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 ASCVD10 risk would fall 21% when ASCVD10 risk was ≥20% and 33% when ASCVD10 risk was <20%; and (3) either all statin-eligible untreated adults or all with ASCVD10 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 ASCVD10 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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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 People2020 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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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. 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. 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. 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, although adverse effects also increase. The current and previous cholesterol guidelines also identified a favorable risk:benefit ratio for statins in adults aged ≥75 years with clinical ASCVD.

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.

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. 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 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%.

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 m² per minute. Chronic kidney disease was defined by estimated glomerular filtration rate of 15 to 59 mL/1.73 m² per minute.

Statin eligibility by the 2013 ACC/AHA Cholesterol Guideline was defined as summarized in Table 1.
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. Dr Robinson, co-author of the 2013 Cholesterol Guideline, summarized safety data on statin therapy, which indicated that the 5-year number needed-to-harm (NNH) was 167 for moderate-intensity and 63 for high-intensity statin therapy. With regard to rhabdomyolysis, a nonsignificant increase with high-versus moderate-intensity statin was noted in 1 meta-analysis (odds ratio 1.66, \( P=0.326 \)). 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\( _{10} \) \( \geq 20\% \) and 33% for ASCVD\( _{10} \) \(< 20\% \); (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 \( \geq 50\% \) decline with high-intensity statins; 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 \( \geq 26\% \) 10-year risk of another CHD event. Patients with CHD risk equivalent status, excluding diabetes mellitus, have a 10-year CHD risk of \( > 20\% \). 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 (\( \approx 795,000 \)) and myocardial infarctions (\( \approx 735,000 \)) in the United States are similar.

ASCVD\( _{10} \), while not required for treating adults aged 21 to 79 years with LDL-C \( \geq 190 \) mg/dL, 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 \( \geq 190 \) 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 | A | Any | 21–75 | High |
| 1. LDL-C \( \geq 190 \) | I | B | \( \geq 190 \) | 21–75 | High |
| 3. Diabetes mellitus—all | I | A | 70–189 | 40–75 | Moderate |
| 4. Diabetes mellitus, ASCVD\( _{10} \) \( \geq 7.5\% \) | Ila | B | 70–189 | 40–75 | High |
| 5. No diabetes mellitus, ASCVD\( _{10} \) \( \geq 7.5\% \) | I | A | 70–189 | 40–75 | Moderate-high |
| 6. No diabetes mellitus, ASCVD\( _{10} \) \( 5\%–7.5\% \) | Ila | 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 \( \gg \) risk; Ila, benefit \( \gg \) 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 χ² 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 | \( P \) Value |
|--------------------------------|---------------------|----------------------------|--------------|
|                                | Taking Statin       | No Statin Therapy          |              |
| NHANES sample, n               | 1016                | 5110                       |              |
| Population, N                  | 32 080 155          | 175 922 845                |              |
| Population, %                  | 15.4                | 84.6                       |              |
| Age, y                         | 60.4±0.4            | 43.2±0.4                   | <0.0001      |
| Male, n (%)                    | 534 (53.9)          | 2406 (47.3)                | 0.005        |
| Female, n (%)                  | 482 (46.1)          | 2704 (52.7)                |              |
| Black, n (%)*                  | 203 (8.9)           | 998 (11.6)                 | <0.0001      |
| White, n (%)†                  | 513 (78.0)          | 2119 (65.9)                |              |
| Hispanic, n (%)                | 225 (7.7)           | 1521 (15.3)                |              |
| Other, n (%)                   | 75 (5.4)            | 472 (7.2)                  |              |
| Visits/y, n (%)                | 0–1                 | 108 (10.4)                 | <0.0001      |
|                                | 2–3                 | 332 (35.6)                 |              |
|                                | ≥4                  | 576 (54.0)                 |              |
| Education, n (%)               | <High school        | 284 (17.7)                 | 0.10         |
|                                | High school         | 251 (25.1)                 |              |
|                                | ≥Some college       | 481 (57.2)                 |              |
| FPL, n (%)                     | <100%               | 149 (8.9)                  | <0.0001      |
|                                | 100–199%            | 212 (16.5)                 |              |
|                                | ≥200%               | 572 (74.6)                 |              |
| Insurance, n (%)               | None                | 82 (5.9)                   | <0.0001      |
|                                | Private             | 367 (48.9)                 |              |
|                                | Medicaid/OG         | 189 (15.4)                 |              |
|                                | Medicare            | 377 (29.8)                 |              |

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, (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, and (3) only statin-eligible adults with ASCVD. 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 | P Value |
|-------|------------|---------------------------|---------|
|       | Taking Statins | No Statin Therapy | Statin Eligible | Statin Ineligible |
| NHANES sample, n | 1016 | 5110 | 1622 | 3488 |
| Population, N | 32 080 | 175 922 | 44 843 | 712 |
| Population, % | 15.4 | 84.6 | 25.5 | 74.5 |
| BMI, kg/m² | 30.3±0.3 | 28.4±0.1 | 29.7±0.2 | 27.9±0.1 |
| Obese, n (%) | 496 (48.0) | 1759 (32.5) | 652 (39.5) | 1107 (30.0) |
| Hypertension, n (%) | 805 (72.9) | 1437 (24.4) | 910 (52.7) | 527 (14.7) |
| SBP, mm Hg | 123.6±0.6 | 118.0±0.4 | 127.5±0.6 | 114.8±0.4 |
| DBP, mm Hg | 68.6±0.5 | 70.2±0.4 | 72.6±0.5 | 69.3±0.4 |
| Total Chol, mg/dL | 180.2±2.1 | 197.6±0.8 | 217.3±1.7 | 190.9±0.8 |
| LDL-Chol, mg/dL | 52.8±0.6 | 54.2±0.3 | 52.4±0.5 | 54.8±0.4 |
| Triglycerides, mg/dL | 134.4±3.4 | 119.0±1.5 | 140.1±3.0 | 111.7±1.5 |
| Diabetes mellitus, n (%) | 434 (32.2) | 567 (7.4) | 451 (23.1) | 116 (2.1) |
| HbA1c <8%, n (%) | 346 (82.6) | 437 (78.1) | 347 (78.1) | 90 (77.8) |
| Cigarette smoker, n (%) | 152 (15.0) | 1139 (21.3) | 429 (27.3) | 710 (19.3) |
| Stage 3–4 CKD, n (%) | 108 (8.5) | 150 (2.5) | 98 (6.3) | 52 (1.2) |
| 10-γ ASCVD risk, n (%) | 17.0±0.8 | 5.2±0.2 | 14.6±0.4 | 2.0±0.1 |
| ASCVD, n (%) | 252 (23.2) | 242 (3.3) | 242 (12.8) | 0 (0) |

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; HbA1c, 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\(_{10}\) \(\geq\)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 \(\geq\)7.5% Taking Moderate- or High-Intensity Statins**

Adults with diabetes mellitus and ASCVD\(_{10}\) risk \(\geq\)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 \(\geq\)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).

**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\(_{10}\), 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 \(\geq\)190                | 142       | 5 016 479     | High            | 9.5                       | 478 091                 | 207 871        | 270 220       | 63.6 | 5.4  | 19 |
| \(\oplus\) DM ASCVD\(_{10}\) \(\geq\)7.5% | 273       | 5 435 130     | Moderate-high\* | 20.3                      | 1 102 617               | 751 566        | 351 051       | 35.0 | 6.5  | 15 |
| \(\oplus\) DM ASCVD\(_{10}\) \(<\)7.5% | 99        | 3 229 536     | Moderate         | 4.3                       | 138 162                 | 94 013         | 44 148        | 32.2 | 1.4  | 73 |
| \(\oplus\) DM ASCVD\(_{10}\) \(\geq\)7.5% | 589       | 16 022 464    | Moderate-High\† | 13.5                      | 2 161 319               | 1 228 995      | 932 324       | 44.8 | 5.8  | 17 |
| \(\oplus\) DM ASCVD\(_{10}\) \(\leq\)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      | 4 484 712     |                | 14.6                      | 6 569 024               | 4 133 133      | 2 435 890     | 41.1 | 5.4  | 18 |
| Only ASCVD\(_{10}\) \(\geq\)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\(_{10}\) \(\geq\)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\(_{10}\) \(\geq\)7.5% | 623       | 16 104 254    |                | 18.1                      | 2 920 220               | 1 830 348      | 1 089 872     | 43.5 | 6.8  | 15 |
| Only ASCVD\(_{10}\) \(<\)7.5%   | 188       | 6 317 602     |                | 5.8                       | 364 292                 | 236 218        | 128 074       | 35.0 | 2.0  | 49 |

ASCVD indicates atherosclerotic cardiovascular disease. \(\oplus\) Statin ASCVD\(_{10}\), n indicates number of ASCVD events over 10 years with statins; \(\oplus\)DM, DM present; \(\oplus\)DM, DM absent; \(\%\)Statin ASCVD\(_{10}\), 10-year ASCVD risk without a statin; \(\%\)Statin ASCVD\(_{10}\), n, number of ASCVD events over 10 years with 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 (\(\oplus\)) diabetes mellitus (DM) and ASCVD\(_{10}\) \(\geq\)7.5% receive high-intensity and 50% receive moderate-intensity statins.

\‡Seven percent of patients with (\(\oplus\)) diabetes mellitus receive high-intensity and 25% receive moderate-intensity statins.

\†Includes ASCVD, LDL \(\geq\)190, and patients with and without diabetes mellitus and 10-year ASCVD risk (ASCVD\(_{10}\)) \(\geq\)7.5% and excludes lower-risk participants with (\(\oplus\)) diabetes mellitus (DM) and ASCVD\(_{10}\) \(<\)7.5% and without (\(\oplus\)) diabetes mellitus (DM) and ASCVD\(_{10}\) \(\leq\)7.4%.

\§Includes only lower-risk participants with diabetes mellitus and ASCVD\(_{10}\) \(<\)7.5% and without diabetes and ASCVD\(_{10}\) \(\geq\)7.5%.

**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 \(\approx\) 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 \(\approx\) 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 \(\geq\)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 \(\approx\) 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
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 ASCVD10 risk of
7.5% to <10% was estimated at $37,000.10 Lowering the treatment threshold further to an ASCVD10 of 4.0% raised the cost/quality-adjusted life-year to $81,000. Treating all adults ≥75 years old with ASCVD10 ≥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 ASCVD10 ≥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

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**Table 5.** Sensitivity Analysis on Percentages of Adults With and Without Diabetes Mellitus and ASCVD10 ≥7.5%* Taking High- and Moderate-Intensity Statins

| Statin Eligible Group | Sample, n | Population, N | Statin Intensity | ASCVD10, % | Change ASCVD10, n | ASCVD10, n | RRR, % | ARR, % | NNT |
|-----------------------|-----------|---------------|-----------------|------------|------------------|-----------|--------|--------|-----|
| 100% Moderate-intensity statin | | | | | | | | | |
| ≥DM ASCVD10 ≥7.5%† | 273 | 5435130 | Moderate | 20.3 | 1162617 | 814563 | 288504 | 28.8 | 5.3 | 19 |
| ≥DM ASCVD10 ≥7.5%† | 589 | 16022464 | Moderate | 13.5 | 2161319 | 1450004 | 711316 | 34.3 | 4.4 | 23 |
| 75% Moderate- and 25% high-intensity statin | | | | | | | | | |
| ≥DM ASCVD10 ≥7.5%† | 273 | 5435130 | Moderate-high | 20.3 | 1162617 | 782347 | 320270 | 32.0 | 5.9 | 17 |
| ≥DM ASCVD10 ≥7.5%† | 589 | 16022464 | Moderate-high | 13.5 | 2161319 | 1374589 | 786730 | 37.9 | 4.9 | 20 |
| 50% Moderate- and 50% high-intensity statin | | | | | | | | | |
| ≥DM ASCVD10 ≥7.5%† | 273 | 5435130 | Moderate-high | 20.3 | 1162617 | 751566 | 351051 | 35.0 | 6.5 | 15 |
| ≥DM ASCVD10 ≥7.5%† | 589 | 16022464 | Moderate-high | 13.5 | 2161319 | 1303415 | 857905 | 41.3 | 5.4 | 19 |
| 25% Moderate- and 75% high-intensity statin | | | | | | | | | |
| ≥DM ASCVD10 ≥7.5%† | 273 | 5435130 | Moderate-high | 20.3 | 1162617 | 722149 | 380468 | 37.8 | 7.0 | 14 |
| ≥DM ASCVD10 ≥7.5%† | 589 | 16022464 | Moderate-high | 13.5 | 2161319 | 1228995 | 932324 | 44.8 | 5.8 | 17 |
| 100% High-intensity statin | | | | | | | | | |
| ≥DM ASCVD10 ≥7.5%† | 273 | 5435130 | High | 20.3 | 1162617 | 694028 | 408588 | 40.5 | 7.5 | 13 |
| ≥DM ASCVD10 ≥7.5%† | 589 | 16022464 | High | 13.5 | 2161319 | 1172783 | 988536 | 47.5 | 6.2 | 16 |

ASCVD indicates atherosclerotic cardiovascular disease; NNH, number needed-to-treat.

*Participants with (≥) diabetes mellitus (DM) and 10-year ASCVD risk (ASCVD10) <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 ASCVD10 ≥7.5% were included.

§Only participants without (≥) DM and ASCVD10 ≥7.5% were included.
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 $\geq 7.5\%$. 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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