

Application of the 2013 American College of Cardiology/American Heart Association Cholesterol Guideline to the Korean National Health and Nutrition Examination Surveys from 1998 to 2012

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Background: The 2013 American College of Cardiology/American Heart Association (ACC/AHA) guideline for the treatment of blood cholesterol recommends statin therapy for individuals at high risk of atherosclerotic cardiovascular disease (ASCVD). The aim of this study was to investigate serial trends in the percentages of Korean adults considered eligible for statin therapy according to the new ACC/AHA cholesterol guideline.

Methods: Data from the Korean National Health and Nutrition Examination Survey (KNHANES) I (1998, $n=7,698$), II (2001, $n=5,654$), III (2005, $n=5,269$), IV (2007 to 2009, $n=15,727$), and V (2010 to 2012, $n=16,304$), which used a stratified, multistage, probability sampling design, were used as representative of the entire Korean population.

Results: The percentage of adults eligible for statin therapy according to the ACC/AHA cholesterol guideline increased with time: 17.0%, 19.0%, 20.8%, 20.2%, and 22.0% in KNHANES I, II, III, IV, and V, respectively ($P=0.022$). The prevalence of ASCVD was 1.4% in KNHANES I and increased to 3.3% in KNHANES V. The percentage of diabetic patients aged 40 to 75 years with a low density lipoprotein cholesterol levels of 70 to 189 mg/dL increased from 4.8% in KNHANES I to 6.1% in KNHANES V. People with an estimated 10-year ASCVD risk $\geq 7.5\%$ and aged 40 to 75 years accounted for the largest percentage among the four statin benefit groups: 9.1% in KNHANES I and 11.0% in KNHANES V.


Conclusion: Application of the 2013 ACC/AHA guideline has found that the percentage of Korean adults in the statin benefit groups has increased over the past 15 years.

Keywords: American Heart Association; Atherosclerosis; Cardiovascular disease; Guideline; Korea

INTRODUCTION

Cardiovascular disease is a leading cause of death worldwide [1]. The American College of Cardiology (ACC) and American Heart Association (AHA) released a new guideline for the treatment of blood cholesterol in November 2013 [2]. The new guideline has been changed significantly from the previous Na-

tional Cholesterol Education Program-Adult Treatment Panel III recommendations. It suggests the new concept of atherosclerotic cardiovascular disease (ASCVD) and pooled cohort equations for estimating the 10-year ASCVD risk. It does not recommend nonstatin therapy and no longer use target levels of low density lipoprotein cholesterol (LDL-C). Instead, the main focus of the new guideline is identification of individuals at risk

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of ASCVD for whom statin therapy may be beneficial.

The prevalence of ASCVD is increasing in many Asian countries [3]. The social and economic implications of this increase in ASCVD prevalence are extensive. In addition to direct economic costs, including healthcare expenditure, indirect costs related to foregone productivity, absenteeism, and premature mortality reinforce the potentially catastrophic economic consequences of the ASCVD issue. South Korea is facing the same situation; the prevalence of ASCVD is increasing, and it has been identified as the second leading cause of death [4].

Cardiovascular risk is lower in Asian countries than in Western countries [5,6]. However, there is no appropriate lipid guideline with clear definition that can identify individuals at cardiovascular risk or who need statin therapy for ASCVD prevention that is specific to Asian populations. No study has reported on percentages of individuals who benefit from statin therapy or the serial trends at the nationwide level in Asian countries.

Therefore, we investigated the number and percentage of people who would be classified into the statin benefit group and the serial trends based on the 2013 ACC/AHA cholesterol guideline using 1998 to 2012 data from the Korean National Health and Nutrition Examination Surveys (KNHANESs), a national dataset that represents the entire Korean population.

METHODS

Data source

In this study, we used the data from KNHANES I (1998, $n=7,698$), II (2001, $n=5,654$), III (2005, $n=5,269$), IV (2007 to 2009, $n=15,727$), and V (2010 to 2012, $n=16,304$). KNHANES is a nationwide, community-based survey that examines the general health and nutrition status of noninstitutionalized civilians in Korea. It is conducted by the Division of Health and Nutritional Survey under the Korean Centers for Disease Control and Prevention (KCDCP). This nationally representative cross-sectional survey includes 5,000 to 6,000 individuals each year as a survey sample and collects information on socioeconomic status, health-related behaviors, quality of life, healthcare utilization, anthropometric measures, biochemical and clinical profiles related to noncommunicable diseases, and dietary intake. Participants were selected from sampling units based on geographic area, sex, and age groups using household registries and a stratified, multistage, clustered, probability sampling design [7]. The sampling method was certified as producing representative sta-

tistics by Statistics Korea (<http://kostat.go.kr/portal/english/index.action>). KNHANES provides statistics as the basis for health-related policies in Korea and serves as a research resource for studies on risk factors and diseases by supporting over 500 publications [8-10]. Each KNHANES was conducted according to the guidelines of the Declaration of Helsinki. All participants in the survey signed an informed consent form. The Institutional Review Board of KCDCP approved the protocol.

Study population

Subjects aged ≥ 20 years who had completed the health examination and health interview survey were included in the analysis. We identified four statin benefit groups based on the 2013 ACC/AHA cholesterol guideline: (1) individuals with ASCVD; (2) those without ASCVD with an LDL-C concentration ≥ 190 mg/dL (≥ 4.9 mmol/L); (3) those with diabetes mellitus and aged 40 to 75 years with LDL-C concentration of 70 to 189 mg/dL (1.8 to 4.9 mmol/L); and (4) those with an estimated 10-year ASCVD risk of $\geq 7.5\%$, aged 40 to 75 years, and with an LDL-C concentration of 70 to 189 mg/dL [2].

The definition of ASCVD including cerebrovascular accident (CVA) and ischemic heart disease (IHD) was based on the questionnaire completed by participants during face-to-face interviews by trained investigators. CVA was determined when a subject was ever told that they had a stroke by a health care professional or was taking medication or having sequelae from that event. Furthermore, IHD was determined based on an affirmative response to any one of the questions about doctor-diagnosed coronary artery disease, angina, or heart attack or current use of antianginal medication. Before 2009, LDL-C level was calculated using Friedewald's equation [11] in individuals with a triglyceride concentration ≤ 400 mg/dL (4.5 mmol/L), and it has been measured directly since KNHANES IV in 2009. Individuals with diabetes mellitus were defined as those with a glycosylated hemoglobin $\geq 6.5\%$, fasting plasma glucose concentration ≥ 126 mg/dL (7 mmol/L), or who reported in the health interview survey as having had a previous diagnosis of diabetes by a physician or being treated with oral antidiabetic agents or insulin.

The estimated 10-year ASCVD risk was calculated using the Pooled Cohort Equations for non-Hispanic Whites, which include age, sex, systolic blood pressure, antihypertensive treatment, levels of total cholesterol and high density lipoprotein cholesterol, smoking status, and history of diabetes mellitus [2]. In KNHANES I (1998) and II (2001), use of lipid-lowering

agents was not assessed in the health interview survey because it was considered to be very low in Korea at that time.

Anthropometric parameters

Anthropometric and laboratory data collected in the KNHANESs were measured as follows. Height was measured to the nearest 0.1 cm using a stadiometer (Seca 210; Seca, Hamburg, Germany), and weight was measured to the nearest 0.1 kg (GL-6000-20; G-tech, Uijeongbu, Korea). Body mass index (BMI) was calculated as body weight (kg) divided by height squared (m²). Waist circumference was measured to the nearest 0.1 cm (Seca 200; Seca). A mercury sphygmomanometer (Baumanometer; Baum, Copiague, NY, USA) was used to measure blood pressure to the nearest 2 mm Hg.

Information about health behaviors such as smoking status, alcohol consumption, physical activity, and medications using lipid-lowering, antidiabetic, and antihypertensive agents was collected in the health questionnaire survey. The lipid-lowering therapy would include not only statins but also drugs other than statins, because the specific class of lipid-lowering agents was not investigated. The health interview was conducted by trained staff members, including physicians, medical technicians, and health interviewers, at a mobile examination center.

Biochemical parameters

Blood samples were drawn from the antecubital vein in the morning after fasting for at least 8 hours. Samples were properly processed, refrigerated at 2°C to 8°C, and immediately sent to the central laboratory (Neodin Medical Institute, Seoul, Korea), where the plasma was separated immediately by centrifugation. The fasting plasma concentrations of glucose and lipids were measured enzymatically. A Hitachi 747 Chemistry Analyzer (Hitachi, Tokyo, Japan) was used in the 1998 and 2001 studies, an Advia 1,650/2,400 analyzer (Siemens, New York, NY, USA) was used in 2005 and 2007, and a Hitachi Automatic Analyzer 7600 was used from 2008 to 2012. To confirm and compare the accuracy and consistency in each survey, commutable frozen serum samples ($n=38$) were taken from normal subjects and patients with dyslipidemia, according to the Clinical and Laboratory Standards Institute guidelines (www.clsi.org). The commutable frozen serum samples were sent to the US Centers for Disease Control and Prevention (Atlanta, GA, USA) and were measured using the standard method. Using the data from the US Centers for Disease Control and Prevention, the conversion rate for KNHANES 2007 was obtained using the Passing-

Bablok regression method. This analysis found that the lipid levels in each survey were statistically well substantiated.

Statistical analysis

All statistical analyses were performed using a complex sample design using SPSS version 20.0 (IBM Co., Armonk, NY, USA). The stratification variables and sampling weights were derived from the sample design for each survey year and were used as designated by the KCDCP. Linear regression analyses were used to compare the percentages of the population classified into statin benefit groups in KNHANES I to V. All data are presented as the mean \pm standard error for continuous variables and as the percentage (standard error) for nominal variables. Statistical significance was defined as $P<0.05$.

RESULTS

Characteristics of participants in the KNHANESs from 1998 to 2012

The baseline characteristics of participants in KNHANES I to V are listed in Table 1. Each year's data are also shown in Supplementary Table 1. During the period, participants' mean age, BMI, and waist circumference increased gradually. The percentages of participants receiving lipid-lowering or antihypertensive therapy also increased with time.

Trends in the percentages of adults in statin benefit groups from 1998 to 2012

The percentages of adults in the total statin benefit groups showed an increasing trend: 17.0%, 19.0%, 20.8%, 20.2%, and 22.0% in KNHANES I, II, III, IV, and V, respectively ($P=0.022$) (Fig. 1). We compared changes in the percentages in four statin benefit groups from KNHANES I to V (Table 2). (1) The prevalence of ASCVD was low in the early KNHANESs (1.4% in KNHANES I and 1.6% in KNHANES II) and increased to $>3\%$ from KNHANES III (2005) through the later surveys ($P=0.075$). Nevertheless, the percentages of adults eligible for statin therapy for primary prevention, without previous ASCVD, increased from 15.6% in KNHANES I to 18.7% in KNHANES V, even though there was no statistical significance ($P=0.071$). Furthermore, when those percentages except for previous ASCVD group were subdivided by year, we could find a significant increasing trend ($P=0.008$): 15.6%, 17.4%, 17.3%, 15.7%, 16.8%, 17.8%, 18.4%, 18.7%, and 18.9% in 1998, 2001, 2005, 2007, 2008, 2009, 2010, 2011, and 2012, respectively. (2) The percentage of

Table 1. Anthropometric and biochemical parameters in the Korean National Health and Nutrition Examination Surveys from 1998 to 2012

Parameter	I 1998	II 2001	III 2005	IV 2007–2009	V 2010–2012
Number	7,698	5,654	5,269	15,727	16,304
Weighted no.	3.10×10^7	2.87×10^7	3.42×10^7	3.35×10^7	3.40×10^7
Age, yr	41.4±0.48	42.2±0.50	43.5±0.50	44.7±0.33	45.3±0.24
Male sex, %	49.0 (0.5)	48.7 (0.6)	48.7 (0.7)	49.2 (0.4)	49.4 (0.4)
BMI, kg/m ²	23.1±0.06	23.4±0.07	23.6±0.08	23.6±0.05	23.7±0.04
WC, cm	80.0±0.20	80.6±0.22	80.6±0.23	81.2±0.19	81.1±0.13
SBP, mm Hg	124.4±0.42	121.6±0.46	117.7±0.44	115.3±0.32	117.4±0.22
Hemoglobin, g/dL	14.1±0.03	13.7±0.03	14.0±0.03	14.0±0.03	14.2±0.02
AST, IU/L	27.9±0.31	22.1±0.22	24.2±0.27	22.5±0.21	22.3±0.14
ALT, IU/L	28.4±0.42	20.4±0.34	22.9±0.45	22.6±0.32	22.1±0.25
Creatinine, mg/dL	0.9±0.004	1.0±0.004	1.0±0.004	0.9±0.005	0.8±0.002
FPG, mg/dL	99.9±0.64	96.3±0.44	93.5±0.40	96.2±0.33	96.5±0.23
HbA1c, % ^a	5.1±0.02	5.7±0.02	7.4±0.11	7.3±0.05	5.7±0.01
TC, mg/dL	185.9±0.78	186.0±0.73	182.6±0.77	185.7±0.58	188.2±0.42
Triglyceride, mg/dL	120.2±1.58	135.2±1.78	121.3±1.86	125.1±1.44	129.9±1.19
HDL-C, mg/dL	50.1±0.24	46.4±0.31	45.3±0.24	48.3±0.18	49.3±0.13
LDL-C, mg/dL	112.2±0.70	112.5±0.64	113.1±0.65	112.5±0.49	114.3±0.34
Diabetes mellitus, %	9.6 (0.5)	8.7 (0.4)	7.0 (0.4)	8.4 (0.3)	9.6 (0.3)
Hypertension, %	24.5 (0.7)	22.3 (0.8)	21.8 (0.8)	20.8 (0.5)	25.2 (0.5)
Current smoker, %	36.0 (0.6)	31.9 (0.7)	25.6 (0.8)	26.3 (0.4)	29.3 (0.5)
Lipid-lowering therapy, %	NA	NA	1.0 (0.1)	2.5 (0.1)	4.6 (0.2)
Antihypertensive therapy, %	7.0 (0.3)	6.9 (0.4)	10.6 (0.5)	13.3 (0.3)	14.9 (0.4)

Values are presented as mean ± standard error or percentage (standard error).

BMI, body mass index; WC, waist circumference; SBP, systolic blood pressure; AST, aspartate transferase; ALT, alanine transferase; FPG, fasting plasma glucose; HbA1c, glycosylated hemoglobin; TC, total cholesterol; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; NA, not assessed.

^aHbA1c levels were measured in adults aged ≥30 years in 1998 and 2000, in patients with diabetes mellitus from 2005 to 2010, and in subjects aged ≥10 years in 2011 and 2012.

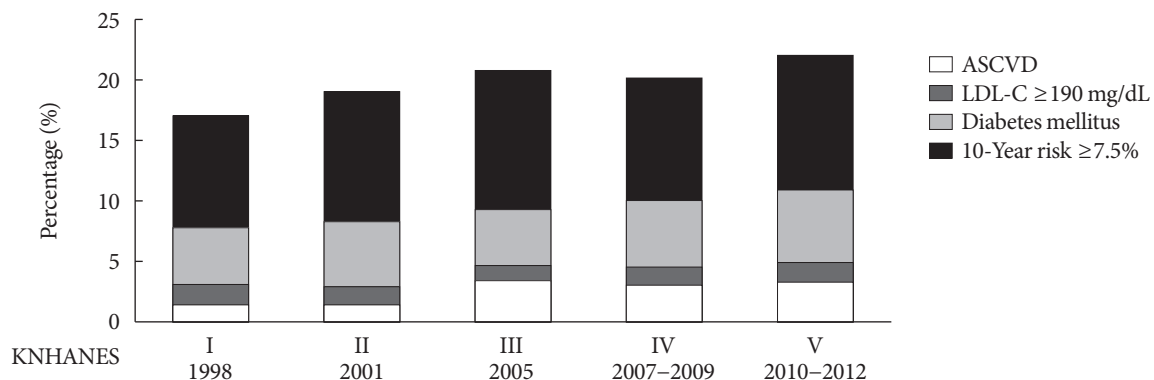


Fig. 1. Annual changes in the percentages of adults in the 1998 to 2012 Korean National Health and Nutrition Examination Surveys (KNHANESs) eligible for 4 statin benefit groups based on the 2013 American College of Cardiology/American Heart Association lipid guideline. ASCVD, atherosclerotic cardiovascular disease; LDL-C, low density lipoprotein cholesterol.

Table 2. Distribution of adults eligible for statin therapy in the 1998 to 2012 Korean National Health and Nutrition Examination Surveys

Variable	I 1998	II 2001	III 2005	IV 2007–2009	V 2010–2012
ASCVD ^a	1.4 (0.1)	1.6 (0.2)	3.5 (0.3)	3.1 (0.2)	3.3 (0.2)
LDL-C \geq 190 mg/dL	1.7 (0.2)	1.2 (0.2)	1.1 (0.2)	1.5 (0.2)	1.6 (0.1)
Diabetes mellitus	4.8 (0.3)	5.6 (0.3)	4.9 (0.3)	5.6 (0.2)	6.1 (0.2)
10-Year risk \geq 7.5%	9.1 (0.4)	10.6 (0.5)	11.3 (0.5)	10.0 (0.3)	11.0 (0.3)
Adults eligible for statin therapy	17.0 (0.7)	19.0 (0.7)	20.8 (0.7)	20.2 (0.4)	22.0 (0.5)
Adults receiving lipid-lowering therapy	NA	NA	1.0 (0.1)	2.5 (0.1)	4.6 (0.2)

Values are presented as percentage (standard error).

ASCVD, atherosclerotic cardiovascular disease; LDL-C, low density lipoprotein cholesterol; NA, not assessed.

^aASCVD was defined as previous history of angina, myocardial infarction, and stroke.

Table 3. Distribution of percentages of adults eligible for statin therapy according to sex and age groups in the 1998 to 2012 Korean National Health and Nutrition Examination Surveys

Age, yr	Men					Women				
	I 1998	II 2001	III 2005	IV 2007–2009	V 2010–2012	I 1998	II 2001	III 2005	IV 2007–2009	V 2010–2012
20–29	0.7 (0.3)	0.9 (0.5)	0.0	0.8 (0.3)	0.6 (0.3)	1.5 (0.5)	0.5 (0.3)	0.1 (0.1)	0.7 (0.3)	0.5 (0.3)
30–39	1.9 (0.5)	1.1 (0.5)	0.8 (0.4)	1.4 (0.3)	2.4 (0.5)	0.5 (0.2)	1.1 (0.5)	0.8 (0.4)	1.0 (0.3)	1.3 (0.4)
40–49	19.4 (1.8)	23.9 (2.0)	21.4 (2.0)	17.3 (1.2)	17.0 (1.2)	6.6 (1.0)	5.6 (0.9)	7.2 (1.3)	6.5 (0.6)	7.7 (0.8)
50–59	56.5 (2.4)	56.2 (3.2)	59.3 (2.7)	47.2 (1.7)	50.0 (1.6)	19.9 (1.8)	18.9 (2.3)	20.2 (2.2)	16.3 (1.1)	16.5 (1.0)
60–69	79.7 (2.2)	92.9 (1.5)	91.1 (1.6)	86.1 (1.4)	89.1 (1.0)	53.8 (2.6)	56.5 (3.0)	53.3 (2.7)	49.7 (1.6)	49.7 (1.5)
70–79 ^a	60.1 (4.3)	79.2 (3.9)	74.3 (4.5)	70.8 (1.9)	72.4 (1.9)	65.9 (3.3)	66.9 (3.7)	73.0 (3.3)	67.9 (1.8)	64.9 (1.8)
70–75	82.3 (4.5)	95.3 (2.5)	94.6 (2.5)	91.2 (1.3)	93.9 (1.2)	88.9 (2.4)	95.6 (1.8)	96.1 (1.6)	93.9 (1.0)	93.8 (0.9)
76–79	3.4 (2.3)	19.2 (7.8)	2.7 (2.7)	16.3 (3.1)	19.1 (2.8)	9.5 (4.1)	5.5 (3.0)	14.4 (3.9)	18.2 (2.6)	12.4 (2.0)
\geq 80	13.6 (8.8)	6.1 (4.8)	5.7 (4.0)	16.8 (3.5)	20.1 (5.0)	10.8 (4.6)	3.8 (2.2)	20.4 (6.2)	11.6 (2.6)	17.4 (3.0)
Percentage of adults aged \geq 20 years eligible for statin therapy, %	20.7 (0.9)	24.3 (1.1)	25.8 (1.1)	25.0 (1.3)	27.7 (0.7)	13.5 (0.7)	13.9 (0.8)	16.1 (0.8)	15.5 (0.5)	16.4 (0.5)

Values are presented as percentage (standard error).

^aThe 70- to 79-year-old group was divided into two groups, 70 to 75 and 76 to 79 years, to assess the percentages of people classified into the statin benefit group before and after the age of 75 years because the third and fourth criteria of the 2013 American College of Cardiology/American Heart Association guideline limits age to 40 to 75 years.

people with LDL-C \geq 190 mg/dL changed little (1.1% to 1.7%) over the survey period ($P=0.922$). However, the percentages of patients taking lipid-lowering therapy increased from 1.0% in KNHANES III to 2.5% and 4.6% in KNHANES IV and V, respectively ($P=0.015$). The percentages of participants with LDL-C \geq 190 mg/dL combined with those taking lipid-lowering therapy increased from 2.1% in KNHANES III to 4.0% and 6.2% in KNHANES IV and V, respectively ($P=0.027$; the use of lipid-lowering agents was not assessed in KNHANES I and II). (3)

The prevalence of diabetes mellitus in people aged 40 to 75 years also increased from 4.8% in KNHANES I to 5.6% in KNHANES IV and 6.1% in KNHANES V ($P=0.139$). (4) The fourth group (individuals with an estimated 10-year ASCVD risk \geq 7.5%, 40 to 75 years of age, with an LDL-C level of 70 to 189 mg/dL, and without ASCVD and diabetes) represented the highest percentage among the four statin benefit groups: 9.1% in KNHANES I and 11.0% in KNHANES V ($P=0.307$). The percentages in each year are also shown in Supplementary Table 2.

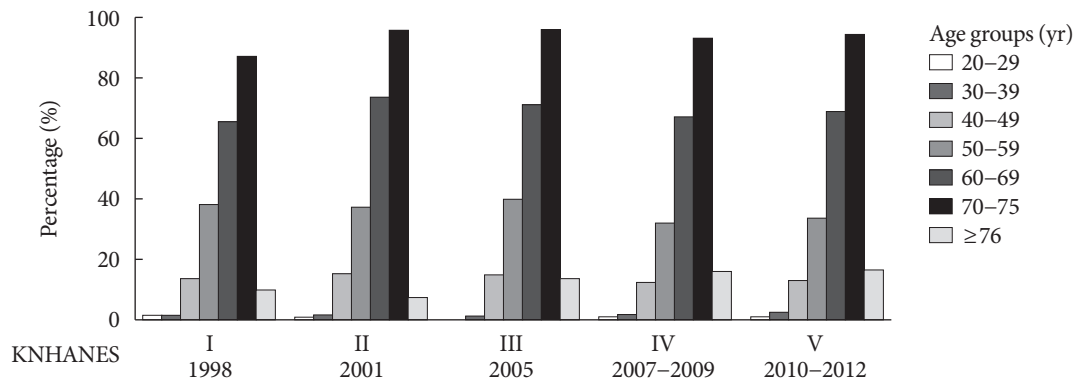


Fig. 2. Age-specific distributions of adults in the 1998 to 2012 Korean National Health and Nutrition Examination Surveys (KNHANESs) eligible for statin treatment based on the 2013 American College of Cardiology/American Heart Association lipid guideline.

Distribution of adults eligible for statin therapy according to sex and age groups

We investigated the distribution of adults eligible for statin therapy according to sex and age (Table 3). Among both men and women, the percentages of adults in the statin benefit groups increased over the 15 years: in men, from 20.7% in KNHANES I to 27.7% in KNHANES V, and in women, from 13.5% in KNHANES I to 16.4% in KNHANES V.

About half of the 50- to 59-year-old age group of men and the 60- to 69-year-old age group of women belonged to the statin benefit groups, and these percentages increased further in the older age groups. In particular, >90% of both men and women aged 70 to 75 years, except in KNHANES I, were found to be eligible for statin therapy (Fig. 2). In adults aged >75 years, the percentage of people eligible for statin treatment declined abruptly because the third and fourth statin benefit groups were limited to those aged 40 to 75 years. The sex- and age-specific distributions in each year are also shown in Supplementary Table 3.

Using the data from KNHANES V, we calculated the 10-year ASCVD risks using the Pooled Cohort Equations in all age groups. Of adults aged 70 years or older, 99.0% had a 10-year ASCVD risk $\geq 7.5\%$ and all adults aged 80 years or older had a risk of $\geq 10.0\%$ (Supplementary Table 4).

DISCUSSION

In these national-scale epidemiological studies, the percentages of Korean adults classified into statin benefit groups based on the 2013 ACC/AHA cholesterol guideline increased from 17.0% in KNHANES I (1998) to 22.0% in KNHANES V (2010

to 2012). This indicates that the numbers of Korean adults eligible for statin therapy have increased from around 6.8 million to around 8.8 million over the past 15 years. Similarly, the increasing trend of statin use can be found in United States. According to National Health and Nutrition Examination Survey data, the percentage of adults aged 20 and over using statins increased from 6.9% to 17.0%, during 1999 to 2012 ($P < 0.001$) [12].

In this study, we found an increasing trend in the percentages of adults eligible for statin therapy for primary prevention. This trend is consistent with the increasing mortality and prevalence of ASCVD in Korea, which accounted for 19.1% of all deaths of Koreans in 2013 [4]. In particular, more than 50% of Korean men aged ≥ 50 years and >50% of Korean women aged ≥ 60 years were found to be eligible for statin therapy according to the 2013 ACC/AHA guideline (Table 3). Among adults aged 70 to 75 years, >90% are recommended to receive statin therapy according to the 10-year ASCVD risk criterion. Among the four statin benefit groups, the group with the highest percentage consisted of people with a 10-year ASCVD risk $\geq 7.5\%$ (Table 2).

In a retrospective cohort study, the median Pooled Cohort Equation score was 10.1 (interquartile range, 4.7 to 20.6) in an Asian ethnic group [13]. However, the actual event rate of ASCVD was 4.9%. Thus, the Pooled Cohort Equations appears to overestimate cardiovascular risk, particularly in Asian population.

We previously reported that the prevalence of hyper-LDL-cholesterolemia increased significantly from 12.1% in the 2007 KNHANES to 15.0% in the 2010 KNHANES when LDL-C ≥ 160 mg/dL was used as a conservative cutoff point [14]. In that study, the percentage of Korean adults taking lipid-lower-

ing agents among those with dyslipidemia was only 3.0% in 2007. It is therefore expected that application of the new cholesterol guideline would also increase in statin use in Korea.

There are several possible reasons for the increasing trend in the percentage of people in the high-risk group requiring statin treatment. First, the population has been aging rapidly in South Korea, which is now one of the fastest-aging countries in the world [15]. Second, the prevalence rates of obesity and metabolic syndrome have been increasing progressively in South Korea [8]. The current analysis shows that the mean age, BMI, and waist circumference have increased continuously in the Korean population, as shown in Table 1.

Considering that the average lifespan has lengthened and that the number of elderly patients with diabetes mellitus has been increasing, it may be counterproductive to limit the age to 40 to 75 years in the third and fourth criteria of the statin benefit groups. Although >90% of seniors belonged to the statin benefit group among those aged 70 to 75 years, the percentage decreased markedly to about 15% among people aged 76 to 79 years. Almost half of the 24 million people with diabetes mellitus are aged >60 years in the USA. In the next 2 decades, their numbers are expected to double and their direct medical costs are expected to triple [16]. Similarly, one-quarter of elderly Koreans aged ≥ 60 years have diabetes mellitus [17,18]. Thus, the number of elderly people with diabetes mellitus is likely to increase further, and the macrovascular complications of this disease will become an important public health issue in many developed and developing countries. Because there is no noticeable difference in the ASCVD risk between people aged 70 to 75 years and those aged ≥ 76 years, it would be inappropriate to set the age limit to 75 years or younger.

In the current study, when the Pooled Cohort Equations were applied to adults without an age limits, nearly all men and women aged >70 years had an estimated 10-year ASCVD risk $\geq 7.5\%$, and all men and women aged >80 years had a 10-year ASCVD risk $\geq 10\%$. These results demonstrate the strong effect of age on the assessment of 10-year ASCVD risk. Thus, the calculated ASCVD risk by the Pooled Cohort Equations seems to be overestimated in the elderly.

We note that older people have less capacity to gain an increase in life expectancy with statin therapy. It took more than 10 years to confirm the beneficial effects of statins on cardiovascular or all-cause mortality in many studies [19-21]. Statin treatment for 3.2 years in high-risk elderly people aged 70 to 82 years provided long-term protection against cardiovascular

events and cardiovascular deaths [22]. However, it did not increase life expectancy, which may reflect the contribution of other causes of mortality. Thus, commencing statin treatment at an earlier age may produce maximum clinical benefits [23]. This may provide one reason for including an age limitation in the definition of statin benefit groups in the new ACC/AHA guideline.

The Pooled Cohort Equations for estimating ASCVD risk were produced from extensive data from several large, racially and geographically varied cohort studies [24-28], including whites and African-Americans, but not many Asians. Furthermore, the new ACC/AHA guideline focuses on ASCVD risk reduction rather than an LDL-C target for determining the prescription of high- and moderate-intensity statin. However, the effects of statin in lowering LDL-C level or reducing coronary heart disease risk may differ between Asians and Westerners. Previous studies have suggested that Asians need a lower dosage or lower intensity of statin compared with Westerners [29,30]. There are few randomized controlled trials of statin treatment in Asian populations [30,31] and Asian-specific risk prediction models of ASCVD have not been published. Further studies regarding ethnic differences and Asian-specific guidelines for cholesterol treatment are needed.

This study has some limitations. First, ASCVD events were determined from questionnaires without objective confirmatory data. However, although clinical ASCVD was not documented by hospital charts, the trained researchers asked the study population in details on event time and reviewed their medication during the face-to-face interviews. Second, the definition of clinical ASCVD was limited to angina, myocardial infarction, and stroke. Other diseases such as transient ischemic attack or peripheral arterial disease were not identified. Third, the measurement methods for several variants have been changed during each period of the investigation, which can be a limitation for analysis of annual changes. But quality controls were performed in every survey at central laboratory to produce standardized values. Moreover, LDL-C level was not measured directly before 2009. We used the calculated LDL-C values obtained using Friedewald's equation, which assumes a triglyceride concentration ≤ 400 mg/dL. Nevertheless, there was a strong correlation between the direct and calculated LDL-C values ($r^2=0.921$, $P<0.001$) using data from KNHANES 2010 to 2012.

Notwithstanding these limitations, the KNHANESs provide national data obtained using a stratified, multistage, probabili-

ty sampling design and give representative estimates of the Korean population covering all adult ages. Each year's biochemical testing was conducted at a central lab and its quality control was managed by the Korean government.

In conclusion, the percentage of Korean adults eligible for statin therapy increased from 17.0% to 22.0% over the past 15 years when classified according to the 2013 ACC/AHA cholesterol guideline. According to this guideline, most old people are classified into the statin benefit group. We believe that Korea is representative of countries experiencing rapid changes in nutrition from a low-fat and low-calorie diet to a high-fat and high-calorie diet. There have also been dramatic changes in behavioral aspects in Korea; for example, low physical activity levels, use of transportation, and easy access to medical care. Given that similar sociobehavioral changes and rapid aging of the population have been found in many Asian countries, more people living in this region will belong to statin benefit groups in the near future.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

ACKNOWLEDGMENTS

This study was supported by Seoul National University Bundang Hospital and Korean Society of Lipidology and Atherosclerosis.

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