ORIGINAL ARTICLE

Application of New Cholesterol Guidelines to a Population-Based Sample

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ABSTRACT

BACKGROUND

The 2013 guidelines of the American College of Cardiology and the American Heart Association (ACC–AHA) for the treatment of cholesterol expand the indications for statin therapy for the prevention of cardiovascular disease.

METHODS

Using data from the National Health and Nutrition Examination Surveys of 2005 to 2010, we estimated the number, and summarized the risk-factor profile, of persons for whom statin therapy would be recommended (i.e., eligible persons) under the new ACC–AHA guidelines, as compared with the guidelines of the Third Adult Treatment Panel (ATP III) of the National Cholesterol Education Program, and extrapolated the results to a population of 115.4 million U.S. adults between the ages of 40 and 75 years.

RESULTS

As compared with the ATP-III guidelines, the new guidelines would increase the number of U.S. adults receiving or eligible for statin therapy from 43.2 million (37.5%) to 56.0 million (48.6%). Most of this increase in numbers (10.4 million of 12.8 million) would occur among adults without cardiovascular disease. Among adults between the ages of 60 and 75 years without cardiovascular disease who are not receiving statin therapy, the percentage who would be eligible for such therapy would increase from 30.4% to 87.4% among men and from 21.2% to 53.6% among women. This effect would be driven largely by an increased number of adults who would be classified solely on the basis of their 10-year risk of a cardiovascular event. Those who would be newly eligible for statin therapy include more men than women and persons with a higher blood pressure but a markedly lower level of low-density lipoprotein cholesterol. As compared with the ATP-III guidelines, the new guidelines would recommend statin therapy for more adults who would be expected to have future cardiovascular events (higher sensitivity) but would also include many adults who would not have future events (lower specificity).

CONCLUSIONS

The new ACC–AHA guidelines for the management of cholesterol would increase the number of adults who would be eligible for statin therapy by 12.8 million, with the increase seen mostly among older adults without cardiovascular disease. (Funded by the Duke Clinical Research Institute and others.)

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This article was published on March 19, 2014, at NEJM.org.

DOI: 10.1056/NEJMoa1315665

Until recently, the guidelines of the Third Adult Treatment Panel (ATP III) of the National Cholesterol Education Program were the recommended guidelines to aid in the treatment of hyperlipidemia in the United States.[1,2] The ATP-III guidelines identified patients with established cardiovascular disease or diabetes and low-density lipoprotein (LDL) cholesterol levels of 100 mg per deciliter (2.59 mmol per liter) or higher as candidates for statin therapy. In addition, the ATP-III guidelines recommended the use of statin therapy for primary prevention in patients on the basis of a combined assessment of LDL cholesterol level and the 10-year risk of coronary heart disease as calculated with the use of the Framingham risk calculator.[1,2]

The 2013 guidelines of the American College of Cardiology and the American Heart Association (ACC–AHA) for the management of cholesterol, which were released in November, substantially modify the previous recommendations.[3] For patients with known cardiovascular disease, the new guidelines expand the treatment recommendation to all adults, regardless of the LDL cholesterol level. For primary prevention, whereas both sets of guidelines recommend statin therapy for patients with an LDL cholesterol level of 190 mg per deciliter (4.91 mmol per liter) or higher, the new guidelines also recommend statin therapy in all persons who have an LDL cholesterol level of 70 mg per deciliter (1.81 mmol per liter) or higher and who also have either diabetes or a 10-year risk of cardiovascular disease of 7.5% or more, as estimated on the basis of new pooled-cohort equations.[4]

Using data from the National Health and Nutrition Examination Surveys (NHANES), we sought to estimate the number of persons in the United States for whom statin therapy would be recommended on the basis of the new guidelines, as compared with the ATP-III guidelines.

METHODS

STUDY POPULATION

In this study, we used fasting sample data collected between 2005 and 2010 as part of the NHANES, a survey designed to provide a representative sample of the civilian noninstitutionalized U.S. population.[5] Of the 3909 NHANES participants between the ages of 40 and 75 years for whom fasting data were available, we excluded 100 participants who had triglyceride levels of more than 400 mg per deciliter (4.52 mmol per liter) and another 36 participants who had missing data with respect to LDL cholesterol. These exclusions resulted in a study sample of 3773 participants who had valid data regarding LDL cholesterol, as calculated with the use of Friedewald's equation.[6] We assessed the eligibility for statin therapy using the 2004-updated ATP-III criteria and also using the 2013 ACC–AHA guidelines (for details, see the Supplementary Appendix, available with the full text of this article at NEJM.org).

STATISTICAL ANALYSIS

We began by determining the proportion of the 3773 participants in the NHANES sample for whom statin therapy would be recommended (i.e., eligible persons) on the basis of the two sets of guidelines. We then used domain analysis to extrapolate the results in our sample of 3773 participants to the population of 115.4 million U.S. adults between the ages of 40 and 75 years who have triglyceride levels below 400 mg per deciliter.[7] All the analyses took into account the complex, multistage probability-sampling design of NHANES and used NHANES-supplied sample weights for participants in the subsample for whom fasting data were available, which account for oversampling of certain segments of the population and nonresponse rates.[7] Missing binary characteristics were assumed to have a "no" answer for this calculation.

We estimated the total number of persons in the United States who would be eligible for statin therapy on the basis of the ATP-III guidelines and the new ACC–AHA guidelines, further stratifying the persons according to sex and the indication for statin therapy. Risk-factor profiles were summarized for persons in each group and for those who were newly eligible for statin therapy. To compare risk-factor profiles of persons without cardiovascular disease who would be eligible for statin therapy for primary prevention on the basis of the ATP-III guidelines, as compared with the new ACC–AHA guidelines, we performed a discordance analysis focusing on persons who would be eligible for statin therapy according to one guideline but not the other. Prespecified age groups of "younger" adults (ages 40 to 59) and "older" adults (ages 60 to 75) were analyzed separately.

Assuming that the mean estimates of the

10-year or 30-year risk of cardiovascular events approximate the actual rates of those events, we used the Framingham risk calculators of D'Agostino et al.[8] and Pencina et al.[9] to estimate the expected rates of cardiovascular events among adults without cardiovascular disease according to the therapy recommended by each guideline. We used the prospective approach of Pencina et al.[10] to estimate the event and nonevent net reclassification indexes, corresponding to the increases in sensitivity and specificity, respectively, when moving from the ATP-III guidelines to the new guidelines (as described in the Supplementary Appendix). To quantify the effect of the risk function used in each guideline, we compared the new ACC–AHA pooled-cohort equations with the ATP-III Framingham risk calculator to determine the proportions of adults who had a 10-year risk of cardiovascular disease of 7.5% or more among those currently without either cardiovascular disease or diabetes who had an LDL cholesterol level of less than 190 mg per deciliter and were not receiving lipid-lowering therapy. All analyses were performed with the use of SAS software, version 9.3.

RESULTS

STUDY SAMPLE

The clinical characteristics of the 3773 participants in the NHANES study sample are provided in Table 1. Of these 3773 participants, 1583 (42.0%) were receiving or would be eligible for statin therapy on the basis of the ATP-III guidelines, as compared with 2135 participants (56.6%) on the basis of the new ACC–AHA guidelines. Under the new guidelines, 599 participants (15.9%) would be newly eligible for statin therapy; this number is higher than the net difference between the two guidelines (552 participants) because some participants who were previously eligible for statin therapy under the ATP-III guidelines would no longer be eligible under the ACC–AHA guidelines.

EXTRAPOLATION OF RESULTS TO U.S. POPULATION

Table 2 shows the extrapolation of NHANES results to the 115.4 million U.S. adults between the ages of 40 and 75 represented in this analysis on the basis of the sample weights in NHANES. An estimated 43.2 million adults (37.5% of the U.S. population; 95% confidence interval [CI], 35.3 to 39.7) would be receiving or be eligible to receive statin therapy, according to the 2004-updated ATP-III guidelines. In contrast, the estimated number of potential statin users would be expanded to 56.0 million (48.6%; 95% CI, 46.3 to 51.0), according to the new ACC–AHA guidelines. An estimated 14.4 million adults would be newly eligible for statin therapy according to the new guidelines, as compared with the ATP-III guidelines. This number would be higher than the net increase of 12.8 million adults, since 1.6 million adults who were previously eligible for statin therapy on the basis of the ATP-III guidelines would no longer be eligible. The median age of adults who would be newly eligible for statin therapy under the new ACC–AHA guidelines is 63.4 years, and 61.7% would be men. The median LDL cholesterol level for these adults is 105.2 mg per deciliter (2.7 mmol per liter).

Figure 1 shows the estimated numbers of adults who would be eligible for statin therapy according to each of the individual criteria in the ATP-III guidelines and the new ACC–AHA guidelines. Among the 115.4 million U.S. adults between the ages of 40 to 75 years who are represented in this analysis, an estimated 25.2 million (21.9%; 95% CI, 19.9 to 23.9) are taking lipid-lowering medication (19.4 million for primary prevention and 5.8 million for secondary prevention) according to the self-report of the NHANES participants. On the basis of the ATP-III guidelines, lipid-lowering therapy would be recommended for an estimated 18.0 million additional adults who are not currently receiving such therapy. In contrast, the new ACC–AHA guidelines would recommend statin therapy for an estimated 30.8 million adults in addition to the 25.2 million already receiving therapy.

The new guidelines increase the estimated number of adults who would be eligible for statin therapy across all categories. The largest increase would occur among adults who have an indication for primary prevention on the basis of their 10-year risk of cardiovascular disease: 15.1 million adults who would be eligible according to the new ACC–AHA guidelines, as compared with 6.9 million who would be eligible according to the ATP-III guidelines (Fig. 1).

Furthermore, 2.4 million adults with prevalent cardiovascular disease and LDL cholesterol levels of less than 100 mg per deciliter who would not be eligible for statin therapy according to the

Table 1. Comparison of the Cardiovascular Risk Profile for U.S. Adults between the Ages of 40 and 75 Years in the NHANES Sample According to Two Guidelines.*

Variable	All Adults (N=3773)	Adults Eligible for Statin Therapy		
		ATP-III Guidelines (N=1583)	ACC–AHA 2013 Guidelines (N=2135)	Newly Eligible Only (N=599)†
Male sex — no. (%)	1854 (49.1)	857 (54.1)	1203 (56.3)	373 (62.3)
Median age (IQR) — yr	56.0 (41.0–73.0)	61.0 (44.0–74.0)	62.0 (45.0–74.0)	65.0 (46.0–74.0)
Cardiovascular disease — no. (%)‡	475 (12.6)	379 (23.9)	475 (22.2)	96 (16.0)
Cholesterol				
Median total (IQR) — mg/dl	199.0 (138.0–272.0)	202.0 (139.0–290.0)	197.0 (137.0–280.0)	186.0 (131.0–250.0)
Median low-density lipoprotein (IQR) — mg/dl	118.0 (64.0–182.0)	122.0 (64.0–198.0)	115.0 (65.0–193.0)	104.0 (70.0–157.0)
Low-density lipoprotein ≥190 mg/dl — no. (%)	129 (3.4)	129 (8.1)	129 (6.0)	0
Median high-density lipoprotein (IQR) — mg/dl	52.0 (33.0–86.0)	49.0 (33.0–78.0)	50.0 (33.0–82.0)	52.0 (31.0–86.0)
Hypertension — no./total no. (%)	1706/3706 (46.0)	1026/1572 (65.3)	1350/2122 (63.6)	345/596 (57.9)
Median systolic blood pressure (IQR) — mm Hg	122.7 (100.0–160.0)	128.0 (102.7–165.3)	128.7 (103.3–166.0)	129.3 (105.3–167.3)
Diabetes — no. (%)	779 (20.6)	612 (38.7)	748 (35.0)	136 (22.7)
Obesity — no./total no. (%)§	1509/3720 (40.6)	758/1559 (48.6)	977/2102 (46.5)	237/589 (40.2)
Current smoking — no./total no. (%)	778/3770 (20.6)	364/1580 (23.0)	496/2133 (23.3)	149/599 (24.9)
Receiving lipid therapy — no. (%)	883 (23.4)	883 (55.8)	883 (41.4)	0

* To convert the values for cholesterol to millimoles per liter, multiply by 0.02586. ACC–AHA denotes American College of Cardiology and American Heart Association, ATP III Third Adult Treatment Panel of the National Cholesterol Education Program, IQR interquartile range, and NHANES National Health and Nutrition Examination Surveys.
† The number of participants who would be newly eligible for statin therapy according to the new ACC–AHA guidelines, as compared with the ATP-III guidelines, is greater than the net difference (552) because some participants who would have been eligible for statin therapy under the ATP-III guidelines would no longer be eligible under the ACC–AHA guidelines.
‡ Cardiovascular disease includes myocardial infarction, angina, and stroke.
§ Obesity was defined as a body-mass index (the weight in kilograms divided by the square of the height in meters) of 30 or more.

ATP-III guidelines would be eligible under the new ACC–AHA guidelines. Finally, the number of adults with diabetes who are eligible for statin therapy would increase from 4.5 million to 6.7 million as a result of the lowering of the threshold for LDL cholesterol treatment from 100 to 70 mg per deciliter. The net increase in the eligibility of 12.8 million adults includes 10.4 million adults in whom statin therapy would be indicated for primary prevention. The increase affects both sexes but is numerically larger among men (Fig. S1 in the Supplementary Appendix).

Given the differences in the guideline recommendations for primary prevention, we specifically examined the percentages of adults without cardiovascular disease who would be eligible for statin therapy according to the two guidelines (Fig. 2). Among adults between the ages of 40 and 59 years, the proportions of those who would be eligible for treatment are similar (27.0% according to the ATP-III guidelines and 29.7% according to the ACC–AHA guidelines). However, we found a substantial difference in eligibility between the two sets of guidelines among older adults between the ages of 60 and 75 years. In this age group, 47.8% of adults would be receiving or be eligible for statin therapy according to the ATP-III guidelines, as compared with 77.3% according to the ACC–AHA guidelines.

In addition, the new guidelines state that it is "reasonable to offer treatment with a moderate intensity statin" to adults without cardiovascular disease and diabetes who have a 10-year risk of cardiovascular disease of 5 to 7.5%.[3] On the basis of the 5% threshold, the estimated percentages of adults who would be eligible for statin therapy would increase to 38.4% among

Table 2. Extrapolation of the Cardiovascular Risk Profile from the NHANES Sample to All U.S. Adults between the Ages of 40 and 75 Years with Respect to Eligibility for Statin Therapy, According to Two Guidelines.*

Variable	All Adults (N=115.4 million)	Adults Eligible for Statin Therapy		
		ATP-III Guidelines (N=43.2 million)	ACC–AHA 2013 Guidelines (N=56.0 million)	Newly Eligible Only (N=14.4 million)
Male sex — no. in millions (%)	55.0 (47.7)	23.3 (54.0)	31.4 (56.0)	8.9 (61.7)
Median age (IQR) — yr	52.5 (40.4–71.5)	57.5 (42.9–72.9)	59.4 (43.0–73.2)	63.4 (44.2–73.5)
Cardiovascular disease — no. in millions (%)	11.8 (10.3)	9.4 (21.7)	11.8 (21.1)	2.4 (17.0)
Cholesterol				
Median total (IQR) — mg/dl	199.0 (139.2–272.1)	200.2 (138.5–292.5)	195.6 (137.1–284.7)	186.6 (133.5–250.0)
Median low-density lipoprotein (IQR) — mg/dl	118.4 (65.4–182.4)	120.4 (62.8–199.3)	114.0 (63.8–194.7)	105.2 (68.3–156.2)
Low-density lipoprotein ≥190 mg/dl — no. in millions (%)	4.1 (3.6)	4.1 (9.5)	4.1 (7.3)	0
Median high-density lipoprotein (IQR) — mg/dl	52.2 (33.8–86.7)	48.4 (32.7–76.9)	49.2 (32.4–79.8)	51.6 (31.3–85.5)
Hypertension — no. in millions/total no. in millions (%)	45.4/113.6 (40.0)	25.6/42.9 (59.7)	32.9/55.7 (59.1)	7.9/14.4 (54.9)
Median systolic blood pressure (IQR) — mm Hg	120.3 (99.1–154.6)	125.1 (101.6–160.4)	125.9 (102.2–161.0)	127.2 (105.1–161.8)
Diabetes — no. in millions (%)	17.1 (14.8)	13.3 (30.8)	16.4 (29.3)	3.1 (21.6)
Obesity — no. in millions/total no. in millions (%)	43.4/113.8 (38.1)	20.3/42.6 (47.7)	25.6/55.2 (46.4)	5.9/14.2 (41.5)
Current smoking — no. in millions/ total no. in millions (%)	23.1/115.3 (20.0)	10.6/43.1 (24.6)	13.7/56.0 (24.5)	3.8/14.4 (26.4)
Receiving lipid therapy — no. in millions (%)	25.2 (21.9)	25.2 (58.4)	25.2 (45.0)	0

* Percentages were calculated before rounding of the numerators and denominators.

younger adults and 87.4% among older adults. Furthermore, among older women without cardiovascular disease who are not receiving lipid-lowering therapy, the proportion that would be eligible for statin therapy would increase from 21.2% according to the ATP-III guidelines to 53.6% according to the ACC–AHA guidelines; on the basis of the 5% risk threshold for treatment, the latter proportion would increase to 72.8%. Among older men without cardiovascular disease who are not receiving lipid-lowering therapy, the proportion that would be eligible for statin therapy would increase from 30.4% according to the ATP-III guidelines to 87.4% according to the ACC–AHA guidelines; on the basis of the 5% risk threshold, the latter proportion would increase to 95.0%. Overall, of the additional 10.4 million adults who would be eligible for statin therapy in primary prevention, 8.3 million would be between the ages of 60 and 75 years.

DISCORDANCE BETWEEN THE TWO SETS OF GUIDELINES

Table 3 presents the numbers of adults without extant cardiovascular disease for whom the recommendations are discordant between the two sets of guidelines. Among adults between the ages of 40 and 59 years, few had discordant recommendations for statin therapy between the two guidelines: 1.8% were reclassified "downward" (i.e., statin therapy was recommended on the basis of the ATP-III guidelines but not the new guidelines), and 4.5% were reclassified "upward" (i.e., statin therapy was recommended on the basis of the new guidelines but not the ATP-III guidelines). In contrast, among adults between the ages of 60 and 75 years, reclassification was substantial, with almost all of it due to upward reclassification (30.3%, as compared with 0.8% reclassified downward). As compared with adults who were reclassified downward in both age

groups, those who were reclassified upward were older, included more men, had a higher systolic blood pressure, had a significantly lower level of LDL cholesterol, and had a higher rate of obesity.

In the two age groups, the 10-year risk of cardiovascular disease, as estimated with the use of the function of D'Agostino et al.,[8] was higher among adults who would be reclassified as being eligible for statin therapy than among those who would no longer be eligible. This finding suggests that with the ACC–AHA guidelines, as compared with the ATP-III guidelines, an in-

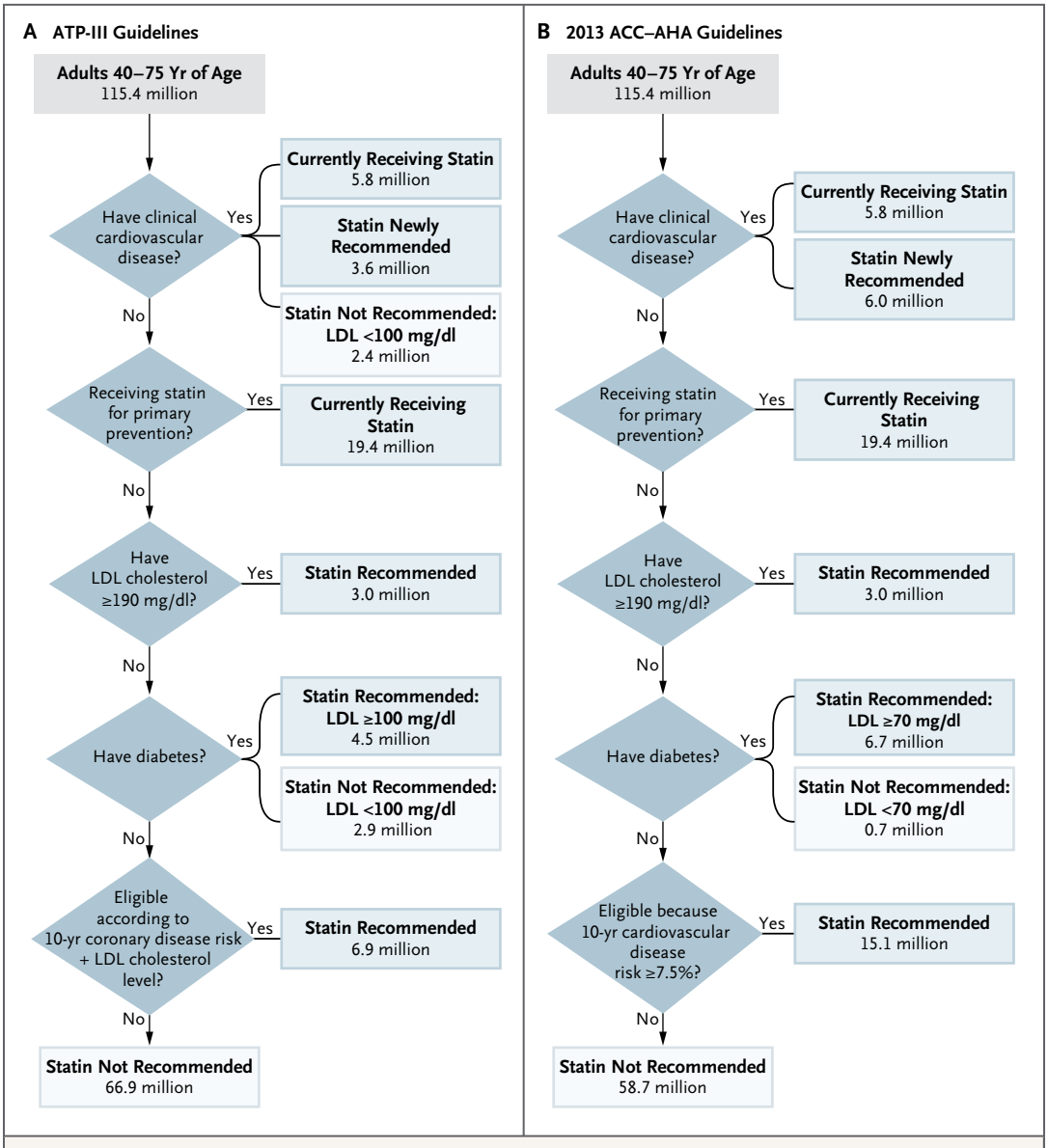

Figure 1. Extrapolation of the NHANES Sample to All U.S. Adults, According to Two Guidelines for the Management of Cholesterol.

Shown are the criteria used to identify adults who would be eligible for statin therapy, indicating the breakdown of statin use and statin recommendations for the 115.4 million adults between the ages of 40 and 75 years on the basis of the guidelines of the Third Adult Treatment Panel (ATP III) of the National Cholesterol Education Program and the 2013 guidelines of the American College of Cardiology and the American Heart Association (ACC–AHA). The ATP-III guidelines use a combination of an assessment of the 10-year risk of coronary disease and the low-density lipoprotein (LDL) level to determine eligibility. To convert the values for cholesterol to millimoles per liter, multiply by 0.02586.

creased number of adults who would be expected to have cardiovascular events would be newly eligible for statin therapy (absolute increase in sensitivity, 16.8 percentage points) but also that an increased number of adults who are not expected to have events would also be eligible (absolute decrease in specificity, 9.2% percentage points).

To determine to what degree the above-mentioned changes can be attributed to the new pooled-cohort equations, we used the ATP-III function (the Framingham risk calculator) to recalculate the 10-year risk. The percentages of adults who would be eligible for statin therapy solely on the basis of a 10-year risk of more than 7.5% were similar with the use of the Framingham risk calculator and the new pooled-cohort equations (19.7% and 24.0%, respectively). These model-based differences were especially small among younger adults (12.4% and 8.9%, respectively) but larger among older adults (39.1% vs. 66.4%).

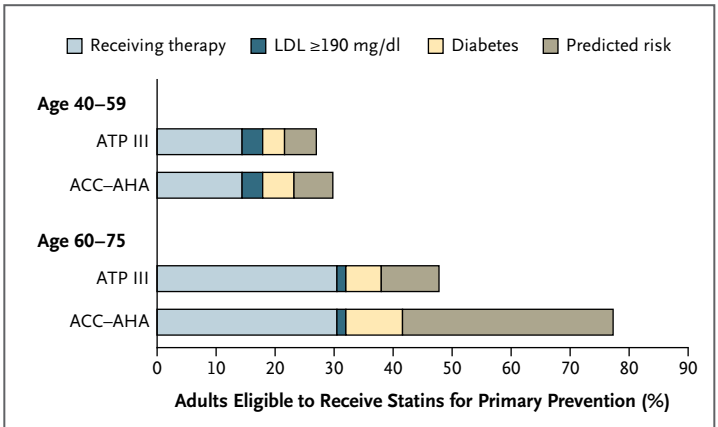

Figure 2. Percent of U.S. Adults Who Would Be Eligible for Statin Therapy for Primary Prevention, According to Set of Guidelines and Age Group.

Shown are the proportions of adults in two age groups (40 to 59 years and 60 to 75 years) without cardiovascular disease who would be eligible for statin therapy for primary prevention of cardiovascular disease under the ATP-III guidelines and the 2013 ACC–AHA guidelines, according to the indication for therapy (elevated LDL cholesterol level, the presence of diabetes, or the predicted risk of a cardiovascular event according to the set of guidelines).

DISCUSSION

The new ACC–AHA cholesterol guidelines differ substantially from the previous ATP-III guidelines, particularly with respect to primary prevention of cardiovascular disease. The ATP-III guidelines place more emphasis on levels of LDL cholesterol to select patients for statin therapy, whereas the new guidelines base the recommendation solely on the 10-year predicted risk, as long as the LDL cholesterol level is 70 mg per deciliter or higher. Using NHANES data, we estimated the effects of these changes on the percentage and mix of the U.S. population for whom statin therapy would be recommended.

We estimate that under the new guidelines, 56.0 million Americans (48.6%) would be eligible for statin therapy, representing almost half of the 115.4 million adults between the ages of 40 and 75 years who have a triglyceride level of less than 400 mg per deciliter. This population would represent a net increase of 12.8 million potential new statin users (an increase of 11.1 percentage points) over the number who would be eligible according to the ATP-III guidelines. The increased number of adults who would be newly eligible for statin therapy suggests higher treatment rates among those expected to have future cardiovascular events (increased sensitivity) but also an increased number of adults receiving therapy who are not expected to have events (decreased specificity).

These new treatment recommendations have a larger effect in the older age group (60 to 75 years) than in the younger age group (40 to 59 years). Although up to 30% of adults in the younger age group without cardiovascular disease would be eligible for statin therapy for primary prevention, more than 77% of those in the older age group would be eligible. This difference might be partially explained by the addition of stroke to coronary heart disease as a target for prevention in the new pooled-cohort equations.[4] Since the prevalence of cardiovascular disease rises markedly with age,[11] the large proportions of older adults who would be eligible for statin therapy may be justifiable. Further research is required to determine whether more aggressive preventive strategies are needed for younger adults.

The new guideline recommendations would also result in more men being newly eligible for statin therapy than women, although the overall percentages of the two sexes that would be eligible for therapy would remain similar. As compared with the ATP-III guidelines, the new guidelines would also expand the eligibility for statin therapy among adults with a higher blood pressure but substantially lower levels of LDL cholesterol.

We also attempted to estimate the likely effect of the full adoption of the new guidelines

on future rates of cardiovascular events. Assuming that the 10-year general cardiovascular risk estimates of D'Agostino et al., when applied to our NHANES sample, would accurately reflect future event rates for the U.S. population, we projected that there will be 11.4 million new cases of cardiovascular disease over the next 10 years among the 103.5 million adults between the ages of 40 and 75 years who do not currently have cardiovascular disease. Using these calculations, we estimated that 16.8% of these 11.4 million adults would be eligible for statin therapy accord-

Table 3. Extrapolation of Results from the NHANES Sample to All U.S. Adults between the Ages of 40 and 75 Years without a Diagnosis of Cardiovascular Disease, According to Concordant and Discordant Recommendations for Statin Use and Age Group.

Variable	Concordant Recommendations		Discordant Recommendations	
	Neither Recommend Statin Therapy	Both Recommend Statin Therapy	Recommended by ATP-III Guidelines but Not ACC–AHA Guidelines	Recommended by ACC–AHA Guidelines but Not ATP-III Guidelines
Age 40 to 59 yr				
NHANES sample — no.	1350	515	40	120
U.S. population estimate — no. in millions	51.4	18.9	1.4	3.4
Male sex (95% CI) — %	42.5 (39.5–45.5)	59.1 (53.4–64.8)	55.5 (40.5–70.6)	79.3 (68.8–89.7)
Mean age (95% CI) — yr	48.0 (47.6–48.4)	51.2 (50.6–51.7)	50.8 (48.6–53.1)	51.7 (50.1–53.3)
Mean low-density lipoprotein cholesterol (95% CI) — mg/dl	119.6 (117.6–121.7)	134.1 (129.2–139.0)	168.7 (165.2–172.1)	109.0 (104.1–113.9)
Hypertension (95% CI) — %	19.7 (17.1–22.4)	48.6 (42.8–54.4)	32.6 (15.4–49.8)	50.4 (41.5–59.3)
Mean systolic blood pressure (95% CI) — mm Hg	117.7 (116.7–118.7)	124.2 (122.7–125.7)	122.5 (117.6–127.4)	132.1 (129.0–135.3)
Diabetes (95% CI) — %	0.5 (0.1–0.9)	21.2 (16.7–25.6)	0	27.3 (19.2–35.4)
Obesity (95% CI) — %	29.7 (26.8–32.6)	49.6 (45.7–53.6)	36.1 (19.5–52.7)	46.4 (34.9–57.9)
Current smoking (95% CI) — %	16.2 (13.3–19.1)	30.4 (25.2–35.6)	56.3 (38.4–74.1)	47.8 (37.3–58.4)
Risk of cardiovascular event (95% CI) — %*				
At 10 yr	5.5 (5.2–5.7)	13.3 (12.4–14.4)	10.7 (9.8–11.7)	15.5 (14.3–16.7)
At 30 yr	25.0 (24.2–25.8)	43.5 (41.7–45.3)	42.1 (40.2–44.0)	47.1 (44.4–49.7)
Age 60 to 75 yr				
NHANES sample — no.	241	642	7	383
U.S. population estimate — no. in millions	6.2	13.3	0.2	8.6
Male sex (95% CI) — %	15.2 (9.5–21.0)	45.1 (40.4–49.9)	28.6 (0–69.7)	54.1 (46.7–61.4)
Mean age (95% CI) — yr	63.6 (63.0–64.2)	67.3 (66.8–67.8)	63.1 (60.4–65.7)	67.2 (66.6–67.8)
Mean low-density lipoprotein cholesterol (95% CI) — mg/dl	114.7 (109.4–120.1)	120.8 (116.9–124.7)	169.9 (161.9–177.9)	116.1 (112.2–120.0)
Hypertension (95% CI) — %	32.9 (25.8–40.1)	72.0 (66.2–77.8)	71.4 (32.9–100)	53.4 (46.2–60.5)
Mean systolic blood pressure (95% CI) — mm Hg	119.2 (116.3– 122.1)	133.0 (130.5–135.5)	117.6 (102.2–133.0)	129.7 (127.3–132.1)
Diabetes (95% CI) — %	4.9 (2.2–7.6)	23.5 (19.4–27.6)	0	8.5 (5.1–11.9)
Obesity (95% CI) — %	35.1 (27.2–43.0)	42.2 (37.7–46.8)	22.9 (0–59.5)	34.3 (28.9–39.7)
Current smoking (95% CI) — %	6.0 (1.3–10.6)	11.7 (8.9–14.5)	0	16.0 (10.3–21.8)
Risk of cardiovascular event at 10 yr (95% CI) — %*	8.3 (7.3–9.2)	24.4 (22.8–25.9)	9.9 (7.4–12.3)	18.0 (17.0–19.1)

* In determining the risk of a cardiovascular event, the 10-year risk was calculated according to the method of D'Agostino et al.,[7] and the 30-year risk was calculated according to the method of Pencina et al.[8] only for adults under the age of 60 years.

ing to the new guidelines but not according to the ATP-III guidelines, a difference of 1.9 million. If statin therapy then reduces the relative cardiovascular risk by 25%, as suggested in meta-analyses of statin use in primary prevention,[12] a total of approximately 475,000 future cardiovascular events would be prevented. More than 90% of this potential benefit would occur among older adults. We based this rough estimate of the benefit on several assumptions, including the applicability and accuracy of the 10-year estimate, full adoption of and adherence to the new guidelines, independence of the relative benefit of statin use from the levels of LDL cholesterol or absolute risk, and the applicability of the 25% risk reduction to the general U.S. population despite differences in the case mix of participants who were enrolled in the trials from which the percentage was derived.

Our study has some potential limitations. First, our results are based on data from 3773 NHANES participants extrapolated to 115.4 million U.S. adults and rely on the accuracy and representativeness of the NHANES data from 2005 through 2010 for the current U.S. population. Second, we could not accurately quantify the effects of the new and the old guidelines on patients who are currently receiving lipid-lowering therapy because we could not determine why lipid-lowering therapy had been initiated. Third, the estimate of the numbers of adults currently receiving statin therapy is based on the participant's declaration in the NHANES sample and therefore may be imprecise. Furthermore, we conservatively assumed that missing binary responses represent a "no" answer, which might have resulted in an underestimate of the rate of statin therapy and other characteristics. Fourth, we did not have data on peripheral vascular disease or transient ischemic attacks and thus may have underestimated the numbers of patients with cardiovascular disease. Fifth, information on family history with respect to premature coronary heart disease was based on myocardial infarction or angina in a first-degree relative under the age of 50 years. This age limit is lower than that used in the ATP-III guidelines, which might have slightly reduced the total number of adults who would be eligible for statin therapy. Finally, we have focused on adults between the ages of 40 and 75 years because the new guidelines are less clear outside this age range.

In addition to these limitations, we may have overestimated changes in statin use under the new guidelines for several reasons. We assumed that membership in one of the groups for whom statin therapy would provide benefit equates with treatment recommendation, whereas the new guidelines call for an informed risk–benefit discussion between the patient and physician before the initiation of statin therapy.[3] In addition, the effect of an expanded treatment recommendation may be limited by a lack of universal implementation. Under the ATP-III guidelines, the number of adults who would be recommended for statin therapy but who have not reported receiving treatment could be as high as 18 million. Thus, it is not clear what effect the new guidelines would have by expanding the number of adults recommended for therapy. Finally, we did not account for treatment adherence, which has been reported to be low.[13,14]

In conclusion, the new ACC–AHA guidelines for the management of blood cholesterol have the potential to increase the net number of new statin prescriptions by 12.8 million, including 10.4 million for primary prevention. As compared with the ATP-III guidelines, the new guidelines would substantially increase the number of adults between the ages of 60 and 75 years and lower the LDL cholesterol levels of those who would be recommended for statin therapy.

Supported in part by Duke Clinical Research Institute's research funds and unrestricted grants from M. Jean de Granpré and Louis and Sylvia Vogel.

Disclosure forms provided by the authors are available with the full text of this article at NEJM.org.

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