Letter to the Editor

Prevalence of High Non-high-density Lipoprotein Cholesterol and Associated Risk Factors in Patients with Diabetes Mellitus in Jilin Province, China: A Cross-sectional Study*

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Dyslipidemia is a risk factor for cardiovascular diseases (CVDs) in patients with diabetes, and non-high-density lipoprotein cholesterol (non-HDL-C) is a better predictor of CVDs than low-density lipoprotein cholesterol (LDL-C) in patients with diabetes. Therefore, we aimed to investigate the distribution of non-HDL-C and the prevalence of high non-HDL-C level in Chinese patients with diabetes mellitus and identify the associated risk factors. Non-HDL-C concentration positively correlated with total cholesterol, triglycerides, and LDL-C concentrations. Although both non-HDL-C and LDL-C concentration both related positively with TC concentration, the magnitude of correlation was relatively higher for non-HDL-C. The prevalence of high non-HDL-C (≥4.14 mmol/L) was higher in two age groups (55-64 years: 46.7%; 65-79 years: 47.3%) than other age groups (18-24 years: 4.2%; 25-34 years: 43.6%; 35-44 years: 38.1%; 45-54 years: 41.0%). It was also higher among overweight (45.1%), generally obese (50.9%), or abdominally obese (47.3%) subjects, compared with normal weight subjects (34.5%). The risk of high non-HDL-C increased with advancing age. Both general obesity [odds ratio (OR)=1.488, 95% confidence interval (CI): 1.003-2.209] and abdominal obesity (OR=1.561, 95% CI: 1.101-2.214) were significantly associated with high non-HDL-C levels.

Diabetes is associated with a greater risk of morbidity and mortality from cardiovascular diseases (CVDs)[1]. The coexistence of diabetes and other risk factors, in particular dyslipidemia, further increases the risk of CVDs[2], and 'lipotoxic' dyslipidemia can accelerate the manifestation and persistence of complications of diabetes[3]. The United Kingdom Prospective Diabetes Study (UKPDS) also showed that dyslipidemia was a risk factor for CVDs in patients with diabetes[4]. Previous studies demonstrated that an elevated level of low-density lipoprotein cholesterol (LDL-C) was a powerful coronary heart disease risk factor and recommended using LDL-C as the primary marker to guide therapy[5]. The Third Adult Treatment Panel (ATP III) of the National Cholesterol Education Program (NCEP) suggested that non-high-density lipoprotein cholesterol (non-HDL-C) be used as a secondary target for lipid control[5]. A recent study also reported that non-HDL-C was a better predictor of CVDs than LDL-C in patients with diabetes[6]. Estimation of non-HDL-C levels, which is calculated by subtracting HDL-C from total cholesterol (TC), does not require measurement of triglyceride (TG) or LDL-C levels, and it is not influenced by plasma TG concentration[5]. Non-HDL-C reflects the concentrations of both cholesterol-rich and TG-rich atherogenic apolipoprotein B-containing lipoproteins, including very-low-density lipoprotein cholesterol (VLDL-C), intermediate-density lipoprotein cholesterol (IDL-C), LDL, and lipoprotein (a)[5]. Most studies on non-HDL-C are performed for normal populations. Very few cross-sectional studies have been performed to investigate the prevalence of high non-HDL-C and associated factors among patients with diabetes in China. In this study, we aimed to describe non-HDL-C levels among patients with diabetes mellitus, examine the prevalence of high non-HDL-C levels and the risk factors influencing high non-HDL-C levels in patients with diabetes mellitus in Jilin Province, China.

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Data for this study were collected from the Survey of Chronic Diseases and Associated Risk Factors among Adults in Jilin Province, China in 2012. The survey was a cross-sectional study that used a multistage cluster random sampling design to select a representative sample of permanent residents aged 18 to 79 years in nine different cities in Jilin Province. The survey is described in detail elsewhere[7]. A total of 16,975 participants completed the survey. Participants with incomplete information on blood glucose or lipid levels were excluded from the present study. Our study sample consisted of 1825 patients with diabetes mellitus, which was defined as fasting plasma glucose (FPG) level ≥7.0 mmol/L, 2-h post prandial plasma glucose (2hPG) concentration ≥11.1 mmol/L, patient administering anti-diabetic medications, or having a history of diabetes mellitus in the past one year.

To account for the complex sampling design, prevalence rates were weighted to produce representative estimates of the total population of Jilin Province. The weights were obtained from the 2010 Chinese population census data and calculated based on four factors: geographical region, residential type (urban/rural), sex, and age.

Of 1825 patients with diabetes mellitus (representing 2,074,217 subjects), 54.4% resided in urban areas while 45.6% resided in rural areas. There was a 56.4% male predominance. The mean age of subjects was 53.20±0.55 years, with 29.0% of them aged 55-64 years, 28.1% aged 45-54 years, and 1.7% aged 18-24 years. Other characteristics of the study sample population are shown in Table S1 (See the BES website: www. besjournal.com).

In our study, the weighted mean levels of TC, TG, LDL-C, HDL-C, and non-HDL-C were 5.31±0.04 mmol/L, 2.98±0.09 mmol/L, 3.11±0.03 mmol/L, 2.13±0.10 mmol/L, and 4.07±0.04 mmol/L, respectively (Table 1). These values were higher than those reported for the general and normal population[8], and these levels are similar to the levels reported by Wagner et al.[9] for patients with type 2 diabetes.

A positive correlation between non-HDL-C and TG concentrations was observed (r=0.531, P<0.001) (Figure 1A), but the correlation between LDL-C and TG concentrations was not significant (r=-0.040, P=0.087) (Table S2, see the BES website: www.besjournal.com). Although both non-HDL-C (r=0.947, P<0.001) (Figure 1B, see the BES website: www.besjournal.com) and LDL-C (r=0.717, P<0.001; Table S2) concentration positively correlated with TC, the magnitude of correlation was relatively higher for the former. Non-HDL-C concentration significantly correlated with LDL-C concentration (r=0.657, P<0.001) (Figure 1C), and non-HDL-C exhibited a significant inverse relationship to HDL cholesterol (r=-0.101, P<0.001) (Figure 1D).

The present data show that non-HDL-C concentration, unlike LDL-C, better correlated with TC concentration. Because non-HDL-C reflects the concentrations of both cholesterol-rich and triglyceride-rich atherogenic apolipoprotein B-containing lipoproteins, including VLDL-C, IDL-C, LDL, and lipoprotein (a), compared with LDL-C, non-HDL-C could be a better atherogenic index for patients with diabetes and hypercholesterolemia and/or hyper triglyceridemia.

According to the NCEP-ATPIII criteria, non-HDL-C levels are routinely calculated as TC levels minus HDL-C level. The reasonable non-HDL-C concentration was 0.78 mmol/L (30 mg/dL higher than LDL-C concentration[5]. Based on the subdivided LDL-C cut-off point, we categorized non-HDL-C concentrations into four levels: <3.37 mmol/L (130 mg/dL), 3.37-4.13 mmol/L (130-159 mg/dL), 4.14-4.90 mmol/L (160-189 mg/dL), and ≥4.92 mmol/L (190 mg/dL). We defined high non-HDL-C concentrations as those >4.14 mmol/L (160 mg/dL). As shown in Table S3 (See the BES website: www. besjournal.com), the non-HDL-concentration for 28.9% of subjects was in the range of 3.37-4.13 mmol/L, for

Table 1. Blood Glucose Concentration and Serum Lipid Levels of Study Subjects in Jilin Province, China, 2012

Variables	Weighted Mean (mmol/L)	SE	95% CI
FPG[a]	8.04	0.09	7.85, 8.22
2hPG[b]	11.39	0.47	10.46, 12.31
TC	5.31	0.04	5.23, 5.38
TG	2.98	0.09	2.80, 3.16
LDL-C	3.11	0.03	3.06, 3.17
HDL-C	1.23	0.10	1.21, 1.25
Non-HDL-C	4.07	0.04	4.00, 4.15

***Note*.** FPG[a], Fasting plasma glucose (1694 study subjects, representing 1,947,369 subjects); 2hPG[b], 2-h post prandial plasma glucose (131 study subjects, representing 126,848 subjects).

23.6% in the range of 4.14-4.91 mmol/L, and for 19.4% it was ≥4.92 mmol/L. The overall prevalence of high non-HDL-C was 43.0% [95 confidence interval (CI)%: 33.9%-46.3%] (Table S4, See the BES website: www.besjournal.com). The odds ratios (ORs) for high non-HDL-C increased with age. Compared to the normal weight group, the OR for high non-HDL-C in the overweight and obesity groups were 1.560 (95% CI: 1.119-2.175) and 1.973 (95% CI: 1.348-2.887), respectively. In the abdominal obesity group, the OR for non-HDL-C was 2.064 (95% CI: 1.436, 2.966). However, the ORs for high non-HDL-C based on variables such as having a family history of dyslipidemia, administering lipid-modifying medication, smoking, drinking, and physical exercise, were not significantly different.

Measurements TG-rich lipoproteins, which are included in non-HDL-C measurements, are of a great significance in clinic because these lipoproteins tend to increase as people advance in age and become more obese, insulin resistant, and hyperglycemic[10]. Moreover, with the increasing prevalence of obesity, metabolic syndrome, and diabetes among adults, using non-HDL-C levels to predict CVDs may become more important[6]. A study by Banu et al.[11] showed that the ages of pre-diabetes and diabetes patients were associated with non-HDL-C levels. Our study also showed that the risk of high non-HDL-C increased with advancing age, but subjects aged 25-34 years had a greater risk of high non-HDL-C (OR=16.628, 95% CI: 1.503-183.994) than two other proceeding age groups: 35-44 years (OR=11.973, 95% CI: 1.351-106.130) and 45-54 years (OR=12.981, 95% CI: 1.486-113.370) (Table 2). This is possibly because the proportion of obese participants in the 25-34 years age group (33.0%) was greater than that in other age groups (less than 29.0%).

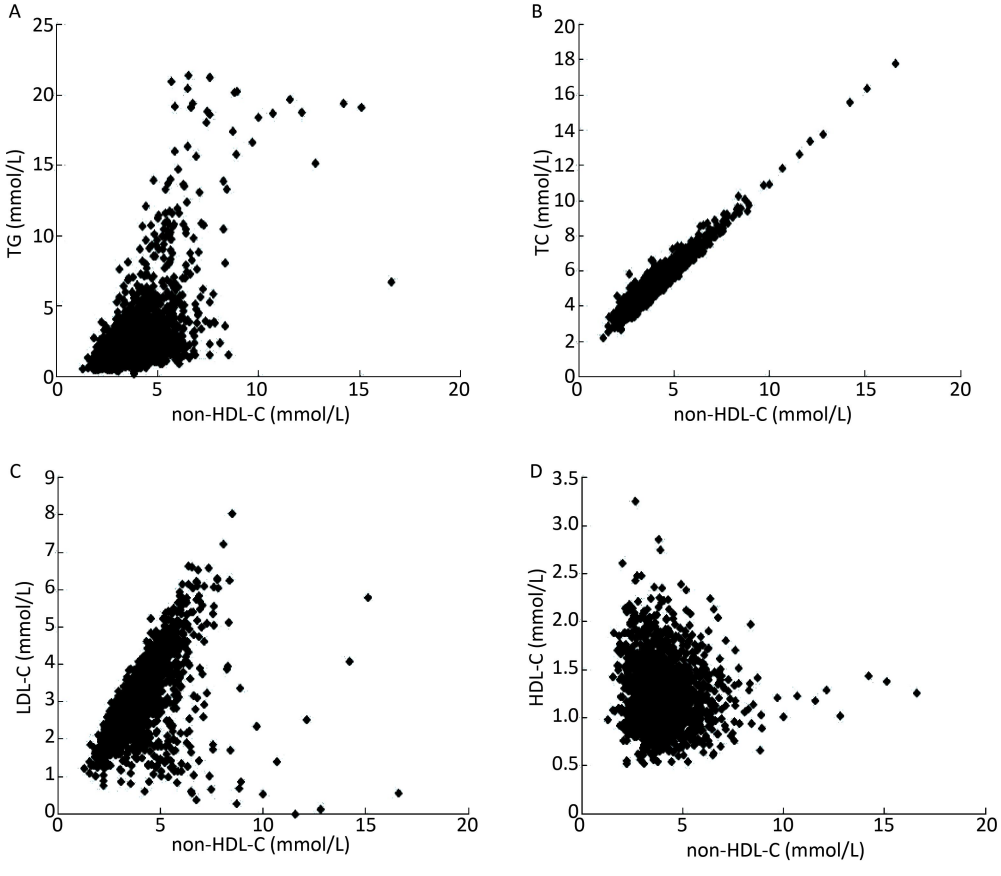

Figure 1. Corrrelations of non-HDL-C and TG (A), TC (B), LDL-C (C), HDL-C (D). TG: triglycerides; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; LDL-C: low-density lipoprotein cholesterol; non-HDL-C: non-high-density lipoprotein cholesterol.

Table 2. Multivariate Logistic Regression Analysis of Factors Influencing High non-HDL-C Levels in Study Subjects in Jilin Province, China, 2012

Variables	Odds Ratio	95% CI	*P*
Age group (years)			0.037
18-	1.000		
25-	16.628	1.503, 183.994	0.022
35-	11.973	1.351, 106.130	0.026
45-	12.981	1.486, 113.370	0.020
55-	16.820	1.924, 147.037	0.011
65-79	16.531	1.864, 146.597	0.012
BMI			0.070
Normal	1.000		
Underweight	0.362	0.098, 1.335	0.127
Overweight	1.246	0.890, 1.746	0.200
Obesity	1.488	1.003, 2.209	0.048
Abdominal obesity			
No	1.000		
Yes	1.561	1.101, 2.214	0.012

Note. Variables with *P*-values ≤0.05 in the univariate logistic regression analysis (Table S4) were included in the multivariate logistic regression model.

Multivariate logistic regression analysis results from the present study suggested that obesity (OR=1.488, 95% CI: 1.003-2.209) and abdominal obesity (OR=1.561, 95% CI: 1.101-2.214) were significantly associated with the prevalence of high non-HDL-C (Table 2). The finding is similar to that from a study conducted by Ram et al.[12], which showed that with increased age and obesity, the degree of insulin resistance becomes more serious in patients with diabetes, leading to a higher prevalence of lipid abnormalities, and most diabetes patients have insulin resistance and lipid metabolism disorders.

In conclusion, our study showed that non-HDL-C concentration positively correlated with TC, TG, and LDL-C concentration. Although both non-HDL-C and LDL-C concentration correlated positively with TC level, the magnitude of correlation was relatively higher for non-HDL-C. The prevalence of high non-HDL-C varied according to age, BMI, and waist circumference in Chinese patients with diabetes mellitus. Our results suggest that we should pay more attention to the level of non-HDL-C in diabetics, especially for older subjects and those who are more obese or abdominally obese. These subjects should monitor and control their blood non-HDL-C levels to prevent complications and deterioration due to diabetes as well as the occurrence of CVDs.

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Table S1. Characteristics of Study Subjects (*n*=1825, representing 2,074,217 subjects) in Jilin Province, China, 2012

Variables	*n*	Weighted Percentage (%)	Estimated Size of Populations
Region			
Urban	893	54.4	1,128,588
Rural	932	45.6	945,630
Gender			
Male	883	56.4	1,169,229
Female	942	43.6	904,988
Age group (years)			
18-	8	1.7	34,766
25-	41	7.1	147,848
35-	192	14.8	307,244
45-	552	28.1	582,875
55-	676	29.0	602,039
65-79	356	19.3	399,442
Income (RMB)			
<500	453	20.6	426,988
500-	363	18.5	383,693
1000-	613	35.6	738,646
2000-	258	16.1	333,986
3000-	138	9.2	190,903
BMI[a]			
Underweight	29	1.5	30,598
Normal	528	29.0	595,483
Overweight	817	45.3	930,458
Obesity	436	24.3	499,351
Abdominal obesity[b]			
No	442	25.8	526,937
Yes	1359	74.2	1,519,119
Family history of dyslipidemia			
No	1751	95.6	1,982,163
Yes	74	4.4	92,055
Taking lipid-modifying medicine			
No	1614	88.9	1,843,688
Yes	211	11.1	230,529
Smoker[c]			
Never	1072	55.6	1,153,964
Now	514	31.2	848,136
Once	239	13.1	272,118
Drinker[d]			
No	1326	69.7	1,444,889
Yes	499	30.3	629,328
Physical exercise[e]			
Never or rare	622	33.7	698,889
Sometimes	323	18.9	391,825
Often	880	47.4	983,504

Note. [a]BMI, Body mass index=weight (kg)/height (m^2), BMI<18.5 kg/m^2 as underweight, 18.5 kg/m^2≤BMI<24.0 kg/m^2 as normal weight, 24.0 kg/m^2≤BMI<28.0 kg/m^2 as overweight, and BMI≥28.0 kg/m^2 as obese; [b]abdominal obesity: waist circumference ≥85 cm for males and ≥80 cm females, respectively; [c]smoker: now (participants who smoked at least one cigarette per day in the past 30 days), and once (participants who smoked in the past but completely abstinent from cigarette use for at least one month); [d]drinking any kind of purchased or homemade alcohol-containing beverages on average more than once a week; [e]physical exercise: never or rare (those who never or seldom exercise), sometimes (participants who exercised one or two times a week), and often (participants who exercised more than three times a week).

Table S2. Relation of Serum non-HDL Cholesterol and LDL Cholesterol to FPG and Other Lipoprotein Variables

Item	Non-HDL-C		LDL-C	
	r	*P*	*r*	*P*
FPG[a]	0.183	<0.001	0.066	0.007
TG	0.531	<0.001	-0.040	0.087
TC	0.947	<0.001	0.717	<0.001
LDL-C	0.657	<0.001	-	-
HDL-C	-0.101	<0.001	0.301	<0.001

***Note*.** [a]fasting plasma glucose (1694 study subjects, representing 1,947,369 subjects).

Table S3. Distribution of non-HDL-C Levels among Study Subjects in Jilin Province, China, 2012

Variables	Non-HDL-C (mmol/L)				*P*
	<3.37	3.37-4.13	4.14-4.91	≥4.92	
Total	28.1 (1.3)	28.9 (1.4)	23.6 (1.5)	19.4 (1.3)	
Region					0.733
Urban	27.1 (1.8)	30.3 (1.9)	23.5 (2.0)	19.1 (1.5)	
Rural	29.2 (2.0)	27.2 (2.0)	23.8 (2.3)	19.8 (2.3)	
Gender					0.778
Male	27.6 (1.9)	30.0 (2.0)	22.8 (2.4)	19.6 (2.0)	
Female	28.7 (1.9)	27.4 (1.8)	24.6 (1.6)	19.2 (1.4)	
Age group (years)					0.607
18-	59.4 (20.8)	36.4 (20.7)	4.2 (4.4)	0.0 (0.0)	
25-	29.8 (9.0)	26.5 (9.3)	21.9 (11.8)	21.7 (12.0)	
35-	32.1 (3.7)	29.8 (4.0)	21.7 (3.3)	16.4 (2.9)	
45-	27.1 (2.1)	31.9 (2.2)	21.2 (1.8)	19.8 (1.8)	
55-	25.3 (1.9)	27.9 (1.9)	25.0 (1.9)	21.7 (1.8)	
65-79	27.2 (2.9)	25.4 (2.8)	28.7 (4.2)	18.6 (2.4)	
Income(RMB)					0.329
<500	29.4 (2.5)	29.4 (2.5)	24.8 (2.3)	16.4 (1.9)	
500-	29.3 (2.8)	29.1 (2.7)	24.6 (2.6)	17.0 (2.2)	
1000-	27.7 (2.3)	24.8 (2.4)	26.8 (3.3)	20.7 (2.0)	
2000-	28.0 (3.5)	33.2 (3.6)	18.4 (2.7)	20.4 (2.7)	
3000-	24.2 (5.5)	35.5 (6.3)	15.8 (3.5)	24.5 (8.8)	
BMI[a]					<0.001
Underweight	66.4 (9.8)	18.9 (6.9)	3.3 (3.3)	11.4 (7.3)	
Normal	37.1 (2.9)	28.5 (2.6)	20.9 (3.2)	13.5 (1.7)	
Overweight	24.7 (1.8)	29.9 (2.1)	23.5 (2.3)	21.9 (1.7)	
Obesity	21.5 (2.5)	27.6 (2.6)	28.5 (2.7)	22.4 (3.7)	
Abdominal obesity					<0.001
No	40.2 (3.3)	29.6 (3.0)	18.2 (3.6)	12.1 (1.8)	
Yes	24.0 (1.4)	28.7 (1.6)	25.4 (1.6)	21.9 (1.6)	
Family history of dyslipidemia					0.835
No	28.0 (1.4)	28.8 (1.4)	23.8 (1.6)	19.4 (1.4)	
Yes	29.6 (6.2)	31.6 (7.9)	18.6 (5.0)	20.2 (4.9)	
Taking lipid-modifying medicine					0.637
No	28.0 (1.4)	28.4 (1.5)	23.8 (1.6)	19.8 (1.4)	
Yes	28.7 (4.2)	32.8 (4.4)	21.8 (3.2)	16.7 (2.6)	
Smoker					0.431
Never	30.3 (1.8)	27.3 (1.7)	23.1 (1.5)	19.3 (1.9)	
Now	24.2 (2.4)	29.6 (2.9)	25.3 (3.8)	20.9 (2.2)	
Once	28.1 (3.3)	33.6 (3.4)	21.7 (2.9)	16.6 (2.7)	
Drinker					0.077
No	27.9 (1.6)	28.7 (1.7)	25.6 (1.9)	17.8 (1.2)	
Yes	28.6 (2.4)	29.4 (2.6)	18.9 (2.0)	23.1 (3.2)	
Physical exercise					0.806
Never or rare	28.2 (2.3)	29.8 (2.5)	22.3 (2.0)	19.6 (2.8)	
Sometimes	27.8 (3.2)	29.5 (3.5)	20.7 (2.6)	22.0 (2.7)	
Often	28.1 (1.9)	28.0 (1.8)	25.6 (2.6)	18.3 (1.5)	

***Note*.** [a]BMI: Body mass index. The numbers in Table S3 mean estimated percentages (standard error).

Table S4. Prevalence and Odds Ratio of High non-HDL-C Levels in Different Groups of Subjects in Jilin Province, China, 2012

Variables	Weighted Prevalence		Odds Ratio (95% CI)	*P*
	n	% (95% CI)		
Region				
Rural	394	43.6 (38.7, 48.6)	1.000	
Urban	395	42.6 (38.5, 46.7)	0.959 (0.737, 1.248)	0.756
Gender				
Female	433	43.8 (40.1, 47.6)	1.000	
Male	356	42.4 (37.6, 47.4)	0.944 (0.734, 1.214)	0.655
Age group (years)				0.022
18-	1	4.2 (0.5, 27.2)	1.000	
25-	15	43.6 (21.9, 68.1)	17.675 (1.649, 189.409)	0.018
35-	74	38.1 (30.8, 46.0)	14.507 (1.608, 122.907)	0.017
45-	232	41.0 (36.7, 45.5)	15.887 (1.847, 136.655)	0.012
55-	310	46.7 (42.5, 51.0)	20.049 (2.333, 172.269)	0.006
65-79	157	47.3 (40.0, 54.8)	20.537 (2.357, 178.948)	0.006
Income (RMB)				0.374
<500	191	41.2 (36.1, 46.4)	1.000	
500-	154	41.7 (36.0, 47.5)	1.019 (0.740, 1.404)	0.906
1000-	277	47.5 (41.6, 53.4)	1.290 (0.936, 1.776)	0.119
2000-	109	38.8 (32.2, 45.7)	0.904 (0.632, 1.292)	0.579
3000-	58	40.3 (26.4, 55.9)	0.780 (0.472, 1.287)	0.331
BMI[a]				<0.001
Normal	184	34.5 (28.5, 41.0)	1.000	
Underweight	4	14.7 (4.8, 37.0)	0.328 (0.093, 1.154)	0.082
Overweight	378	45.1 (40.6, 49.6)	1.560 (1.119, 2.175)	0.009
Obesity	215	50.9 (44.4, 57.4)	1.973 (1.348, 2.887)	<0.001
Abdominal obesity				
No	136	30.3 (23.7, 37.7)	1.000	
Yes	638	47.3 (43.7, 50.8)	2.064 (1.436, 2.966)	<0.001
Family history of dyslipidemia				
No	694	43.6 (40.2, 47.1)	1.000	
Yes	95	38.5 (31.0, 46.5)	0.830 (0.472, 1.460)	0.517
Taking lipid-modifying medicine				
No	694	43.6 (40.2, 47.1)	1.000	
Yes	95	38.5 (31.0, 46.5)	0.810 (0.566, 1.158)	0.247
Smoker				0.273
Never	468	42.4 (38.5, 46.4)	1.000	
Now	228	46.2 (39.6, 52.9)	1.166 (0.852, 1.597)	0.338
Once	93	38.3 (31.7, 45.3)	0.843 (0.606, 1.173)	0.311
Drinker				
No	581	43.5 (39.8, 47.3)	1.000	
Yes	208	42.0 (36.2, 48.1)	0.943 (0.706, 1.260)	0.691
Physical exercise				0.866
Never or rare	375	42.0 (36.6,47.6)	1.000	
Sometimes	146	42.7 (36.2,49.4)	1.030 (0.723, 1.468)	0.600
Often	268	43.9 (39.2,48.7)	1.083 (0.804, 1.459)	0.870

Note. [a]BMI: Body mass index.