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ORIGINAL ARTICLE

Trends of Dyslipidemia in Korean Youth According to Sex and Body Mass Index: Based on the Korea National Health and Nutrition Examination Survey (2007- 2018)

Kyungchul Song, MD[1], Soyoung Jeon, MS[2], Hye Sun Lee, PhD[2], Han Saem Choi, MD[1], Junghwan Suh, MD[1], Ahreum Kwon, MD[1], Ho-Seong Kim, MD, PhD[1], Hyun Wook Chae, MD[1]

From the [1]Department of Pediatrics, Severance Children's Hospital, Endocrine Research Institute, Yonsei University College of Medicine, Seoul, Korea and [2]Biostatistics Collaboration Unit, Yonsei University College of Medicine, Seoul, Korea

The authors declare no conflicts of interest.

Corresponding Author: Hyun Wook Chae, Department of Pediatrics, Severance Children's Hospital, Endocrine Research Institute, Yonsei University College of Medicine, Seoul, Korea.
E-mail: hopechae@yuhs.ac

Tel: (+82) 2-2019-3350; Fax: (+82) 2-393-9118

Key Words: Lipids; Prevalence; Child; Adolescent

List of Abbreviations:

ASCVD Atherosclerotic cardiovascular disease

TG Triglycerides

HDL-C High-density lipoprotein cholesterol

LDL-C Low-density lipoprotein cholesterol

KNHANES Korea National Health and Nutrition Examination Survey

BMI Body mass index

WC Waist circumference

Objective To assess trends of dyslipidemia among youth, we investigated secular trends in serum lipid levels from 2007 to 2018 and the current prevalence of dyslipidemia in Korean children and adolescents.

Study design This cross-sectional study investigated lipid profiles of 10,734 youths aged 10–18 years using data from phases Ⅳ–Ⅶ of the Korea National Health and Nutritional Examination Survey. We assessed age-, sex-, and body mass index (BMI)-adjusted mean levels of lipids at each survey.

Results Mean levels of total cholesterol, LDL-C, and non-HDL-C levels increased from phase Ⅳ to Ⅶ. Among boys, the prevalence of acceptable levels of total cholesterol, LDL-C, and non-HDL-C decreased significantly (P = .005, p = 0.001, and p < 0.001, respectively). In girls, the prevalence of acceptable levels of total cholesterol, LDL-C, HDL-C, and non-HDL-C decreased significantly (p = 0.003, p = 0.005, p = 0.008 and p = 0.013, respectively). In BMI- and age-specific analyses, worsening trends in total cholesterol, LDL-C, and non-HDL levels were more apparent in youths with a normal BMI and young age.

Conclusions Dyslipidemia trends are worsening in Korean youth, even in those with a normal BMI and young age. Thus, future cardiovascular disease risk may increase and

comprehensive management plans are required for youth with overweight or obesity and those with a normal BMI and young age.

Metabolism of cholesterol is closely related to the onset and progression of atherosclerotic cardiovascular disease (ASCVD).[1] Thus, changes in cholesterol levels in the population impact the incidence of ASCVD, which is the most common cause of death worldwide.[2-4] A prospective study reported that high triglycerides (TG) and low high-density lipoprotein cholesterol (HDL-C) is positively associated with the incidence of ASCVD.[3] Law et al found that a reduction of 10% in the low-density lipoprotein cholesterol (LDL-C) level lowers the risk of ischemic heart disease by 50% in adults.[5]

Dyslipidemia in youth is one of the risk factors of adulthood cardiovascular disease. A serial cross-sectional study reported that the prevalence of pediatric dyslipidemia had decreased from 1999 to 2016 but was still high at 19–25% in US youths.[6] One study showed adverse trends in lipid levels by comparing the prevalence of dyslipidemia in 2004 and 2014 in China.[7] In Korea, Lim et al reported that pediatric dyslipidemia was prevalent in 19.7% of the population based on the data from the Korea National Health and Nutrition Examination Survey (KNHANES) Ⅳ (2007–2009).[8] Despite the apparent adverse health impact of dyslipidemia, investigations on secular trends in lipid levels are scarce. Consequently, the investigation of secular trends in pediatric lipid levels may anticipate the future prevalence of adulthood cardiovascular disease as well as inform public health efforts regarding resource needs for pediatric dyslipidemia.[6]

Therefore, this study aimed to investigate secular trends in serum lipid levels from 2007 to 2018 in Korean children and adolescents using the KNHANES data. Specifically, our objectives were to investigate the serial trends in childhood lipid levels and dyslipidemia for

12 years, according to age, sex, and body mass index (BMI), and the current prevalence of pediatric dyslipidemia in Korea.

Methods

This was a cross-sectional study of 10,734 youths aged 10–18 years included in the four phases of KNHANES: IV (2007–2009), V (2010–2012), VI (2013–2015), and VII (2016–2018). Data from the KNHANES I (1998), II (2001), and III (2005) were excluded because they did not involve consecutive years. The study design and patient inclusion flowchart are shown in Figure 1 (available at www.jpeds.com).

KNHANES is a national survey with a stratified and multistage sampling design, approved and conducted by the Korea Centers for Disease Control and Prevention, based on the National Health Promotion Act. This cross-sectional and nationally representative survey has been performed to identify the health behaviors of the Korean population and the current status of chronic diseases since 1998. The survey involves a two-stage stratified sampling method using sampling units and households as the first and second sampling units, respectively. Health surveys, examinations, and nutrition surveys are conducted for household members.[9]

The present study was performed in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (IRB) of Yonsei University Gangnam Severance Hospital (IRB no.: 3-2020-0081). Written informed consent from statutory representatives was obtained for the children enrolled in this study.

Study Variables

Data on age, sex, anthropometric measurement, and plasma lipid levels were collected. Height and weight were measured by well-trained examiners with participants wearing light clothing and no shoes. Height was measured to the nearest 0.1 cm using a portable stadiometer (range, 850–2060 mm; Seriter, Holtain Ltd., Crymych, UK). Weight was measured with participants in the upright position to the nearest 0.1 kg using a calibrated balance beam scale (Giant 150N; HANA, Seoul, Korea). BMI was calculated as the weight divided by the height squared. Waist circumference (WC) was measured at the narrowest point between the lower borders of the rib cage and the iliac crest at the end of normal expiration, and the waist-to-height ratio was calculated as WC (cm)/height (cm). Height, weight, and BMI were presented as Z-score values based on the 2017 Korean National Growth Charts.[10] Children were classified as normal (<85th percentile), overweight (85th to <95th percentile), or obese (≥95th percentile) according to BMI. Central obesity was defined as a WC >90th percentile using Korean waist reference data.[11] We assessed the age-, sex-, and BMI-adjusted mean levels of lipids at each survey. Additionally, we assessed the proportion of youth with overweight and obesity among the participants with an adverse level of any lipid. A 24-hour dietary recall method with self-reported questionnaires was used to assess the dietary intake of calories, carbohydrates, proteins, and fats.

Measurement of Serum Lipid Levels

Blood samples were collected from the antecubital vein following an 8-hour fast and then processed and immediately refrigerated. The serum levels of total cholesterol, HDL-C, and TG were measured using the Advia 1650/2400 (Siemens, New York, NY, USA) in the 2007

survey and the Hitachi Automatic Analyzer 7600/7600-210 (Hitachi, Tokyo, Japan) in the 2008–2018 surveys. The LDL-C level was calculated using the Friedewald formula (LDL-C = total cholesterol − [HDL-C + (TG/5)]). TG/5 was used for serum samples with TG values ≤400 mg/dL, whereas it was set as missing for samples with TG levels >400 mg/dL.[12] The non-HDL-C level was calculated as the difference between total cholesterol and HDL-C values.[13] The cut-off points for acceptable and adverse lipid levels were defined according to the pediatric lipid guidelines as follows:[14,15] acceptable: total cholesterol level <170 mg/dL, LDL-C level <110 mg/dL, TG level <90 mg/dL, HDL-C level ≥45 mg/dL, and non-HDL-C level <120 mg/dL; and adverse: total cholesterol level ≥200 mg/dL, LDL-C level ≥130 mg/dL, TG level ≥130 mg/dL, HDL-C level <40 mg/dL, and non-HDL-C level ≥145 mg/dL.

Statistical Analyses

The sampling weights were considered in all analyses to report representative estimates of the Korean population. All continuous variables are expressed as weighted means with standard errors, and categorical variables are expressed as weighted percentages with standard errors. We analyzed the changes in the mean lipid levels and proportion of participants with acceptable and adverse lipid levels across the KNHANES phases (IV-VII). Moreover, we analyzed the change in the mean lipid levels across the KNHANES phases after dividing the participants into subgroups according to sex, age, and BMI groups. One-way analysis of variance was used to compare the mean values of the continuous variables including the mean lipid levels. The Rao-Scott chi-square test was used to compare categorical variables including the prevalence of acceptable and adverse lipid levels. All statistical analyses for the complex survey design with clustering, stratification, and unequal weighting of the KNHANES sample were performed using SAS, version 9.4 (SAS Inc., Cary,

NC, USA). Significance was determined as $p < 0.05$.

Results

Baseline Characteristics and Trends in Mean Lipid Levels and Dyslipidemia

The unweighted sample sizes in the KNHANES Ⅳ (2007–2009), Ⅴ (2020–2012), Ⅵ (2013–2015), and Ⅶ (2016–2018) were 2657, 2379, 1841, and 1854, respectively. Table Ⅰ shows the participant characteristics according to sex across the KNHANES phases. Among boys, the proportion of participants with central obesity represented by WC increased ($p = 0.005$), whereas the proportions of those with overweight and obesity did not show significant changes. The daily fat intake increased from KNHANES Ⅳ to Ⅵ among boys and girls ($p < 0.001$). Figure 2 shows the changes in the mean lipid levels from KNHANES Ⅵ through the following phases. Mean levels of total cholesterol, LDL-C, and non-HDL-C increased from KNHANES Ⅳ, Ⅴ, and Ⅵ to Ⅶ among both sexes. Among boys, the prevalence of participants with acceptable levels of total cholesterol, LDL-C, and non-HDL-C decreased ($p = 0.005$, $p = 0.001$ and $p < 0.001$, respectively), and the prevalence of participants with adverse levels of these lipids increased from KNHANES Ⅵ to Ⅶ ($p = 0.011$, $p = 0.020$ and $p = 0.005$, respectively). In girls, the prevalence of participants with acceptable levels of total cholesterol, LDL-C, HDL-C, and non-HDL-C decreased ($p = 0.003$, $p = 0.005$, $p = 0.008$ and $p = 0.013$, respectively), and the prevalence of participants with adverse levels of all lipid profiles increased from KNHANES Ⅳ to Ⅶ (total cholesterol, $p = 0.013$; LDL-C, $p = 0.015$; TG, $p = 0.030$; HDL-C, $p = 0.003$; non-HDL-C, $p = 0.002$). The prevalence of adverse levels of any lipid level increased from KNHANES Ⅵ to Ⅶ in boys ($p = 0.017$). Among the youth with dyslipidemia, 36.5% of boys and 29.7% of girls were overweight or obese in the last

phase of the KNHANES.

Trends in Mean Lipid Levels and Dyslipidemia According to Sex and BMI

In sex- and BMI-specific analyses, adverse trends in total cholesterol, LDL-C, and non-HDL levels were more apparent in boys with normal BMI ($p < 0.001$, $p = 0.003$, and $p = 0.004$, respectively) than in those who were overweight ($p = 0.062$, $p = 0.032$ and, $p = 0.077$, respectively) and obese ($p = 0.132$, $p = 0.338$, and $p = 0.037$, respectively) (Table Ⅱ [available at www.jpeds.com] and Figure 3, A–E). Among girls, the mean levels of total cholesterol, LDL-C, and non-HDL-C increased significantly from KNHANES Ⅳ to Ⅶ in participants with a normal BMI ($p < 0.001$, $p = 0.003$, and $p = 0.004$, respectively) and those who were overweight ($p = 0.001$, $p = 0.004$, and $p = 0.004$, respectively), but not in those who were obese (Figure 4). In contrast, the TG level increased significantly from KNHANES Ⅵ to Ⅶ in girls with obesity ($p = 0.011$) but not in those with a normal BMI or overweight.

Trends in Mean Lipid Levels and Dyslipidemia According to Sex and Age

In sex- and age- specific analyses, the mean total cholesterol, LDL-C, and non-HDL-C levels increased from KNHANES Ⅴ to Ⅶ in the overall population of boys (Table Ⅲ; available at www.jpeds.com). In addition, mean levels of total cholesterol and LDL-C were higher in boys aged 10–12 years than in boys aged 13–18 years. Among girls, the mean total cholesterol, LDL-C, and non-HDL-C levels increased from KNHANES Ⅳ to Ⅶ in participants aged 10–12 years ($p = 0.004$, $p = 0.003$, and $p = 0.044$, respectively) and 16–18 years ($p < 0.001$, $p = 0.007$, and $p = 0.006$, respectively). In the overall population, the prevalence of acceptable levels of total cholesterol, LDL-L, and non-HDL-C generally

decreased, whereas the prevalence of those with adverse levels of total cholesterol, LDL-C, and non-HDL-C generally increased (Table Ⅳ and Table Ⅴ; both available at www.jpeds.com).

Discussion

Our data revealed worsening trends in total cholesterol, LDL-C, and non-HDL-C levels among Korean youth. This trend was seen in youth with a normal BMI, overweight, and obesity. Additionally, the trends in lipid levels were unfavorable in children aged 10–12 years and adolescents. Overall, the prevalence of participants with acceptable levels of total cholesterol, LDL-C, and non-HDL-C decreased, whereas the prevalence of those with adverse levels increased. In the last phase of the KNHANES, the proportions of participants with adverse levels of any lipid were 28.1% in boys and 29.7% in girls, the proportions of participants with overweight or obesity were 21.7% in boys and 19.3% in girls, and the proportions of participants with dyslipidemia were 39.5% in boys and 29.7% in girls.

A previous systematic analysis of 3 million subjects worldwide reported that the mean total cholesterol levels had decreased from 1980 to 2008 in western countries, whereas the corresponding values had increased in East and Southeast Asia.[16] In 2008, the mean global total cholesterol levels were 179.4 mg/dL for men and 184.1 mg/dL for women. Among Korean adults, the mean levels of total cholesterol and HDL-C increased from 2005 to 2015 according to a KNHANES-based study.[17] In 2007–2009, the mean total cholesterol levels were 187.7 mg/dL for men and 187.9 mg/dL for women. In our study, the mean total cholesterol levels were 161.2 mg/dL for boys and 168.9 mg/dL for girls in the last phase.

Among youth, favorable trends in total cholesterol, HDL-C, and non-HDL-C levels were

observed from 1996 to 2016 in the US.[6] The mean levels of total cholesterol, HDL-C, non-HDL-C, TG, and LDL-C were 155 mg/dL, 55 mg/dL, 100 mg/dL, 63 md/dL, and 86 mg/dL, respectively. Further, dyslipidemia was prevalent in 15.2% of children and 25.2% of adolescents at the end of the study. Among the Danish youth, dyslipidemia was prevalent in 6.4% of the subjects from 2010 to 2015 in a population-based cohort study.[18] In a German cohort study conducted between 2011 and 2015, adverse levels of total cholesterol, LDL-C, and HDL-C were prevalent in 7.8%, 6.1%, and 9.0% of the youth, respectively.[19]

In Asia, a study of 14,872 Japanese children from 1993 to 2008 showed no significant trends in total cholesterol, HDL-C, or non-HDL-C levels.[20] In contrast, Chinese youth demonstrated adverse trends in lipid levels from 2004 to 2014 in a cross-sectional study.[7] A meta-analysis conducted in China reported that the overall prevalence of dyslipidemia was 31.6% in children aged 7–18 years and 9.0% in children aged 2–6 years.[21] In Iran, the prevalence of dyslipidemia was 34.3% of adolescents.[22] Although our results were opposite to the favorable trends in western countries, such as the US, they were consistent with observations in Asia.[6,7,16] The difference between western countries and Asian countries may be associated with development status.[7] Among the Asian countries, the lipid trend in Japan was different from that in other countries.[20] Although lipid levels usually increase with economic development and urbanization, it may be offset later through healthier diets and medical interventions.[16]

We found no significant trends in the prevalence of overweight and obesity. Globally, the prevalence of overweight and obesity is increasing among both adults and youth.[23,24] The global age-standardized prevalence of obesity increased from 0.9% to 7.8% in boys and from 0.7% to 5.6% in girls, from 1975 to 2016, in a population-based study.[24] The mean BMI increased for both sexes in East and South Asia, and for boys in Southeast Asia. Meanwhile,

it was recently reported to have flattened in north western Europe, high-income English-speaking regions, and Asia-Pacific regions. In addition, a systematic review reported that the prevalence of central obesity increased from 16.3% in 1985–1999 to 33.9% in 2010–2014, among the population aged 15–40 years.[25] Among Korean youth, central obesity was prevalent in 7.2% of boys and 9.0% of girls from 2008 to 2010 in a KNHANES-based study.[26] The prevalence rates were 11.54% in boys and 10.49% in girls in this recent phase of the KNHANES.

Our study cannot explain the exact cause of adverse trends in lipid levels. However, the increased prevalence of boys with central obesity in our study may be attributed to the trends in adverse lipid levels. WC is positively associated with dyslipidemia in youth.[7] In addition, fat intake increased in our study. Song et al reported that dietary intake of total fat and saturated fatty acids had increased among Korean adolescents from 2007 to 2017.[27] Another Korean study showed that calorie intake and fat intake increased from 2008 to 2017 among youth.[28] The increasing trend in intake of calories and fats may help explain the worsening trend in lipid levels among Korean youth.

This study has some limitations. First, this was a cross-sectional study exclusive to Korean., Second, confounding factors such as pubertal status and physical activity were not considered. Third, defining obesity and overweight according to the BMI percentile does not consider lean and fat body mass. Fourth, accurate information on saturated fat was not included in the KHANES data set. Further studies are required to determine the causes for the observed trends in lipid levels.

In conclusion, our results indicate worsening trends in lipid levels and the prevalence of dyslipidemia among youth in Korea. Furthermore, these adverse trends were seen even in youth with a normal BMI and young age. These findings suggest an increased risk of

cardiovascular disease among the youth in the future. Consequently, further efforts are required to manage lipid levels for all Korean youth, not just those with overweight or obesity.

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Figure Legends

Figure 1 Flowchart of study population; online only.

KNHANES, Korea National Health and Nutrition Examination Survey.

Figure 2. Trends in mean levels of lipids in boys (A) and girls (B). Changes in mean lipid levels from KNHANES Ⅵ through the following phases. The black solid line is total cholesterol, the dashed line is low-density lipoprotein cholesterol, the dotted line is non-high-density lipoprotein cholesterol, the gray solid line is triglycerides, and the black narrow line is high-density lipoprotein cholesterol.

KNHANES, Korea National Health and Nutrition Examination Survey.

Figure 3. Trends in mean levels of lipids in boys according to BMI groups (normal, overweight, and obesity).

Changes in mean lipid levels from KNHANES Ⅳ to the following phases. The solid line is the total group, the dotted line is the normal group, the dashed line is the overweight group, and the black narrow line is the obesity group. (A) Total cholesterol; (B) low-density lipoprotein cholesterol; (C) non-high-density lipoprotein cholesterol; (D) triglycerides; and (E) high-density lipoprotein cholesterol levels.

BMI, body mass index; *KNHANES*, Korea National Health and Nutrition Survey.

Figure 4. Trends in mean levels of lipids in girls according to BMI groups (normal,

overweight, and obesity).

Changes in mean lipid levels from KNHANES Ⅳ to the following phases. The solid line is the total group, the dotted line is the normal group, the dashed line is the overweight group, and the black narrow line is the obesity group. (A) Total cholesterol; (B) low-density lipoprotein cholesterol; (C) non-high-density lipoprotein cholesterol; (D) triglycerides; and (E) high-density lipoprotein cholesterol levels.

BMI, body mass index; *KNHANES*, Korea National Health and Nutrition Survey.

1 **Table Ⅰ.** Characteristics of subjects according to sex

	Male sex (n=4651)						Female sex (n=4080)					
Phase	Overall	Ⅳ	Ⅴ	Ⅵ	Ⅶ	*p*	Overall	Ⅳ	Ⅴ	Ⅵ	Ⅶ	*p*
Unweighted number	4651	1410	1278	990	973		4080	1247	1101	851	881	
Age, y	14.29 (0.04)	14.11 (0.08)	14.27 (0.08)	14.36 (0.09)	14.49 (0.09)	0.011	14.25 (0.05)	14.07 (0.08)	14.23 (0.11)	14.32 (0.10)	14.41 (0.11)	0.046
Height SDS	0.24 (0.02)	0.25 (0.03)	0.21 (0.04)	0.22 (0.04)	0.29 (0.04)	0.597	0.19 (0.02)	0.15 (0.04)	0.20 (0.04)	0.15 (0.05)	0.27 (0.04)	0.108
Weight SDS	0.09 (0.02)	0.08 (0.04)	0.01 (0.05)	0.18 (0.05)	0.13 (0.05)	0.048	0.08 (0.02)	-0.04 (0.04)	0.07(0.05)	0.18 (0.05)	0.13 (0.044)	0.003
BMI SDS	-0.04 (0.02)	-0.06 (0.04)	-0.13 (0.05)	0.08 (0.05)	-0.01 (0.05)	0.027	-0.02 (0.02)	-0.14 (0.05)	-0.04 (0.05)	0.13 (0.05)	-0.01 (0.05)	0.001
BMI percentile						0.255						0.266
Normal	79.18 (0.70)	79.42 (1.23)	80.73 (1.40)	77.81 (1.51)	78.32 (1.50)		81.75 (0.71)	83.58 (1.27)	81.43 (1.47)	80.90 (1.46)	80.66 (1.52)	
Overweight	10.00 (0.49)	11.10 (0.95)	9.42 (0.96)	9.72 (0.97)	9.57 (0.99)		8.93 (0.49)	9.35 (0.89)	8.89 (1.00)	8.81 (1.02)	8.57 (1.04)	
Obesity	10.82 (0.55)	9.48 (0.97)	9.85 (1.06)	12.47 (1.21)	12.11 (1.25)		9.32 (0.56)	7.07 (0.98)	9.68 (1.16)	10.29 (1.20)	10.76 (1.17)	
WC	72.25 (0.19)	71.91 (0.34)	71.29 (0.37)	73.11 (0.41)	73.05 (0.40)	0.001	67.54 (0.17)	67.08 (0.30)	67.32 (0.35)	68.41 (0.34)	67.52 (0.33)	0.026
WC >90th percentile	9.14 (0.50)	7.76 (0.85)	7.37 (0.90)	10.77 (1.12)	11.54 (1.19)	0.005	10.39 (0.57)	8.96 (0.91)	11.27 (1.23)	11.05 (1.20)	10.49 (1.19)	0.424
WHtR	0.437 (0.001)	0.437 (0.002)	0.432 (0.002)	0.442 (0.002)	0.439 (0.002)	0.009	0.429 (0.001)	0.428 (0.002)	0.427 (0.002)	0.434 (0.002)	0.427 (0.002)	0.035
Energy (kcal)	2341.07 (17.80)	2134.85 (28.02)	2406.60 (35.23)	2470.29 (40.09)	2393.83 (38.28)	<0.001	1847.19 (14.20)	1741.94 (24.20)	1906.67 (28.26)	1900.17 (32.32)	1850.25 (28.73)	<0.001
Carbohydrate (g)	355.14 (2.61)	337.60 (4.34)	369.10 (5.05)	362.93 (5.95)	352.40 (5.66)	<0.001	284.84 (2.18)	278.93 (3.94)	296.08 (4.12)	285.94 (4.78)	277.40 (4.64)	0.007
Protein (g)	85.17 (0.88)	75.24 (1.12)	88.68 (1.96)	89.88 (2.00)	88.93 (1.82)	<0.001	65.46 (0.71)	60.77 (1.03)	67.61 (1.32)	67.20 (1.86)	66.88 (1.39)	<0.001
Fat (g)	62.21 (0.74)	53.02 (1.12)	63.36 (1.51)	68.57 (1.58)	66.15 (1.67)	<0.001	48.65 (0.64)	42.48 (1.00)	50.72 (1.37)	51.57 (1.35)	50.78 (1.36)	<0.001
Total cholesterol, mg/dL	155.58 (0.50)	154.78 (0.97)	153.35 (1.02)	153.80 (0.96)	161.20 (0.99)	<0.001	164.20 (0.49)	161.35 (0.83)	163.46 (1.05)	163.94 (1.02)	168.90 (1.04)	<0.001
LDL-C, mg/dL	89.84 (0.43)	88.84 (0.81)	88.80 (0.87)	87.51 (0.85)	94.78 (0.87)	<0.001	95.09 (0.43)	92.57 (0.72)	94.93 (0.92)	95.05 (0.90)	98.47 (0.92)	<0.001

TG, mg/dL	85.27 (0.98)	88.61 (2.02)	81.25 (1.79)	86.33 (2.15)	84.87 (1.86)	0.047	87.38 (0.91)	90.42 (1.74)	85.91 (1.97)	84.00 (1.65)	88.66 (1.79)	0.040
HDL-C, mg/dL	49.51 (0.17)	48.36 (0.30)	49.37 (0.36)	50.60 (0.36)	50.09 (0.34)	<0.001	52.34 (0.19)	50.80 (0.34)	52.45 (0.43)	53.21 (0.38)	53.28 (0.39)	<0.001
Non-HDL-C, mg/dL	106.07 (0.48)	106.42 (0.94)	103.98 (0.93)	103.21 (0.90)	111.11 (0.96)	<0.001	111.86 (0.47)	110.55 (0.82)	111.01 (0.99)	110.73(0.98)	115.62 (1.01)	0.004
Acceptable lipid levels, %												
Total cholesterol <170 mg/dL	72.33 (0.76)	73.49 (1.34)	75.52 (1.51)	72.43 (1.51)	66.73 (1.71)	0.005	61.88 (0.90)	66.08 (1.54)	62.63 (1.88)	62.44 (1.88)	55.17 (1.92)	0.003
LDL-C <110 mg/dL	81.86 (0.65)	83.27 (1.13)	83.22 (1.26)	83.15 (1.26)	77.05 (1.54)	0.001	76.49 (0.81)	80.79 (1.23)	75.98 (1.73)	76.88 (1.70)	71.32 (1.81)	0.005
TG <90 mg/dL	65.79 (0.86)	65.20 (1.47)	68.07 (1.77)	63.80 (1.86)	65.75 (1.79)	0.357	63.27 (0.90)	61.26 (1.66)	65.98 (1.92)	64.47 (1.83)	61.42 (1.73)	0.156
HDL-C ≥45 mg/dL	65.52 (0.86)	60.75 (1.60)	63.86 (1.78)	69.05 (1.66)	70.25 (1.68)	<0.001	76.46 (0.80)	71.95 (1.54)	75.84 (1.70)	79.54 (1.44)	79.75 (1.57)	0.008
Non-HDL-C <120 mg/dL	73.26 (0.74)	73.06 (1.34)	76.24 (1.45)	76.68 (1.42)	66.39 (1.65)	<0.001	67.12 (0.86)	69.38 (1.49)	68.01 (1.81)	68.40 (1.83)	61.98 (1.79)	0.013
Adverse lipid levels, %												
Total cholesterol ≥200 mg/dL	6.13 (0.41)	6.29 (0.71)	5.30 (0.79)	4.65 (0.76)	8.45 (1.02)	0.011	9.43 (0.52)	7.80 (0.82)	9.02 (1.07)	8.93 (1.06)	12.43 (1.22)	0.013
LDL-C ≥130 mg/dL	5.07 (0.38)	4.35 (0.60)	4.96 (0.78)	4.05 (0.67)	7.18 (0.96)	0.020	7.28 (0.46)	5.98 (0.77)	6.95 (0.93)	6.60 (0.91)	9.98 (1.13)	0.015
TG ≥130 mg/dL	13.48 (0.62)	14.59 (1.16)	12.90 (1.25)	13.83 (1.32)	12.43 (1.20)	0.594	13.53 (0.64)	15.21 (1.17)	12.84 (1.26)	10.53 (1.18)	15.23 (1.45)	0.030
HDL-C <40 mg/dL	15.58 (0.62)	19.77 (1.26)	16.30 (1.28)	11.66 (1.10)	13.13 (1.12)	<0.001	9.39 (0.55)	12.76 (1.10)	9.53 (1.23)	7.61 (0.98)	6.76 (0.95)	0.003
Non-HDL-C ≥145 mg/dL	7.52 (0.46)	9.39 (0.97)	5.67 (0.79)	5.49 (0.80)	9.44 (1.07)	0.005	9.64 (0.54)	9.17 (0.96)	8.21 (1.01)	8.10 (1.03)	13.44 (1.32)	0.002
Adverse level of any lipid	28.76 (0.78)	32.01 (1.47)	28.86 (1.59)	25.05 (1.59)	28.10 (1.58)	0.017	27.44 (0.84)	29.17 (1.56)	26.58 (1.66)	24.00 (1.67)	29.70 (1.84)	0.075
BMI percentile among youth with dyslipidemia						0.685						0.685
Normal	62.51 (1.48)	62.69 (2.57)	65.34 (2.95)	60.43 (3.39)	60.46 (3.02)		70.95 (1.58)	70.52 (2.97)	70.31 (3.28)	73.28 (3.42)	70.29 (2.95)	
Overweight	16.62 (1.15)	18.13 (2.10)	15.83 (2.34)	16.65 (2.37)	15.36 (2.34)		10.76 (0.98)	13.12 (1.90)	10.01 (1.97)	8.67 (2.07)	10.33 (1.85)	
Obesity	20.87 (1.33)	19.18 (2.36)	18.83 (2.60)	22.92 (2.93)	24.18 (2.87)		18.28 (1.44)	16.36 (2.68)	19.68 (3.05)	18.05 (3.03)	19.38 (2.81)	

2 *SDS*, standard deviation score; *BMI*, body mass index; *WC*, waist circumference; *WHtR*, waist-to-height ratio; *LDL-C*, low-density lipoprotein cholesterol; *TG*,

triglycerides; *HDL-C*, high-density lipoprotein cholesterol.

Continuous variables are presented as the mean (standard error), and categorical data as the percentage (standard error).

Table Ⅱ. Trends in the mean lipid levels according to sex and BMI classification

	Male (n=4,651)						Female (n=4,080)					
Phase	Overall	Ⅳ	Ⅴ	Ⅵ	Ⅶ	*p*	Overall	Ⅳ	Ⅴ	Ⅵ	Ⅶ	*p*
Total cholesterol, mg/dL												
Normal	152.95 (0.53)	151.71 (1.04)	150.91 (1.05)	151.61 (1.00)	158.54 (1.00)	<0.001	163.03 (0.53)	160.11 (0.87)	162.79 (1.12)	162.83 (1.13)	167.32 (1.12)	<0.001
Overweight	161.51 (1.59)	161.33 (2.80)	157.58 (3.06)	158.52 (3.03)	169.63 (3.71)	0.062	165.17 (1.45)	161.71 (2.62)	158.88 (2.75)	166.99 (2.85)	175.68 (2.85)	0.001
Obesity	169.40 (1.67)	172.881 (2.64)	169.26 (4.51)	163.84 (3.08)	171.72 (2.70)	0.132	173.49 (1.90)	175.47 (3.84)	173.26 (4.32)	170.11 (3.44)	175.34 (3.41)	0.675
LDL-C, mg/dL												
Normal	87.13 (0.44)	86.52 (0.86)	86.06 (0.85)	84.67 (0.89)	91.78 (0.85)	<0.001	93.61 (0.46)	91.24 (0.74)	93.68 (0.96)	93.56 (0.97)	96.65 (1.00)	0.003
Overweight	95.19 (1.37)	92.38 (2.29)	93.17 (2.69)	93.42 (2.47)	103.67 (3.34)	0.032	97.44 (1.33)	94.54 (2.62)	93.78 (2.55)	97.41 (2.45)	105.87 (2.61)	0.004
Obesity	104.74 (1.54)	104.27 (2.46)	107.08 (4.22)	100.63 (2.82)	107.10 (2.47)	0.338	105.83 (1.63)	105.65 (3.48)	106.53 (3.49)	104.76 (3.07)	106.25 (2.92)	0.980
TG, mg/dL												
Normal	77.98 (0.93)	78.87 (1.53)	74.20 (1.65)	80.51 (2.29)	79.13 (2.09)	0.071	83.28 (0.92)	86.65 (1.77)	81.11 (1.96)	80.75 (1.74)	83.97 (1.81)	0.070
Overweight	110.56 (4.55)	123.25 (11.05)	108.37 (7.43)	105.33 (7.43)	99.36 (6.23)	0.299	94.06 (2.97)	95.71 (5.09)	91.60 (6.07)	94.72 (7.49)	94.11 (5.01)	0.965
Obesity	115.29 (3.21)	129.69 (7.58)	113.07 (5.46)	107.84 (6.51)	110.52 (5.16)	0.130	116.98 (3.92)	128.03 (9.03)	121.05 (8.68)	100.30 (4.83)	119.47 (7.33)	0.011
HDL-C, mg/dL												
Normal	50.71 (0.19)	49.39 (0.32)	50.59 (0.40)	51.91 (0.41)	51.43 (0.40)	<0.001	53.29 (0.21)	51.66 (0.35)	53.64 (0.46)	54.01 (0.42)	54.28 (0.44)	<0.001
Overweight	46.02 (0.44)	45.62 (0.82)	44.37 (0.75)	47.43 (1.04)	47.22 (0.80)	0.027	50.03 (0.49)	48.03 (0.80)	49.16 (0.91)	52.37 (1.23)	51.41 (0.83)	0.004
Obesity	43.92 (0.41)	42.96 (0.72)	44.15 (0.92)	44.85 (0.90)	43.70 (0.70)	0.406	46.21 (0.59)	44.22 (1.36)	45.52 (1.24)	47.62 (1.10)	47.25 (0.92)	0.161

Non-HDL-C, mg/dL												
Normal	102.23 (0.48)	102.32 (0.97)	100.32 (0.92)	99.69 (0.94)	107.11 (0.93)	<0.001	109.74 (0.49)	108.45 (0.81)	109.16 (1.02)	108.82 (1.04)	113.04 (1.07)	0.004
Overweight	115.49 (1.52)	115.71 (2.89)	113.22 (2.70)	111.09 (2.67)	122.41 (3.59)	0.077	115.15 (1.43)	113.68 (2.60)	109.73 (2.73)	114.63 (2.78)	124.27 (3.01)	0.004
Obesity	125.48 (1.63)	129.92 (2.65)	125.11 (4.30)	118.99 (2.92)	128.02 (2.76)	0.037	127.28 (1.92)	131.25 (4.18)	127.74 (4.29)	122.49 (3.33)	128.09 (3.27)	0.389

2 *BMI*, body mass index; *LDL-C*, low-density lipoprotein cholesterol; *TG*, triglycerides; *HDL-C*, high-density lipoprotein cholesterol.

3 Continuous variables are presented as the mean (standard error), and categorical data as percentages (standard error).

1 **Table Ⅲ.** Trends of mean lipid levels according to sex and age groups

	Male (n=4,651)						Female (n=4,080)					
Phase	Overall	Ⅳ	Ⅴ	Ⅵ	Ⅶ	*p*	Overall	Ⅳ	Ⅴ	Ⅵ	Ⅶ	*p*
Total cholesterol, mg/dL												
10-12y	164.24 (0.77)	164.80 (1.47)	161.52 (1.54)	163.10 (1.40)	168.36(1.62)	0.016	165.77 (0.81)	162.36 (1.17)	165.85 (1.81)	167.21 (1.98)	169.10 (1.54)	0.004
13-15y	150.70 (0.77)	149.70 (1.38)	148.40 (1.54)	149.34 (1.59)	156.62 (1.59)	<0.001	161.74 (0.80)	159.44 (1.41)	161.66 (1.41)	160.78 (1.55)	165.84 (2.07)	0.081
16-18y	153.42 (0.82)	150.74 (1.40)	151.46 (1.82)	151.28 (1.62)	160.33 (1.58)	<0.001	165.21 (0.90)	162.36 (1.55)	163.25 (2.09)	164.32 (1.70)	171.31 (1.69)	<0.001
LDL-C, mg/dL												
10-12y	95.34 (0.67)	96.20 (1.28)	93.45 (1.28)	93.27 (1.30)	98.82 (1.48)	0.014	95.26 (0.69)	91.80 (1.05)	95.93 (1.46)	97.42 (1.75)	97.24 (1.32)	0.003
13-15y	86.18 (0.67)	84.93 (1.11)	85.34 (1.30)	83.76 (1.51)	91.65 (1.41)	<0.001	93.46 (0.70)	91.05 (1.16)	94.37 (1.29)	92.78 (1.38)	96.26 (1.85)	0.070
16-18y	88.96 (0.74)	85.99 (1.23)	88.34 (1.68)	86.87 (1.43)	94.70 (1.41)	<0.001	96.44 (0.78)	94.88 (1.40)	94.69 (1.74)	95.30 (1.44)	101.19 (1.56)	0.007
TG, mg/dL												
10-12y	80.99 (1.57)	84.89 (2.82)	76.82 (2.95)	77.64 (3.49)	84.24 (3.38)	0.125	97.22 (1.85)	98.16 (3.22)	98.70 (3.95)	91.31 (3.57)	100.07 (4.04)	0.330
13-15y	86.81 (1.88)	90.83 (4.21)	82.22 (2.79)	91.10 (3.87)	82.61 (4.02)	0.134	86.92 (1.58)	94.28 (3.34)	80.78 (3.00)	83.79 (2.72)	87.65 (3.05)	0.018
16-18y	87.17 (1.38)	89.78 (2.52)	83.91 (2.88)	88.11 (2.94)	87.02 (2.70)	0.488	80.07 (1.28)	79.08 (1.94)	80.83 (3.26)	78.81 (2.41)	81.47 (2.27)	0.815
HDL-C, mg/dL												
10-12y	53.12 (0.32)	51.62 (0.52)	53.29 (0.63)	54.99 (0.70)	53.30 (0.72)	0.002	52.16 (0.29)	51.25 (0.46)	51.85 (0.62)	53.20 (0.60)	52.80 (0.65)	0.045
13-15y	48.13 (0.25)	46.96 (0.42)	47.75 (0.51)	49.11 (0.54)	49.18 (0.53)	0.002	51.57 (0.34)	49.54 (0.56)	52.02 (0.71)	52.46 (0.72)	52.81 (0.66)	<0.001

16-18y	47.99 (0.27)	46.79 (0.47)	47.74 (0.60)	48.82 (0.54)	48.81 (0.50)	0.009	53.18 (0.33)	51.66 (0.57)	53.28 (0.75)	53.88 (0.66)	54.01 (0.64)	0.021
Non-HDL-C, mg/dL												
10-12y	111.11 (0.72)	113.18 (1.38)	108.23 (1.34)	108.12 (1.36)	115.05 (1.61)	<0.001	113.60 (0.76)	111.10 (1.13)	114.00 (1.62)	114.01 (1.90)	116.31 (1.49)	0.044
13-15y	102.57 (0.76)	102.74 (1.40)	100.65 (1.45)	100.23 (1.59)	107.44(1.65)	0.006	110.17 (0.77)	109.90 (1.36)	109.63 (1.36)	108.32 (1.46)	113.03 (2.06)	0.321
16-18y	105.42 (0.80)	103.95 (1.42)	103.72 (1.74)	102.47 (1.55)	111.52 (1.59)	<0.001	112.03 (0.86)	110.70 (1.53)	109.97 (1.96)	110.44 (1.57)	117.29 (1.70)	0.006

2 *LDL-C*, low-density lipoprotein cholesterol; *TG*, triglycerides; *HDL-C*, high-density lipoprotein cholesterol.

3 Values are presented as percentages (standard error).

Table Ⅳ. Trends in the prevalence of acceptable lipid levels according to sex and age groups

	Male (n=4,651)						Female (n=4,080)					
Phase	Overall	Ⅳ	Ⅴ	Ⅵ	Ⅶ	*p*	Overall	Ⅳ	Ⅴ	Ⅵ	Ⅶ	*p*
Total cholesterol, mg/dL												
10-12y	61.00 (1.37)	61.69 (2.28)	65.34 (2.90)	58.52 (2.90)	56.42 (2.89)	0.118	57.19 (1.48)	63.94 (2.27)	53.83 (3.19)	56.09 (3.39)	52.64 (3.09)	0.020
13-15y	78.32 (1.19)	79.40 (2.11)	80.83 (2.28)	79.88 (2.36)	71.77 (2.77)	0.040	65.78 (1.47)	68.05 (2.47)	67.44 (2.97)	67.43 (3.01)	59.11 (3.37)	0.119
16-18y	75.55 (1.29)	78.34 (2.19)	78.69 (2.57)	75.47 (2.73)	69.22 (2.81)	0.033	62.02 (1.60)	66.06 (2.92)	65.01 (3.45)	62.72 (3.07)	53.67 (3.21)	0.026
LDL-C, mg/dL												
10-12y	76.20 (1.18)	76.29 (1.92)	77.20 (2.57)	76.84 (2.39)	73.98 (2.55)	0.806	75.87 (1.33)	82.19 (2.00)	72.89 (2.73)	70.96 (3.29)	75.36 (2.76)	0.010
13-15y	85.32 (1.02)	88.03 (1.75)	86.31 (1.86)	85.96 (2.13)	79.57 (2.57)	0.030	78.89 (1.27)	81.57 (1.97)	78.75 (2.69)	81.95 (2.46)	72.38 (3.02)	0.036
16-18y	83.05 (1.12)	84.90 (1.96)	85.13 (2.16)	85.08 (2.20)	76.98 (2.63)	0.022	74.81 (1.43)	78.66 (2.27)	75.86 (3.13)	76.78 (2.72)	67.60 (3.19)	0.035
TG, mg/dL												
10-12y	70.58 (1.33)	67.30 (2.34)	72.47 (2.80)	75.57 (2.58)	67.83 (2.81)	0.093	55.04 (1.58)	53.92 (2.63)	56.46 (3.25)	56.47 (3.42)	53.51 (3.48)	0.864
13-15y	65.88 (1.38)	65.57 (2.47)	66.78 (2.47)	60.94 (3.07)	70.55 (3.17)	0.151	63.49 (1.56)	57.94 (2.94)	71.47 (2.89)	63.93 (3.31)	60.91 (3.20)	0.010
16-18y	62.01 (1.47)	62.91 (2.59)	65.72 (3.01)	57.96 (3.10)	60.69 (3.06)	0.299	69.54 (1.47)	71.68 (2.42)	68.29 (3.39)	70.81 (2.92)	67.42 (2.84)	0.695
HDL-C, mg/dL												
10-12y	77.61 (1.15)	73.80 (2.13)	77.06 (2.33)	82.20 (2.16)	79.57 (2.45)	0.055	76.67 (1.22)	73.49 (2.11)	75.96 (2.43)	82.81 (2.50)	75.90 (2.78)	0.057
13-15y	59.88 (1.42)	52.80 (2.54)	58.56 (2.85)	63.96 (2.91)	66.99 (2.96)	0.002	73.47 (1.45)	65.95 (2.77)	76.15 (2.81)	74.56 (3.05)	79.12 (2.76)	0.006
16-18y	61.38 (1.57)	56.82 (2.93)	58.23 (3.54)	64.33 (2.91)	67.00 (2.83)	0.055	79.01 (1.30)	76.72 (2.34)	75.47 (2.95)	81.52 (2.25)	82.99 (2.55)	0.102
Non-HDL-C, mg/dL												
10-12y	67.29 (1.31)	65.93 (2.23)	71.57 (2.72)	69.76 (2.70)	60.79 (2.80)	0.028	62.80 (1.46)	68.64 (2.33)	57.47 (2.97)	61.56 (3.41)	62.06 (3.11)	0.036
13-15y	77.18 (1.21)	78.40 (2.15)	77.69 (2.37)	80.33 (2.30)	71.37 (2.87)	0.079	70.20 (1.42)	71.03 (2.39)	72.86 (2.92)	72.52 (2.81)	63.57 (3.25)	0.092
16-18y	74.26 (1.31)	74.20 (2.32)	78.63 (2.51)	78.25 (2.59)	65.99 (2.99)	0.002	67.73 (1.51)	68.38 (2.64)	71.65 (3.25)	69.80 (2.98)	60.60 (3.09)	0.054

LDL-C, low-density lipoprotein cholesterol; *TG*, triglycerides; *HDL-C*, high-density lipoprotein cholesterol.

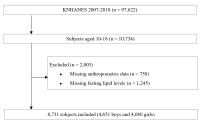
Values are presented as percentages (standard error).

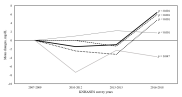
Table V. Trends in the prevalence adverse lipid levels according to sex and age groups

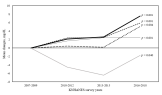
	Male (n=4,651)						Female (n=4,080)					
Phase	Overall	IV	V	VI	VII	*p*	Overall	IV	V	VI	VII	*p*
Total cholesterol, mg/dL												
10-12y	9.86 (0.85)	10.54 (1.45)	8.35 (1.82)	7.83 (1.50)	13.03 (2.00)	0.170	9.78 (0.93)	5.33 (1.08)	11.29 (2.04)	13.76 (2.56)	10.31 (1.82)	0.006
13-15y	4.01 (0.55)	4.08 (0.99)	2.97 (0.91)	3.16 (1.10)	6.23 (1.50)	0.185	8.06 (0.82)	8.17(1.41)	5.55 (1.45)	6.58 (1.50)	12.39 (2.19)	0.025
16-18y	5.22 (0.66)	4.64 (1.17)	5.05 (1.39)	3.77 (1.11)	7.33 (1.56)	0.281	10.39 (0.97)	9.77 (1.64)	10.36 (2.15)	7.44 (1.67)	13.96 (2.24)	0.139
LDL-C, mg/dL												
10-12y	7.17 (0.72)	6.87 (1.24)	5.81 (1.38)	6.40 (1.34)	10.36 (1.89)	0.158	6.53 (0.76)	3.43 (0.85)	7.58 (1.61)	8.66 (2.12)	7.55 (1.64)	0.046
13-15y	3.51 (0.51)	2.79 (0.77)	3.37 (0.96)	2.13 (0.90)	6.21 (1.49)	0.046	6.21 (0.70)	6.25 (1.30)	4.27 (1.21)	5.35 (1.28)	9.37 (1.82)	0.077
16-18y	4.89 (0.64)	3.60 (0.98)	5.79 (1.51)	4.17 (1.09)	5.96 (1.44)	0.439	8.84 (0.91)	8.12 (1.56)	8.85 (1.99)	6.18 (1.56)	12.20 (2.10)	0.145
TG, mg/dL												
10-12y	12.10 (0.98)	14.39 (1.90)	11.17 (1.99)	9.78 (1.74)	12.24 (2.06)	0.355	20.19 (1.31)	21.99 (2.16)	20.03 (2.73)	14.56 (2.54)	23.47 (3.09)	0.119
13-15y	5.71 (0.65)	6.86 (1.37)	4.15 (1.03)	4.16 (1.20)	7.84 (1.59)	0.110	12.13 (1.06)	15.51 (2.08)	9.29 (1.91)	10.16 (1.90)	13.03 (2.42)	0.113
16-18y	13.98 (1.05)	16.07 (1.93)	13.30 (2.31)	13.96 (2.20)	12.49 (1.87)	0.646	9.58 (0.91)	8.46 (1.43)	10.58 (2.08)	7.90 (1.80)	11.27 (1.82)	0.493
HDL-C, mg/dL												
10-12y	9.92 (0.83)	12.39 (1.53)	10.54 (1.85)	6.03 (1.33)	9.25 (1.68)	0.048	9.32 (0.84)	10.68 (1.55)	11.52 (1.82)	6.88 (1.76)	7.18 (1.51)	0.130
13-15y	14.10 (1.03)	13.30 (1.78)	13.94 (2.00)	16.78 (2.30)	12.50 (2.25)	0.532	10.85 (0.99)	15.87 (2.07)	7.38 (1.64)	10.05 (2.01)	9.11 (2.04)	0.009
16-18y	17.24 (1.21)	22.22 (2.77)	17.90 (2.37)	13.41 (2.11)	14.63 (2.11)	0.037	8.11 (0.84)	11.50 (1.73)	9.92 (2.04)	6.00 (1.38)	4.50 (1.25)	0.008
Non-HDL-C, mg/dL												
10-12y	10.06 (0.81)	13.03 (1.57)	7.19 (1.47)	6.94 (1.35)	12.67 (2.06)	0.005	9.93 (0.93)	7.99 (1.35)	10.39 (1.96)	10.83 (2.29)	11.24 (2.00)	0.566
13-15y	18.51 (1.08)	24.05 (2.15)	19.50 (2.31)	14.11 (1.90)	14.31 (1.99)	0.002	8.02 (0.79)	8.56 (1.41)	4.88 (1.20)	6.18 (1.45)	12.91 (2.18)	0.002
16-18y	7.25 (0.79)	8.60 (1.57)	5.89 (1.51)	5.68 (1.41)	8.68 (1.71)	0.349	10.89 (1.00)	10.91 (1.82)	9.50 (2.03)	7.78 (1.77)	15.42 (2.33)	0.056

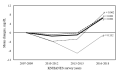
TC, total cholesterol; *LDL-C*, low-density lipoprotein cholesterol; *TG*, triglycerides; *HDL-C*, high-density lipoprotein cholesterol.

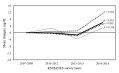
Values are presented as percentages (standard error).

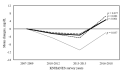


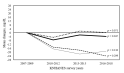


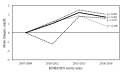


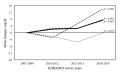


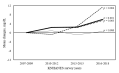


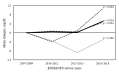


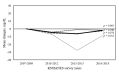


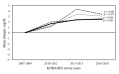












STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5-6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*5-6*
Bias	9	Describe any efforts to address potential sources of bias	N/A
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5-6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6-7
		(*b*) Describe any methods used to examine subgroups and interactions	6-7
		(*c*) Explain how missing data were addressed	4
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	N/A
		(*e*) Describe any sensitivity analyses	N/A

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	4
		(b) Give reasons for non-participation at each stage	4
		(c) Consider use of a flow diagram	4
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7
		(b) Indicate number of participants with missing data for each variable of interest	5
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	N/A
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	N/A
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	N/A
		Cross-sectional study—Report numbers of outcome events or summary measures	7-9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	N/A
		(*b*) Report category boundaries when continuous variables were categorized	7-9
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7-9
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	11-12
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	1

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.