change), small HDL (−36.5% change), and large HDL (−81.6% change) were no longer significant after this adjustment (Table 3).

Lipoprotein particle subclass size analysis

Age-adjusted average VLDL particle size was significantly ($P < .001$) larger in both women (Table 2) and men (Table 3) in Hawaii, and age-adjusted average LDL and HDL particle sizes were significantly ($P < .001$) smaller in both genders in Hawaii. Adjustment for age and CVD risk factors reduced the difference in average VLDL size compared to the age-adjusted model for both women (−18.1% change) and men (−42.8% change), and the significance of the difference was also reduced for both genders. For women, additional adjustment for BMI further reduced the difference in average VLDL particle size (−23.6% change), and also reduced the significance of the difference. For men, differences in average particle size for VLDL (−78.6% change) and HDL (−61.5% change) were no longer significant after this adjustment.

Discussion

The data presented here indicate that Japanese Americans have significantly greater concentrations of lipoprotein particles implicated in atherogenesis in other studies,^{16–18,20,21} including large VLDL, small LDL, and small HDL, compared with Japanese in Japan. Average LDL and HDL particle sizes are also significantly smaller in Japanese Americans. Conversely, Japanese Americans have significantly lower concentrations of putatively cardioprotective large HDL particles compared to Japanese in Japan.

In contrast to other studies in which authors compare lipoprotein particles in populations with differing lifestyles, the present study compares two genetically similar populations. Much of the population of Japan has undergone major changes in diet and lifestyle since the end of World War II. These include a substantial increase in cholesterol intake, likely attributable to an increase in “western” foods in the diet. Cigarette smoking and relatively high alcohol consumption are still common among Japanese men in Japan.^{3,4} However, there is little evidence to date of an increase in CHD mortality rates in Japan since World War II.^{5,27} The Japanese participants in this study were born after 1945 and are thus

representative of the first generation of “westernized” Japanese. In contrast, the Japanese-American participants in Hawaii are third- and fourth-generation descendants of the original Japanese immigrants; therefore a significant proportion of the “westernization” process occurred in previous generations. Detailed standardized dietary data, such as that available in this study is often not available for population comparisons, especially in different countries or even for regions of countries.

The samples studied here reflect the expected risk factor patterns. Japanese men in Japan are leaner, drink more alcohol, smoke more cigarettes, and have a greater intake of cholesterol than Japanese Americans in Hawaii.⁴ On the basis of these differences, Japanese in Japan might be expected to have rates of atherosclerotic disease comparable with those seen in the United States. However, Japanese in Japan have significantly lower concentrations of lipoprotein particles implicated in atherogenesis, and significantly greater concentrations of putatively cardio-protective lipoprotein particles than Japanese Americans.

The differences in BMI between Japanese in Japan and Japanese Americans may partially explain the differences in lipoprotein particle subclass profiles, as indicated by a marked reduction in the difference between certain lipoprotein particle measures with adjustment for BMI. These effects were most notable for total LDL particle concentration and large HDL particle concentration for both genders, total VLDL particle concentration for women, and large VLDL concentration and average HDL particle size for men.

Factors that affect lipoprotein particle concentration and size are not well understood; however, body weight is likely an important contributor to triglyceride levels and lipoprotein particle profiles. For example, a low fat diet has been shown to reduce LDL particle size in men and women, and concentrations of medium and large HDL, and IDL in men.²⁸ The same diet decreases small VLDL and large HDL particle concentrations in women. Greater dietary intake of carbohydrates, particularly those with a high glycemic index, has been shown to increase levels of small, dense LDL and HDL,²⁹ as seen in the present study for men but not women. However, body weight appears to have a much larger effect than other factors in the present study.

There are several limitations in the current study. The samples in this study, although population-based, are relatively small. For this reason some potentially clinically significant differences might be expected not to reach statistical significance. However, this underscores the importance of the significant differences that were seen. Study samples were nonfasting and although there do not appear to be substantial differences in the distribution of time since last meal between the populations, the exact content of that meal was not determined making it difficult to adjust for the effects. There are few data on such effects and we cannot, with this data set, determine the contribution of such factors to our findings. The three Japanese subpopulations may not be totally representative of the population of Japan. However, both rural and urban populations are represented and the variations between these populations for the measures in question are relatively small. Both the Hawaii and Japan populations are entirely Japanese by decent, and are genetically similar. Although that lack of genetic diversity that makes this specific comparison less complex, it is possible that different effects could be seen in other ethnic groups.

In conclusion, the data presented here show significant differences in VLDL, LDL, and HDL subclass particle concentrations and sizes between ethnic Japanese growing up in two different environments. These differences may contribute to the continued lower rates of CHD in Japan despite traditional risk factor profiles that have become similar to those seen in the United States and high smoking rates in Japan. Such endpoint analyses are beyond the scope of this data set. However, it is likely that lifestyle factors, such as smoking rate and consumption of carbohydrates, fish, soy products, alcohol, omega-3 fatty acids, and antioxidants, contribute to the differences in lipoprotein particles, directly and/or through their effect on BMI. The complexity of the many measures created by lipoprotein particle analyses and their varying and intercorrelated relationships with the many potential lifestyle and environmental factors makes interpretation of the findings in this and other such studies difficult. More focused analyses such as that planned for this data set and in other studies in the future should help to better understand lifestyle effects on lipoprotein particles and to improve our understanding of the effects of lipoprotein particle distribution on CHD risk in these and other populations. It has been suggested that this field would significantly profit from increased collaboration of nutrition studies conducted by international groups such as that begun here.³⁰

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Demographic, anthropometric and biochemical characteristics of participants in Japan and Hawaii: INTERLIPID 1997–1999

Table 1

	Men		Women		P value
	Hawaii	Japan	Hawaii	Japan	
Age, years	50.7 ± 5.1	49.6 ± 5.4	49.8 ± 4.9	49.1 ± 5.3	ns
BMI, kg/m ²	28.6 ± 4.6	23.5 ± 2.7	25.7 ± 5.5	23.2 ± 3.1	<.001
Hypertension, % *	33	17	27	11	<.001
Smoking, %					
Never	44	19	77	94	
Former	47	25	19	1	
Current	9	56	4	5	<.001
Cholesterol intake, mg/d	316 ± 137	433 ± 169	240 ± 117	352 ± 137	<.001
Alcohol intake, g/d	10.5 ± 15.9	30.4 ± 24.7	1.2 ± 4.9	3.4 ± 5.4	<.01
Alcohol use, %					
Never	7	2	26	14	
Former	16	1	30	2	
Current	77	97	44	84	<.001
Saturated fat intake, g/d	25.9 ± 9.8	15.5 ± 5.1	19.5 ± 7.2	14.4 ± 4.9	<.001
Menopause, %					
Pre-	—	—	47	45	
Current	—	—	23	12	
Post	—	—	30	43	<.01
Total cholesterol [†]	209.7 ± 29.7	199.5 ± 29.1	210.6 ± 31.9	201.8 ± 31.8	<.05
LDL cholesterol [†]	135.3 ± 27.9	124.0 ± 28.6	136.3 ± 33.4	126.1 ± 29.6	<.01
HDL cholesterol [†]	50.4 ± 10.2	54.4 ± 13.4	59.9 ± 13.2	60.1 ± 14.0	ns
Triglycerides, nonfasting [†]	226.4 ± 49.6	158.0 ± 102.7	156.6 ± 90.8	109.5 ± 56.7	<.001

Data values are mean ± SD or percentage.

BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; ns, not significant.

* Hypertension was defined as systolic blood pressure ≥ 140 mm Hg, diastolic blood pressure of ≥ 90 mm Hg, or receiving antihypertensive drugs.

Enzymatically-derived measurements from serum samples (mg/dL).

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NMR measurements of lipoprotein subclasses for women from Hawaii and Japan: INTERLIPID 1997–1999

Table 2

	Hawaii (n = 102)	Japan (n = 415)	Age adjusted*	Age, RF adjusted	Age, RF, BMI adjusted
	Median (range)		P values		
Particle concentration, nmol/L					
Total VLDL	82.2 (19.6–278.3)	63.0 (0–243.8)	<.001	<.05 (–38.5%) [‡]	ns (–77.9%)
Small VLDL	44.6 (0–101.6)	40.0 (0–141.0)	ns	ns --	ns --
Medium VLDL	36.3 (2.3–177.0)	17.7 (0–137.7)	<.001	<.01 (–28.1%)	<.01 (–47.4%)
Large VLDL	2.4 (0.1–25.7)	0.3 (0–18.0)	<.001	<.001 (–5.9%)	<.001 (–14.3%)
Total LDL, nmol/L	1484 (760–2767)	1127 (584–2469)	<.001	<.01 (–24.4%)	ns (–64.2%)
IDL	10.6 (0–86.4)	0 (0–131.4)	<.001	<.001 (–39.6%)	<.001 (–68.1%)
Small LDL	976 (222–2332)	452 (0–1902)	<.001	<.001 (–1.2%)	<.001 (–23.2%)
Large LDL	416 (91–861)	627 (150–1225)	<.001	<.001 (–13.7%)	<.001 (–14.4%)
Total HDL, μ mol/L	35.0 (24.1–63.3)	27.2 (16.0–53.0)	<.001	<.001 (+14.8%)	<.001 (+22.1%)
Small HDL	21.0 (9.8–40.3)	16.3 (6.3–33.5)	<.001	<.001 (+5.4%)	<.001 (+3.7%)
Medium HDL	5.0 (0–20.6)	0.2 (0–21.4)	<.001	<.001 (–7.3%)	<.001 (–12.3%)
Large HDL	8.2 (0.9–21.7)	9.9 (1.3–22.2)	<.001	<.05 (+2.3%)	ns (–77.4%)
Particle size, nm					
VLDL	52.6 (38.8–75.2)	46.3 (28.2–124.8)	<.001	<.01 (–18.1%)	<.05 (–23.6%)
LDL	20.8 (19.7–22.3)	21.8 (19.8–23.0)	<.001	<.001 (–14.1%)	<.001 (–24.2%)
HDL	9.2 (8.5–9.9)	9.7 (8.3–10.9)	<.001	<.001 (–2.0%)	<.001 (–14.0%)

Adjusted P values are from median regression analysis.

BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NMR, nuclear magnetic resonance; ns, not significant; RF, risk factor; VLDL, very-low-density lipoprotein.

* The unadjusted comparisons (not shown) give very similar results to that of age-adjusted comparisons.

[‡] Percent change in the difference compared to the age-adjusted model.

Table 3

NMR measurements of lipid subclasses for men from Hawaii and Japan: INTERLIPID 1997–1999

	Hawaii(n = 96)	Japan (n = 400)	Age adjusted*	Age, RF Adjusted	Age, RF, BMI Adjusted
	Median (range)		P values		
Particle concentration, nmol/L					
Total VLDL	102.1 (31.0–308.5)	90.1 (0–292.9)	ns	ns --	ns --
Small VLDL	49.2 (7.7–107.9)	45.9 (0–213.7)	ns	ns --	ns --
Medium VLDL	49.0 (2.4–187.9)	35.9 (0–194.2)	<.01	ns(– 6.4%) [‡]	ns(–51.1%)
Large VLDL	5.3 (0–60.8)	0.9 (0–61.1)	<.001	<.001(– 7.5%)	ns (–70.0%)
Total LDL, nmol/L	1510 (778–2148)	1345 (392–2521)	<.001	<.05 (+14.2%)	ns (–69.8%)
IDL	26.3 (0–123.8)	5.3 (0–139.9)	<.001	<.001 (+11.1%)	<.001 (–16.2%)
Small LDL	1286 (219–2019)	864 (0–2183)	<.001	<.001 (+19.4%)	<.01 (–31.0%)
Large LDL	254 (11–805)	479 (0–1324)	<.001	<.001 (+3.5%)	<.001 (–33.8%)
Total HDL, μ mol/L	32.8 (21.3–53.4)	29.6 (15.6–51.9)	<.001	<.05 (– 9.2%)	<.05 (–10.0%)
Small HDL	22.8 (11.6–39.2)	19.5 (7.9–35.2)	<.001	<.01 (–14.9%)	ns (–36.5%)
Medium HDL	4.0 (0–15.7)	1.2 (0–19.5)	<.001	<.001 (– 3.2%)	<.05 (–43.8%)
Large HDL	5.2 (0.7–13.3)	7.5 (1.1–22.5)	<.001	<.05 (– 12.1%)	ns (–81.6%)
Particle size, nm					
VLDL	54.0 (32.9–81.8)	46.2 (24.0–124.9)	<.001	<.05 (–42.8%)	ns (–78.6%)
LDL	20.1 (19.5–22.2)	21.0 (19.1–22.9)	<.001	<.001 (+4.4%)	<.001 (–45.6%)
HDL	8.9 (8.4–9.8)	9.2 (8.5–10.5)	<.001	<.001 (+11.5%)	ns (–61.5%)

Adjusted P values are from median regression analysis.

BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NMR, nuclear magnetic resonance; ns, not significant; RF, risk factor; VLDL, very-low-density lipoprotein.

* The unadjusted comparisons (not shown) give very similar results to that of age-adjusted comparisons.

[‡] Percent change in the difference compared with the age-adjusted model.