ORIGINAL RESEARCH

2013 ACC/AHA Cholesterol Guideline and Implications for Healthy People 2020 Cardiovascular Disease Prevention Goals

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***Background*—**Healthy People 2020 aim to reduce fatal atherosclerotic cardiovascular disease (ASCVD) by 20%, which translates into 310 000 fewer events annually assuming proportional reduction in fatal and nonfatal ASCVD. We estimated preventable ASCVD events by implementing the American College of Cardiology/American Heart Association (ACC/AHA) 2013 Cholesterol Guideline in all statin-eligible adults. Absolute risk reduction (ARR) and number needed-to-treat (NNT) were calculated.

***Methods and Results*—**National Health and Nutrition Examination Survey data for 2007–2012 were analyzed for adults aged 21 to 79 years and extrapolated to the US population. Literature-guided assumptions were used including (1) low-density lipoprotein cholesterol falls 33% with moderate-intensity statins and 51% with high-intensity statins; (2) for each 39 mg/dL decline in low-density lipoprotein cholesterol, 10-year $ASCVD_{10}$ risk would fall 21% when $ASCVD_{10}$ risk was ≥20% and 33% when $ASCVD_{10}$ risk was <20%; and (3) either all statin-eligible untreated adults or all with $ASCVD_{10}$ risk ≥7.5% would receive statins. Of 175.9 million adults aged 21 to 79 years not taking statins, 44.8 million (25.5%) were statin eligible. Treating all statin-eligible adults would prevent an estimated 243 589 ASCVD events annually (ARR 5.4%, 10-year NNT 18). Treating all statin-eligible adults with $ASCVD_{10}$ risk ≥7.5% reduces the number treated to 32.2 million (28.2% fewer), whereas ASCVD events prevented annually fall only 10.5% to 217 974 (6.8% ARR, NNT 15).

***Conclusions*—**Implementing the ACC/AHA 2013 Cholesterol Guideline in all untreated, statin-eligible adults could achieve ≈78% of the Healthy People 2020 ASCVD prevention goal. Most of the benefit is attained by individuals with 10-year ASCVD risk ≥7.5%.
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Key Words: cardiovascular disease • cholesterol • epidemiology • guideline • primary prevention • secondary prevention • statin

In the US, ≈735 000 myocardial infarctions and 795 000 strokes occur annually, resulting in ≈500 000 deaths including ≈130 000 deaths from stroke and ≈370 000 deaths from coronary disease.[1,2] In 2010, ischemic heart disease was the leading cause of life lost in the United States at 7.2 million life years with stroke third at 1.9 million years.[3] Healthy People[4] 2020 goals include reducing deaths from heart disease and stroke 20%.[5] Hypercholesterolemia is a major, modifiable risk factor for coronary heart disease (CHD) and stroke.[6] Statins are beneficial for the primary and secondary prevention of fatal and nonfatal CHD and stroke.[7,8]

The American College of Cardiology/American Heart Association (ACC/AHA) 2013 Cholesterol Guideline, hereafter the 2013 Cholesterol Guideline, would treat ≈12.8 million additional adults aged 40 to 75 years old for hypercholesterolemia than recommended in the National Cholesterol Education Program/Adult Treatment Panel–3 guideline (NCEP/ATP-3).[9] Moreover, the atherosclerotic cardiovascular

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disease (ASCVD) risk calculator in the 2013 Cholesterol Guideline is more strongly associated with coronary calcium scores and cardiovascular outcomes than is the CHD risk equation in ATP-3.[10] These observations suggest that cardiovascular health could be improved and Healthy People 2020 goals advanced by implementing the 2013 Cholesterol Guideline.

A prior analysis indicated that full implementation of the 2013 Cholesterol Guideline would prevent an additional ≈475 000 cardiovascular events over 10 years compared with full implementation of the Adult Treatment Panel (ATP)-3 Guideline.[9] A cost-effectiveness analysis suggested that lowering the threshold for intervention from a 10-year ASCVD risk ($ASCVD_{10}$) from ≥7.5% to ≥3.0% would prevent an additional 161 650 ASCVD events over 10 years and was cost effective, especially with low-cost statins.[11] In both reports, only adults aged 40 to 75 years were included, and statins were assumed to reduce CHD by 25% and stroke by 17%, given a 39-mg/dL reduction in low-density lipoprotein cholesterol (LDL-C).

The 2013 Cholesterol Guideline extends to a broader age range than 40 to 75 years for adults with clinical atherosclerotic cardiovascular disease or low-density lipoprotein cholesterol (LDL-C) ≥190 mg/dL.[6] Moreover, the percentage and absolute reduction in LDL-C are dose dependent with high-intensity statins more effective than moderate-intensity statins in reducing ASCVD,[6,8,12–16] although adverse effects also increase.[16–19] The current and previous cholesterol guidelines also identified a favorable risk:benefit ratio for statins in adults aged ≥75 years with clinical ASCVD.[6,20,21]

Given the importance of ASCVD prevention, we examined the impact of implementing the 2013 Cholesterol Guideline on 2 key outcomes. One outcome was to estimate the number of ASCVD events that could be prevented in the United States by providing statins to currently untreated but statin-eligible adults 21 to 79 years old. A second outcome was to calculate absolute risk reduction (ARR) and 10-year number needed-to-treat (NNT) to prevent a major ASCVD event. This information is important for assessing clinical resource requirements and risk:benefit ratio. Study findings have potentially important implications for healthcare delivery, policy, and payment to enhance cardiovascular health promotion and disease prevention.

Methods

The National Health and Nutrition Examination Surveys (NHANES) assess health and nutritional status in a representative sample of the US noninstitutionalized civilian population. All adults provided written consent, which was approved by the National Center for Health Statistics.[22,23]

Participants included adults aged 21 to 79 years in NHANES 2007–2012 with ≥1 recorded blood pressure (BP) and a complete lipid profile.

Statin use was determined from medications reportedly taken in the prior 30 days and a match to known statins.

Race/ethnicity was determined by self-report and separated into non-Hispanic white (white), non-Hispanic black (black), Hispanic ethnicity, and other.

BP was measured and analyzed according to NHANES guidelines.[22–24] *Hypertension* was defined by systolic BP ≥140 and/or diastolic BP ≥90 mm Hg or positive response to "Are you currently taking prescribed medication to lower your BP?" Systolic BP of 60 to 300 mm Hg and diastolic BP of 30 to 240 mm Hg were accepted as valid.

Prevalent diabetes mellitus included (1) *diagnosed diabetes mellitus* defined by positive response(s) to ≥1 question, "Have you ever been told by a doctor that you have diabetes mellitus ?" or "Are you now taking insulin?" or "Are you now taking diabetic pills to lower your blood sugar?" and (2) *undiagnosed diabetes mellitus* was defined by negative responses to the questions and fasting glucose ≥126 mg/dL or glycosylated hemoglobin ≥6.5%.[25]

Lipid/Lipoprotein Values

As shown in Figure 1, fewer than half of adult participants in NHANES provided fasting blood samples. Total cholesterol and high-density lipoprotein cholesterol (HDL-C) were measured on all participants regardless of fasting status, whereas triglycerides were measured and LDL-C calculated only from fasting samples. For patients with triglyceride levels >400 mg/dL (n=128, representing 3 627 587 US adults [aged 21–79 years]), LDL-C was not calculated. Total cholesterol of 40 to 800 mg/dL, HDL-C of 2 to 140 mg/dL, LDL-C of 20 to 700 mg/dL, and triglycerides of 20 to 12 000 mg/dL were accepted as valid.

Inclusion and Exclusion Criteria

Adult men and women aged 21 to 79 years were included with a valid BP and complete lipid profile including calculated LDL-C. Exclusion criteria were self-reported congestive heart failure and estimated glomerular filtration rate <15 mL/1.73 m^2 per minute.[5] Chronic kidney disease was defined by estimated glomerular filtration rate of 15 to 59 mL/1.73 m^2 per minute.[26]

Statin eligibility by the 2013 ACC/AHA Cholesterol Guideline was defined as summarized in Table 1.[6]

For the main analysis, we assumed that 75% of adults without diabetes mellitus and $ASCVD_{10}$ ≥7.5% (1A for moderate- to high-intensity statin) and 50% with diabetes mellitus and $ASCVD_{10}$ ≥7.5% (IIaB for high-intensity statin)

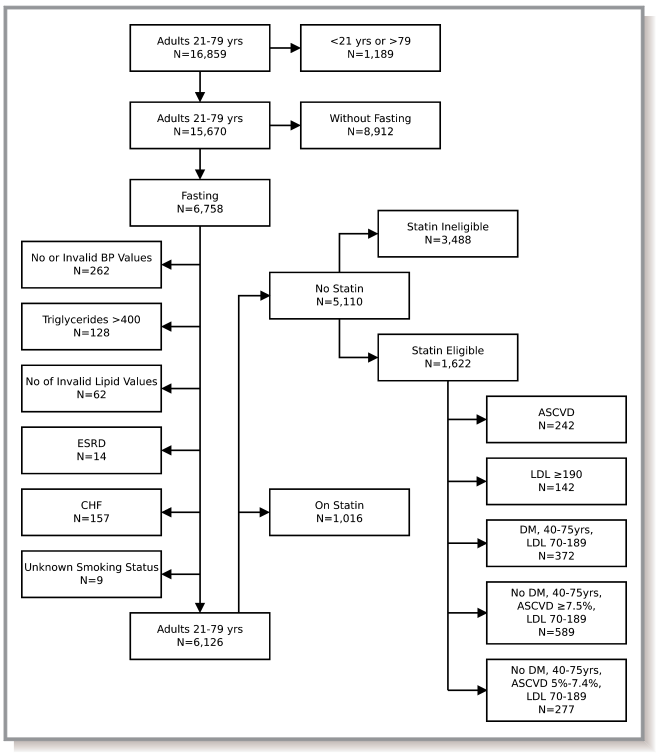

Figure 1. Flow diagram showing derivation of the study sample with numbers and reasons for exclusion from consideration for statin therapy (left). Among adults not taking statins, the numbers of statin-ineligible and eligible adults are also shown (right).

would receive high-intensity statin. Assumptions reflect arbitrary estimates of how informed clinicians would balance recommendations and benefit:risk information. For every 2 additional cases of incident diabetes mellitus with high- versus moderate-intensity statin in patients with CHD, 6.5 fewer major vascular events occur.[16] Dr Robinson, co-author of the 2013 Cholesterol Guideline, summarized safety data on statin therapy,[14,27,28] which indicated that the 5-year number needed-to-harm (NNH) was ≈167 for moderate-intensity and 63 for high-intensity statin therapy.[19] With regard to rhabdomyolysis, a nonsignificant increase with high- versus moderate-intensity statin was noted in 1 meta-analysis (odds ratio 1.66, P=0.326).[18] Given uncertainty over what intensity statin therapy clinicians would prescribe, a sensitivity analysis was performed for these 2 groups by varying the percentages on moderate- and high-intensity statins from 0% to 100%.

Estimated Decline in $ASCVD_{10}$ With Statin Therapy

Assumptions included (1) for each 39-mg/dL decline in LDL-C, ASCVD events would fall 21% for $ASCVD_{10}$ ≥20% and 33% for $ASCVD_{10}$ <20%[15]; (2) LDL–C would fall 33% with moderate-intensity and 51% with high-intensity statin therapy, that is, the conservative end of the estimated 30% to <50% LDL-C reduction with moderate-intensity and ≥50% decline with high-intensity statins[6,29]; and (3) for patients with prior stroke or myocardial infarction in whom $ASCVD_{10}$ is not calculated, a 39% 10-year risk was assigned. In subjects with angina or transient ischemic attack, a 10-year risk of 31.5% was assigned. Estimates were derived as follows. Adults with clinical CHD have a ≥26% 10-year risk of another CHD event. Patients with CHD risk equivalent status, excluding diabetes mellitus,[6] have a 10-year CHD risk of >20%.[20,30,31] Respective risks of 26% and 21% were multiplied by 1.5, which assumes $ASCVD_{10}$ event rates were 50% greater than 10-year CHD risk alone. This assumption is conservative, as annual numbers of strokes (≈795 000) and myocardial infarctions (≈735 000) in the United States are similar.[1,2]

$ASCVD_{10}$, while not required for treating adults aged 21 to 79 years with LDL-C ≥190 mg/dL,[6] was calculated to estimate absolute risk reduction (ARR) and number needed-to-treat (NNT). The ACC/AHA ASCVD risk calculator accepts ages 20 to 79 years and limits total cholesterol values to a maximum of 320 mg/dL. In NHANES 2007–2012, 0.59% of adults aged 21 to 79 years in the fasting sample used for this analysis had total cholesterol levels of >320, and all of them had LDL-C levels of ≥190 mg/dL. Total cholesterol values >320 were entered as 320 in the ASCVD risk calculator.

Table 1. Summary of Statin-Eligible Groups in the 2013 ACC/AHA Cholesterol Guideline

2013 Guideline Statin-Eligible Groups[6]	COR	LOE	LDL-C, mg/dL	Age, y	Statin Intensity
1. ASCVD	I IIa	A B	Any	21–75 ≥75	High Moderate-high
2. LDL-C ≥190	I	B	≥190	21–75	High
3. Diabetes mellitus—all	I	A	70–189	40–75	Moderate
4. Diabetes mellitus, $ASCVD_{10}$ ≥7.5%	IIa	B	70–189	40–75	High
5. No diabetes mellitus, $ASCVD_{10}$ ≥7.5%	I	A	70–189	40–75	Moderate-high
6. No diabetes mellitus, $ASCVD_{10}$ 5–>7.5%	IIa	B	70–189	40–75	Moderate

ACC/AHA indicates American College of Cardiology/American Heart Association; ASCVD, atherosclerotic cardiovascular disease; A, multiple randomized clinical trials or meta-analyses; B, single randomized trial or nonrandomized studies; COR, class of recommendation; I, benefit ⋙ risk; IIa, benefit ≫ risk; LDL-C, low-density lipoprotein cholesterol; LOE, level of evidence.

Data Reporting and Analysis

SAS Enterprise Guide 7.1 was used for all analyses and accounts for complex sampling characteristics of NHANES. One-half of NHANES participants were studied in the morning and were instructed to fast at least 9 hours before their examination. Triglyceride and calculated LDL-C values are provided only for the fasting participants studied in the morning. Because fasting is an important defining characteristic of subjects in our analysis, the fasting sample weight, WTSAF2YR, was used.

Descriptive statistics including mean and SE were generated. Wald's F test was applied for continuous variables, and the Rao–Scott modified χ^2 test was used for categorical variables. ASCVD reduction was calculated with the use of PROC SURVEYMEANS. Absolute risk reduction (ARR) and number needed-to-treat (NNT) were calculated using PROC SURVEYMEANS. Two-sided $P<0.05$ were accepted as significant.

Table 2. Demographic, Educational, and Economic Characteristics of Adults 21–79 Years by Statin Use and Eligibility Status

Group	All Adults			Adults Not Taking Statins		
Variable/Subgroup	Taking Statin	No Statin Therapy	*P* Value	Statin Eligible	Statin Ineligible	*P* Value
NHANES sample, n	1016	5110		1622	3488	
Population, N	32 080 155	175 922 845		44 843 712	131 079 133	
Population, %	15.4	84.6		25.5	74.5	
Age, y	60.4±0.4	43.2±0.4	<0.0001	57.8±0.3	38.1±0.4	<0.0001
Male, n (%)	534 (53.9)	2406 (47.3)	0.005	932 (58.0)	1474 (43.7)	<0.0001
Female, n (%)	482 (46.1)	2704 (52.7)		690 (42.0)	2014 (56.3)	
Black, n (%)*	203 (8.9)	998 (11.6)	<0.0001	411 (15.3)	587 (10.3)	<0.0001
White, n (%)†	513 (78.0)	2119 (65.9)		648 (67.6)	1471 (65.4)	
Hispanic, n (%)	225 (7.7)	1521 (15.3)		454 (11.8)	1067 (16.5)	
Other, n (%)	75 (5.4)	472 (7.2)		109 (5.4)	363 (7.8)	
Visits/y, n (%)						
0–1	108 (10.4)	2149 (39.9)	<0.0001	556 (33.2)	1593 (42.2)	<0.0001
2–3	332 (35.6)	1364 (28.5)		403 (24.6)	961 (29.9)	
≥4	576 (54.0)	1596 (31.5)		662 (42.1)	934 (27.9)	
Education, n (%)						
<High school	284 (17.7)	1323 (17.3)	0.10	531 (22.3)	792 (15.6)	<0.0001
High school	251 (25.1)	1104 (20.8)		392 (24.0)	712 (19.7)	
≥Some college	481 (57.2)	2680 (62.0)		698 (53.8)	1982 (64.8)	
FPL, n (%)						
<100%	149 (8.9)	1040 (14.9)	<0.0001	317 (14.5)	723 (15.0)	0.60
100–199%	212 (16.5)	1272 (20.5)		428 (21.7)	844 (20.0)	
≥200%	572 (74.6)	2369 (64.6)		724 (63.7)	1645 (64.9)	
Insurance, n (%)						
None	82 (5.9)	1531 (23.5)	<0.0001	406 (19.5)	1125 (24.9)	<0.0001
Private	367 (48.9)	2323 (57.8)		548 (44.3)	1775 (62.4)	
Medicaid/OG	189 (15.4)	717 (10.5)		256 (12.0)	461 (10.0)	
Medicare	377 (29.8)	536 (8.2)		412 (24.2)	124 (2.7)	

Continuous variables (age) are presented as mean±1 SE. Categorical variables are presented as NHANES sample number (n) and percentage (%) of US population represented by NHANES sample number. The sum of n-values for participant subgroups on variables, such as visits and education, do not always equal overall NHANES sample N because of missing data. Sample weights on subjects with data were adjusted by NHANES so that summation of subgroup percentages reflect 100% of the US population N for that column, such as taking statins, no statin therapy, statin eligible, and statin ineligible. ASCVD indicates atherosclerotic cardiovascular disease; Educ, highest education level attained; FPL, federal poverty level; N, number represented in US population by NHANES sample; NHANES, national health and nutrition examination surveys; OG, other government.

*Non-Hispanic black.

†Non-Hispanic white.

Results

The process for selecting adults for statin eligibility and the number of adults in each statin-eligible group are provided in Figure 1. As shown, 6758 adults 21 to 79 years old were included in the fasting sample for NHANES 2007–2012; 128 (1.9%), or an estimated 3 627 587 adults, had triglyceride levels >400 mg/dL and were excluded from consideration for statin eligibility.

Comparison of Adults Reporting and Not Reporting Current Statin Use

Statin users comprised 32 million (15.4%) of 208 million US adults aged 21 to 79 years. Compared with adults not reporting statin use, those taking statins (1) were older and more likely to be male and white, (2) more often had health insurance, (3) had incomes ≥200% of the federal poverty level, and (4) had more healthcare visits in the previous year, higher body mass indices, and more prevalent obesity, hypertension, diabetes mellitus, stage 3 to 4 chronic kidney disease, clinical ASCVD, systolic BP, and triglycerides but lower diastolic BP, total cholesterol, LDL-C, and HDL-C levels and fewer cigarette smokers (Tables 2 and 3).

Comparing Statin-Eligible and -Ineligible Adults

Of an estimated 175.9 million adults not reporting statin use, 44.8 million (25.5%) were statin eligible by the 2013 Cholesterol Guideline.[3] Compared with statin-ineligible adults, the statin-eligible group (1) was older, more often male and white or black, and less often Hispanic; (2) had lower educational attainment but similar incomes; (3) more often had health insurance; (4) reported more healthcare visits; (5) more often had hypertension, diabetes mellitus, and chronic kidney disease and smoked cigarettes; and (6) had higher body mass index, systolic and diastolic BP, total cholesterol and LDL-C, and triglycerides but lower HDL-C (Tables 2 and 3).

Estimates of ASCVD Prevention in Statin-Eligible Adults Not Taking Statins

Data are provided for the number of adults in the various groups of statin-eligible adults, (1) all statin-eligible adults combined, (2) only statin-eligible adults with $ASCVD_{10}$ ≥7.5%, and (3) only statin-eligible adults with $ASCVD_{10}$ <7.5%. Treating all statin-eligible adults is estimated to prevent 2 435 890 events over 10 years or 243 589 events/year. For this group, ARR is 5.4%, with 10-year NNT of 18. Treating

Table 3. Selected Medical Characteristics of Adults Aged 21–79 Years by Statin Use and Eligibility Status

Group	All Adults			Adults Not Taking Statins		
Variable/Subgroup	Taking Statins	No Statin Therapy	*P* Value	Statin Eligible	Statin Ineligible	*P* Value
NHANES sample, n	1016	5110		1622	3488	
Population, N	32 080 155	175 922 845		44 843 712	131 079 133	
Population, %	15.4	84.6		25.5	74.5	
BMI, kg/m^2	30.3±0.3	28.4±0.1	<0.0001	29.7±0.2	27.9±0.1	<0.0001
Obese, n (%)	496 (48.0)	1759 (32.5)	<0.0001	652 (39.5)	1107 (30.0)	<0.0001
Hypertension, n (%)	805 (72.9)	1437 (24.4)	<0.001	910 (52.7)	527 (14.7)	<0.0001
SBP, mm Hg	123.6±0.6	118.0±0.4	<0.0001	127.5±0.6	114.8±0.4	<0.0001
DBP, mm Hg	68.6±0.5	70.2±0.4	0.0004	72.6±0.5	69.3±0.4	<0.0001
Total Chol, mg/dL	180.2±2.1	197.6±0.8	<0.0001	217.3±1.7	190.9±0.8	<0.0001
HDL-Chol, mg/dL	52.8±0.6	54.2±0.3	0.02	52.4±0.5	54.8±0.4	0.0001
LDL-Chol, mg/dL	100.5±1.7	119.7±0.6	<0.0001	136.8±1.5	113.8±0.6	<0.0001
Triglycerides, mg/dL	134.4±3.4	119.0±1.5	<0.0001	140.1±3.0	111.7±1.5	<0.0001
Diabetes mellitus, n (%)	434 (32.2)	567 (7.4)	<0.0001	451 (23.1)	116 (2.1)	<0.0001
HbA_{1c} <8%, n (%)	346 (82.6)	437 (78.1)	0.20	347 (78.1)	90 (77.8)	0.96
Cigarette smoker, n (%)	152 (15.0)	1139 (21.3)	<0.0001	429 (27.3)	710 (19.3)	<0.0001
Stage 3–4 CKD, n (%)	108 (8.5)	150 (2.5)	<0.0001	98 (6.3)	52 (1.2)	<0.0001
10-y ASCVD risk, n (%)	17.0±0.8	5.2±0.2	<0.0001	14.6±0.4	2.0±0.1	<0.0001
ASCVD, n (%)	252 (23.2)	242 (3.3)	<0.0001	242 (12.8)	0 (0)	<0.0001

Continuous variables are presented as mean±1 SE. Categorical variables are presented as NHANES sample number (n) and percentage (%) of US population represented by NHANES sample number. ASCVD indicates atherosclerotic cardiovascular disease; BMI, body mass index; Chol, cholesterol; CKD, chronic kidney disease; D, diastolic; HbA_{1c}, glycosylated hemoglobin; HDL, high-density lipoprotein; LDL, low-density lipoprotein: NHANES, national health and nutrition examination surveys; OG, other governmental insurance; SBP, systolic blood pressure.

only statin-eligible adults with $ASCVD_{10}$ ≥7.5% prevents an estimated 2 179 743 events over 10 years or 217 974 events/year; ARR is 6.8% with NNT of 15. For statin-eligible adults with $ASCVD_{10}$ <7.5%, ARR is 2.0% with NNT of 49. Table 3 also provides data assuming that 75% and 50% of all statin-eligible adults receive statins with the expected proportionate reductions in numbers of individuals treated and ASCVD events prevented (Table 4).

Changes in ARR and NNT When Varying the Proportion of Adults With $ASCVD_{10}$ Risk ≥7.5% Taking Moderate- or High-Intensity Statins

Adults with diabetes mellitus and $ASCVD_{10}$ risk ≥7.5% have a 1A recommendation for moderate-intensity and a IIaB recommendation for high-intensity statins (Table 4, Figure 2). Adults without diabetes mellitus and $ASCVD_{10}$ risk ≥7.5% have a 1A recommendation for moderate- to high-intensity statins. The absolute number of ASCVD events prevented and ARR increase as the proportion of adults on high-intensity statins increases (Table 5), whereas NNT falls (Figure 2).

Discussion

Statins are recommended for the primary and secondary prevention of CHD and stroke.[5–7] Given projections for a rapidly growing burden of cardiovascular disease in the United States,[32] the role of statins merits attention. In the United States, there are more statin-eligible adults not receiving statins than adults reporting statin use (Table 2). If all statin-eligible adults were treated, or roughly 44.8 million individuals, then ≈243 589 ASCVD events annually or 2 435 890 events over 10 years (Table 4) could be prevented. The number of ASCVD events prevented is ≈78% of the Healthy People 2020 goal for cardiovascular disease prevention. Implementing the 2013 Cholesterol Guideline in statin-eligible US adults is also relatively efficient with ARR of 5.4% and 10-year NNT of 18.

Treating only statin-eligible adults with 10-year ASCVD risk ≥7.5% reduces the number of adults treated by 12.6 million individuals or 28.2% from 44.8 to 32.2 million. Yet, the number of ASCVD events prevented annually falls only 10.5% from 243 589 to 217 974, which is ≈70% of the Healthy People 2020 goal. For this higher-risk group, ARR is 6.8% with 10-year NNT of 15. The 2013 Cholesterol Guideline is less

Table 4. ASCVD Events Prevented in 10 Years by Statin-Eligible Group and When the Percentages of Statin-Eligible Adults on Statins Vary

Variable Statin-Eligible Group	Sample, n	Population, N	Statin Intensity	∅Statin $ASCVD_{10}$, %	∅Statin $ASCVD_{10}$, n	⊕Statin $ASCVD_{10}$, n	Change $ASCVD_{10}$ Events, n	$ASCVD_{10}$ RRR, %	$ASCVD_{10}$ ARR, %	NNT
ASCVD	242	5 734 435	High	36.6	2 098 412	1 472 264	626 148	30.2	10.9	9
LDL ≥190	142	5 016 479	High	9.5	478 091	207 871	270 220	63.6	5.4	19
⊕DM $ASCVD_{10}$ ≥7.5%	273	5 435 130	Moderate-high*	20.3	1 102 617	751 566	351 051	35.0	6.5	15
⊕DM $ASCVD_{10}$ <7.5%	99	3 229 536	Moderate	4.3	138 162	94 013	44 148	32.2	1.4	73
∅DM $ASCVD_{10}$ ≥7.5%	589	16 022 464	Moderate-High†	13.5	2 161 319	1 228 995	932 324	44.8	5.8	17
∅DM $ASCVD_{10}$ 5–7.4%	277	9 405 669	Moderate	6.3	590 423	378 424	211 999	35.9	2.3	44
100% statin-eligible treated	1622	44 843 712		14.6	6 569 024	4 133 133	2 435 890	41.1	5.4	18
Only $ASCVD_{10}$ ≥7.5%‡	1246	32 208 508		18.1	5 840 439	3 660 696	2 179 743	43.5	6.8	15
Only $ASCVD_{10}$ <7.5%§	376	12 635 205		5.8	728 585	472 437	256 147	35.0	2.0	49
75% statin-eligible treated	1216	33 632 784		14.6	4 926 768	3 099 850	1 826 918	41.1	5.4	18
Only $ASCVD_{10}$ ≥7.5%‡	934	24 156 381		18.1	4 380 329	2 745 522	1 634 807	43.5	6.8	15
Only $ASCVD_{10}$ <7.5%§	282	9 476 403		5.8	546 439	354 328	192 110	35.0	2.0	49
50% statin-eligible treated	811	22 421 856		14.7	3 284 512	2 066 567	1 217 945	41.1	5.4	18
Only $ASCVD_{10}$ ≥7.5%‡	623	16 104 254		18.1	2 920 220	1 830 348	1 089 872	43.5	6.8	15
Only ASCVD10 <7.5%§	188	6 317 602		5.8	364 292	236 218	128 074	35.0	2.0	49

ASCVD indicates atherosclerotic cardiovascular disease. ⊕ Statin $ASCVD_{10}$, n indicates number of ASCVD events over 10 years with statins; ⊕DM, DM present; ∅DM, DM absent; ∅Statin $ASCVD_{10}$, %, 10-year ASCVD risk without a statin; ∅Statin $ASCVD_{10}$, n, number of ASCVD events over 10 years without a statin; ARR, absolute risk reduction; DM, diabetes mellitus; NNT, 10-year number needed-to-treat to prevent an ASCVD event; RRR, relative risk reduction.

*Fifty percent of patients with (⊕) diabetes mellitus (DM) and $ASCVD_{10}$ ≥7.5% receive high-intensity and 50% receive moderate-intensity statins.

†Seventy-five percent of patients without (∅) diabetes mellitus receive high-intensity and 25% receive moderate-intensity statins.

‡Includes ASCVD, LDL ≥190, and patients with and without diabetes mellitus and 10-year ASCVD risk ($ASCVD_{10}$) ≥7.5% and excludes lower-risk participants with (⊕) diabetes mellitus (DM) and $ASCVD_{10}$ <7.5% and without (∅) diabetes mellitus (DM) and $ASCVD_{10}$ 5–7.4%.

§Includes only lower risk participants with diabetes mellitus and $ASCVD_{10}$ <7.5% and without diabetes and $ASCVD_{10}$ 5–7.4%.

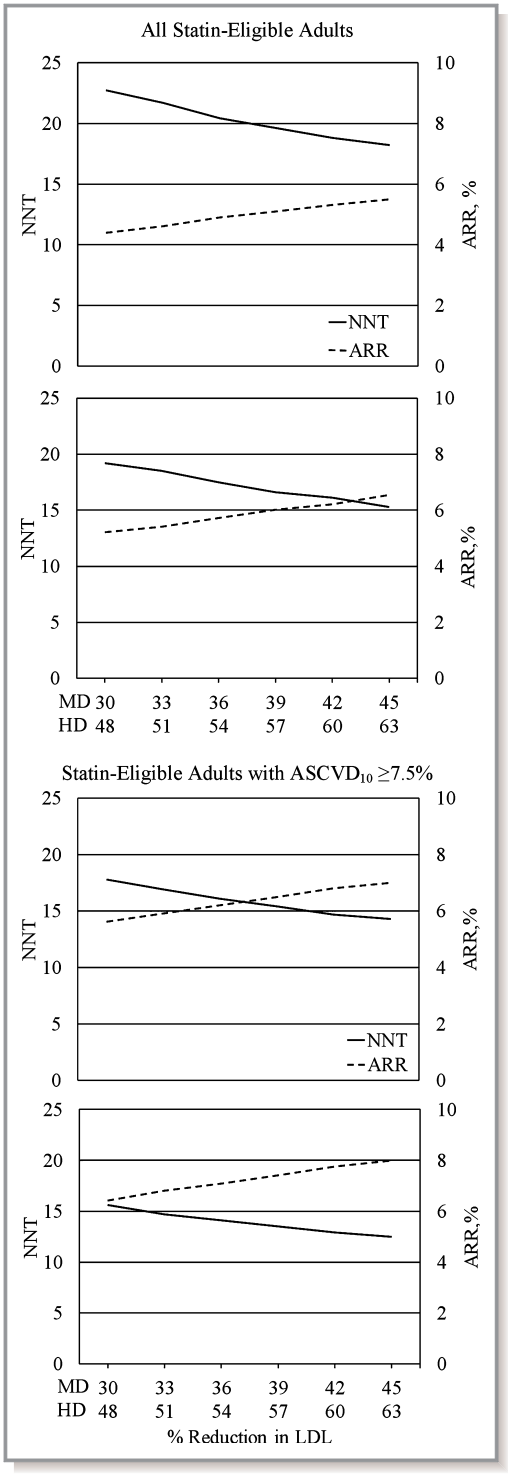

Figure 2. Absolute risk reduction (ARR) in 10-year risk for atherosclerotic cardiovascular disease $(ASCVD)_{10}$ and number needed-to-treat (NNT) to prevent an ASCVD event are depicted for adults with and without diabetes mellitus and with $ASCVD_{10}$ ≥7.5%. The data points reflect changes in ARR and NNT as the proportion of individuals taking moderate-dose (MD) and high-dose (HD) statins varies from 0% to 100% in 25% increments.

efficient for untreated, statin-eligible adults with 10-year ASCVD risk <7.5%, that is, treating 12.6 million adults in this group would prevent ≈256 147 events over 10 years or 25 615 annually, with ARR of 2.0% and 10-year NNT of 49.

The feasibility of identifying and treating 100% of statin-eligible but untreated adults is low. As an initial step, treating 50% of untreated, statin-eligible adults would also have a positive impact on Healthy People 2020 goals for cardiovascular disease prevention and is credible for several reasons. First, 2 of 3 statin-eligible but untreated adults report ≥2 healthcare visits annually (Table 2), which indicates opportunities for assessing ASCVD risk and statin eligibility. Second, 80% are insured, which suggests some financial support for screening and treatment. Third, treating half of statin-eligible adults and continuing treatment in those currently on statins would bring statin therapy to 71% of statin-eligible adults. This is comparable to the proportion of all adults with hypertension receiving pharmacotherapy since 2007–2008.[22] Fourth, the majority of statin-eligible but untreated adults also have hypertension with the majority receiving treatment and having ≥2 healthcare visits annually.[22] Fifth, most statins are available as generics with several on discount formularies at <$50/year.[33] Individuals prescribed generic statins experience fewer cardiovascular events and deaths than do individuals prescribed proprietary statins,[34] which suggests the former are more likely than the latter to obtain and take statin medications. Sixth, the percentage of adults taking statins is growing faster than percentages of adults taking antihypertensive medications; that is, the prescribing gap between statins and antihypertensive medications is closing.[35] The points provided could support a more ambitious target than treating 50% of untreated, statin-eligible adults. Yet, the 50% target is an important step in moving to even higher treatment levels. The impact of raising the percentage of statin-eligible adults taking statins from 50% to 75% is enumerated in Table 4.

Our principal analysis assumed that among adults with ASCVD ≥7.5%, 50% of those with diabetes mellitus would receive moderate-intensity and the other would receive 50% high-intensity statin. For the subset without diabetes mellitus, 25% were estimated to receive moderate- and 75% to receive high-intensity statin. Since those were only estimates, sensitivity analyses were conducted, which varied the proportion taking moderate- and high-intensity statins from 0% to 100%. ARR and the number of ASCVD events prevented rose as the proportion taking high-intensity statins increased, whereas the NNT to prevent an ASCVD event fell (Table 5, Figure 2).

Cost-effectiveness of statin therapy, while not the focus of our report, is relevant in extending treatment to millions of additional statin-eligible patients. The cost per quality adjusted life-year for adults with 10-year $ASCVD_{10}$ risk of

Table 5. Sensitivity Analysis on Percentages of Adults With and Without Diabetes Mellitus and $ASCVD_{10}$ ≥7.5%* Taking High- and Moderate-Intensity Statins

Variable Statin Eligible Group	Sample, n	Population, N	Statin Intensity	∅Statin $ASCVD_{10}$, %	∅Statin $ASCVD_{10}$, n	⊕Statin $ASCVD_{10}$, n	Change $ASCVD_{10}$ Events, n	$ASCVD_{10}$ RRR, %	$ASCVD_{10}$ ARR, %	NNT
100% Moderate-intensity statin										
⊕DM $ASCVD_{10}$ ≥7.5%†	273	5 435 130	Moderate	20.3	1 102 617	814 563	288 504	28.8	5.3	19
∅DM $ASCVD_{10}$ ≥7.5%‡	589	16 022 464	Moderate	13.5	2 161 319	1 450 004	711 316	34.3	4.4	23
75% Moderate-, 25% high-intensity statin										
⊕DM $ASCVD_{10}$ ≥7.5%†	273	5 435 130	Moderate-high	20.3	1 102 617	782 347	320 270	32.0	5.9	17
∅DM $ASCVD_{10}$ ≥7.5%‡	589	16 022 464	Moderate-high	13.5	2 161 319	1 374 589	786 730	37.9	4.9	20
50% Moderate- and 50% high-intensity statin										
⊕DM $ASCVD_{10}$ ≥7.5%†	273	5 435 130	Moderate-high	20.3	1 102 617	751 566	351 051	35.0	6.5	15
∅DM $ASCVD_{10}$ ≥7.5%‡	589	16 022 464	Moderate-high	13.5	2 161 319	1 303 415	857 905	41.3	5.4	19
25% Moderate- and 75% high-intensity										
⊕DM $ASCVD_{10}$ ≥7.5%†	273	5 435 130	Moderate-high	20.3	1 102 617	722 149	380 468	37.8	7.0	14
∅DM $ASCVD_{10}$ ≥7.5%‡	589	16 022 464	Moderate-high	13.5	2 161 319	1 228 995	932 324	44.8	5.8	17
100% High-intensity statin										
⊕DM $ASCVD_{10}$ ≥7.5%†	273	5 435 130	High	20.3	1 102 617	694 028	408 588	40.5	7.5	13
∅DM $ASCVD_{10}$ ≥7.5%‡	589	16 022 464	High	13.5	2 161 319	1 172 783	988 536	47.5	6.2	16

ASCVD indicates atherosclerotic cardiovascular disease; NNT, number needed-to-treat.
*Participants with (⊕) and without (∅) diabetes mellitus (DM) and 10-year ASCVD risk ($ASCVD_{10}$) <7.5% have an indication only for moderate-intensity statins and were excluded. Participants with ASCVD and LDL ≥190 have an indication for high-intensity statins and were excluded.
†Only participants with (⊕) diabetes mellitus (DM) who also had $ASCVD_{10}$ ≥7.5% were included.
‡Only participants without (∅) DM and $ASCVD_{10}$ ≥7.5% were included.

7.5% to <10% was estimated at $37 000.[10] Lowering the treatment threshold further to an $ASCVD_{10}$ of 4.0% raised the cost/quality-adjusted life-year to $81 000. Treating all adults ≥75 years old with $ASCVD_{10}$ ≥7.5% led to a cost estimate of $25 200 per disability-adjusted life-year.[36] The incremental cost-effectiveness ratio per quality-adjusted life-year for high- versus moderate-dose statins was <$50 000, a commonly accepted threshold for cost-effectiveness, assuming a cost differential of <$1.70/day between the 2 statin doses.[37]

Safety is another important consideration when increasing the proportion of adults receiving statin therapy. Dr Robinson, co-author of the 2013 Cholesterol Guideline,[6] summarized safety data on statin therapy,[14,27,28] which indicated that the 5-year NNH was ≈167 for moderate- and 63 for high-intensity statin therapy.[19] With regard to the risk-to-benefit considerations with high- versus moderate-intensity statin therapy, and assuming a linear relationship between 1- and 5-year risk, the 5-year NNT in adults with CHD taking high- versus moderate-intensity statin is 31 to prevent a major vascular event versus an NNH of 100 for diabetes mellitus.[15] Analyses from JUPITER indicate that statin-related diabetes mellitus reflects a shortening of the latent period from prediabetes to diabetes mellitus by a few weeks. In JUPITER, only minimal changes in the fasting glucose and glycosylated hemoglobin values were observed among all statin-treated participants.[27]

Limitations include a small sample of the US civilian population, partially explained by missing LDL-C in over half of NHANES adults as previously noted (Figure 1).[22] Health care is dynamic, and data from 2007 to 2012 may not reflect current realities. The potential for ASCVD prevention is limited by clinical barriers, such as lack of data to assess eligibility and failure to assess eligibility when data are available or to prescribe statins when appropriate for ASCVD risk. Patients may fail to fill prescriptions or persist in taking statins, yet substantial persistence with statin therapy at 3 years was documented.[38] And, widely available, low-cost generic statins improve outcomes relative to proprietary statins.[33,34]

In summary, Healthy People 2020 aims to reduce CHD and stroke by 20%.[5] Our estimates suggest that implementing the 2013 Cholesterol Guideline in all statin-eligible adults, or ≈44.8 million individuals, would accomplish >75% of the Healthy People 2020 annual goal for ASCVD prevention. Implementing the 2013 Cholesterol Guideline in all statin-eligible adults with $ASCVD_{10}$ ≥7.5% could achieve ≈70% of Healthy People 2020 goals, while reducing the number of adults initiated on statin therapy to 32.2 million. An initial

step of treating only half of statin-eligible adults would make a substantial impact in reducing cardiovascular events. Given the projected health benefits and in view of clinical safety and cost-effectiveness considerations, public health, healthcare policy, and population healthcare initiatives to effectively implement the 2013 Cholesterol Guideline appear justified, especially for those with a 10-year ASCVD risk of ≥7.5%. These initiatives have the potential to enhance success with an important Healthy People 2020 goal for cardiovascular disease prevention and to attenuate a large projected increase in the burden of ASCVD.[32]

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