

JAMA | Original Investigation

Projected Changes in Statin and Antihypertensive Therapy Eligibility With the AHA PREVENT Cardiovascular Risk Equations

James A. Diao, MD, MPhil; Ivy Shi, MD; Venkatesh L. Murthy, MD, PhD; Thomas A. Buckley, BS; Chirag J. Patel, PhD; Emma Pierson, PhD; Robert W. Yeh, MD, MSc; Dhruv S. Kazi, MD, MS; Rishi K. Wadhera, MD, MPP, MPhil; Arjun K. Manrai, PhD

IMPORTANCE Since 2013, the American College of Cardiology (ACC) and American Heart Association (AHA) have recommended the pooled cohort equations (PCEs) for estimating the 10-year risk of atherosclerotic cardiovascular disease (ASCVD). An AHA scientific advisory group recently developed the Predicting Risk of cardiovascular disease EVENTS (PREVENT) equations, which incorporated kidney measures, removed race as an input, and improved calibration in contemporary populations. PREVENT is known to produce ASCVD risk predictions that are lower than those produced by the PCEs, but the potential clinical implications have not been quantified.

OBJECTIVE To estimate the number of US adults who would experience changes in risk categorization, treatment eligibility, or clinical outcomes when applying PREVENT equations to existing ACC and AHA guidelines.

DESIGN, SETTING, AND PARTICIPANTS Nationally representative cross-sectional sample of 7765 US adults aged 30 to 79 years who participated in the National Health and Nutrition Examination Surveys of 2011 to March 2020, which had response rates ranging from 47% to 70%.

MAIN OUTCOMES AND MEASURES Differences in predicted 10-year ASCVD risk, ACC and AHA risk categorization, eligibility for statin or antihypertensive therapy, and projected occurrences of myocardial infarction or stroke.

RESULTS In a nationally representative sample of 7765 US adults aged 30 to 79 years (median age, 53 years; 51.3% women), it was estimated that using PREVENT equations would reclassify approximately half of US adults to lower ACC and AHA risk categories (53.0% [95% CI, 51.2%-54.8%]) and very few US adults to higher risk categories (0.41% [95% CI, 0.25%-0.62%]). The number of US adults receiving or recommended for preventive treatment would decrease by an estimated 14.3 million (95% CI, 12.6 million-15.9 million) for statin therapy and 2.62 million (95% CI, 2.02 million-3.21 million) for antihypertensive therapy. The study estimated that, over 10 years, these decreases in treatment eligibility could result in 107 000 additional occurrences of myocardial infarction or stroke. Eligibility changes would affect twice as many men as women and a greater proportion of Black adults than White adults.

CONCLUSION AND RELEVANCE By assigning lower ASCVD risk predictions, application of the PREVENT equations to existing treatment thresholds could reduce eligibility for statin and antihypertensive therapy among 15.8 million US adults.

JAMA. 2024;332(12):989-1000. doi:10.1001/jama.2024.12537
Published online July 29, 2024.

◀ Viewpoint page 961 and Editorial page 967

+ Supplemental content

+ CME Quiz at jamacmelookup.com

Author Affiliations: Author affiliations are listed at the end of this article.

Corresponding Author: Arjun K. Manrai, PhD, Department of Biomedical Informatics, Harvard Medical School, 10 Shattuck St, Boston, MA 02115 (Arjun_Manrai@hms.harvard.edu).

The global burden of atherosclerotic cardiovascular disease (ASCVD) necessitates attention to modifiable risk factors, including elevated blood pressure and low-density lipoprotein (LDL) cholesterol levels.¹ Since 2013, the American College of Cardiology (ACC) and American Heart Association (AHA) have recommended statin therapy for primary prevention based on 10-year ASCVD risk, as calculated using the pooled cohort equations (PCEs).^{2,3} In 2017 and 2018, the ACC and AHA issued additional risk-based guidelines for primary prevention with blood pressure medications or high-intensity statins.³⁻⁵ Although influential, the PCEs underlying these guidelines have faced scrutiny over potential overestimation of risk,⁶ omission of important kidney and metabolic factors,^{7,8} and the inclusion of Black race as an input.^{9,10}

In response, an AHA scientific advisory group developed the Predicting Risk of cardiovascular disease EVENTS (PREVENT) equations in 2023.¹¹ Compared with the PCEs, the new PREVENT equations for ASCVD incorporate the estimated glomerular filtration rate (eGFR), extend the accepted age range to include younger adults, and no longer use race as an input.^{11,12} Whereas the PCEs were developed using 5 research cohort studies,² PREVENT was developed using larger and more recent datasets derived from both research cohort studies and electronic medical records.^{11,12} Validation data reported by the PREVENT investigators showed improved calibration in contemporary populations,¹¹ but questions remain regarding external validity given the limitations of electronic medical record data^{13,14} and following recent increases in cardiovascular disease mortality.¹⁵

Although PREVENT has not yet been recommended to replace the PCEs, the rationale supporting current treatment thresholds does not depend on the choice of risk equation, and an accompanying AHA scientific statement asserted that “the risk assessed by PREVENT may be implemented in the existing ACC/AHA prevention guideline framework.”¹² Using nationally representative data from the National Health and Nutrition Examination Surveys (NHANES) of 2011 to March 2020,¹⁶ this study sought to estimate the number of US adults who may experience changes in risk categories, treatment eligibility, or clinical outcomes if PREVENT were to be recommended without concomitant changes to treatment criteria.

Methods

Study Population

We analyzed data from NHANES 2011 to 2020, comprising serial cross-sectional samples of the civilian noninstitutionalized US population. These data included questionnaire responses, including age, gender, race and ethnicity, and medical history; physical examination measurements, including blood pressure levels; laboratory testing results, including serum cholesterol levels; and prescription medication data. Details on the categorization of self-reported race and ethnicity are provided in the eMethods in Supplement 1. NHANES suspended collection of the 2019 to 2020 survey cycle in March 2020 due to the COVID-19 pandemic. These incomplete data from 2019 to 2020 were combined with survey data from preceding years to create a nationally representative prepanemic sample.

Key Points

Question How many US adults are estimated to experience changes in treatment eligibility when evaluated using the American Heart Association Predicting Risk of cardiovascular disease EVENTS (PREVENT) equations vs the pooled cohort equations?

Findings In this nationally representative study of 7765 US adults aged 30 to 79 years, it was estimated that using PREVENT would decrease the number of US adults receiving or recommended for statin therapy by 14.3 million and antihypertensive therapy by 2.62 million. Over 10 years, reductions in treatment eligibility could result in an estimated 107 000 additional occurrences of myocardial infarction or stroke.

Meaning Application of the PREVENT equations to current risk-based treatment thresholds could reduce eligibility for statin and antihypertensive therapy among 15.8 million US adults, with substantial implications for public health.

Our study used data from participants examined in a morning session after fasting at least 8.5 hours. From this subsample, we excluded participants with self-reported age younger than 30 years or older than 79 years, self-reported pregnancy, or positive urinary pregnancy test results. We also excluded participants with missing values for serum creatinine, which is needed to calculate eGFR; total or high-density lipoprotein cholesterol, which are required inputs for both risk equations; or triglycerides, which are needed to estimate LDL cholesterol levels using the Martin-Hopkins method.¹⁷ We excluded participants with triglyceride levels above 400 mg/dL because the Martin-Hopkins method is not recommended above this threshold. Written informed consent was obtained following protocols approved by the National Center for Health Statistics.

Statistical Analyses

We calculated 10-year ASCVD risk predictions using the PCEs among participants aged 40 to 79 years without prior myocardial infarction or stroke and using PREVENT equations among participants aged 30 to 79 years without prior myocardial infarction, stroke, or heart failure. We did not calculate other outputs of the PREVENT equations, which include the 30-year risk of ASCVD or the 10- or 30-year risks of heart failure or total cardiovascular disease. Further details about each risk equation and their implementation are provided in the eMethods in Supplement 1. We then compared risk predictions among participants with valid inputs for both the PCEs and PREVENT, including those aged 40 to 79 years with no history of myocardial infarction, stroke, or heart failure. Lines of best fit were calculated using ordinary least squares with zero intercept to analyze calibration differences. A regression slope of more than 1 indicates that PREVENT assigned higher risk estimates, whereas a slope of less than 1 indicates that the PCEs assigned higher risk estimates.

We estimated the number of US adults classified in each ACC/AHA risk category when using either PREVENT or the PCEs. Categories included low risk (<5.0%), borderline risk (5.0% to <7.5%), intermediate risk (7.5% to <20%), and high risk (≥20%). We then estimated eligibility for statin and antihypertensive therapy using Class I recommendations from the

2019 ACC/AHA guidelines on primary prevention,⁵ with eligibility criteria detailed in the eMethods in [Supplement 1](#). We defined treatment eligibility as individuals receiving or recommended for treatment, following the approach used by Pencina et al.¹⁸ Based on this definition, individuals already receiving treatment were included in eligibility counts for both PREVENT and the PCEs and therefore did not contribute to estimates of eligibility differences. However, some of these individuals who qualified for risk-based treatment when evaluated using the PCEs may not have qualified when evaluated using PREVENT. To balance this conservative analysis, we conducted a sensitivity analysis that modeled treated individuals as untreated by adjusting their measured blood pressure and cholesterol levels based on the expected changes from blood pressure medications¹⁹ and lipid-lowering medications²⁰⁻²² (eMethods in [Supplement 1](#)).

We estimated the expected clinical outcomes of eligibility changes for statin or antihypertensive therapy, including changes to the 10-year incidence of ASCVD events and new-onset diabetes. To calculate changes in the number of US adults receiving treatment, we multiplied the number of US adults with eligibility changes by adherence rates to treatment guidelines for primary prevention. Guideline adherence rates for each treatment were calculated as the proportion of US adults receiving treatment among those recommended for treatment after applying blood pressure and cholesterol adjustments to model baseline untreated values. To estimate the change in 10-year incidence for ASCVD events, we summed the absolute risk reductions that would no longer be accrued in the newly ineligible population. Absolute risk reductions were derived by multiplying the relative risk reduction associated with therapy²³⁻²⁵ by each patient's absolute risk as calculated using PREVENT. The increase in 10-year incidence for new-onset diabetes associated with statin therapy was assumed to be 1% based on randomized trial data.^{24,25} Further details are provided in the eMethods and in [eTable 3 in Supplement 1](#).

Lastly, we compared the populations eligible for statin therapy when assessed using PREVENT or the PCEs by characterizing their respective demographic and risk profiles among untreated US adults with no other indications for statin therapy. We also estimated the number of US adults eligible for statin or antihypertensive therapy when varying the risk-based treatment threshold. Population-wide estimates and CIs were adjusted using the NHANES survey weights and design for the fasting subsample. Survey weights were combined across survey cycles and scaled to the April 2020 US Census count for adults aged 30 to 79 years (eMethods in [Supplement 1](#)). This study adhered to Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines for cross-sectional studies.

Results

Study Sample

Of the 45 462 individuals participating in NHANES cycles spanning 2011 to March 2020, 20 205 (44.4%) were aged 30 to 79 years. Among this age range, the fasting subsample was com-

posed of 8459 individuals. A total of 694 participants were excluded, including 420 (5.0%) with missing blood pressure measurements, 119 (1.4%) with missing cholesterol or serum creatinine measurements, 117 (1.4%) with triglyceride levels greater than 400 mg/dL, and 38 (0.45%) who were pregnant. The final study sample was composed of 7765 participants representing 187 million US adults, including expected proportions across gender (51.3% women) and age (median 53 ± 13 years) and with oversampling of racial and ethnic minoritized groups (24.7% Hispanic, 22.9% Black, and 13.4% Asian participants) ([Table](#)). Additional data on demographics, medical conditions, laboratory measures, and medications are provided in [eTable 1 in Supplement 1](#). Characteristics of the 545 participants (7.0%) with out-of-range laboratory values are provided in [eTable 2 in Supplement 1](#).

Comparison of Predicted Risk

Participants with valid risk estimates from both the PCEs and PREVENT included those aged 40 to 79 years with no history of myocardial infarction, stroke, or heart failure. Among this population, 10-year ASCVD risk estimates calculated using PREVENT were lower than those calculated using the PCEs across all subgroups of age, gender, and race and ethnicity ([Figure 1](#)). After survey adjustment, the mean 10-year ASCVD risk calculated using PREVENT was lower than the mean risk calculated using the PCEs (4.6% and 9.0%, respectively). Similarly, the survey-weighted regression slope of 10-year ASCVD risk calculated using PREVENT compared with that calculated using the PCEs was 0.43 (95% CI, 0.42-0.44), indicating lower risk predictions when using PREVENT.

Bland-Altman analysis showed smaller differences in predicted risk between the PCEs and PREVENT among persons at low risk and greater differences among persons at high risk ([eFigure 1 in Supplement 1](#)). Relatedly, Black, male, and older persons aged 70 to 79 years would experience larger decreases in risk (regression slopes of 0.41, 0.42, and 0.39, respectively) compared with Hispanic persons, women, and younger persons aged 40 to 49 years (regression slopes of 0.44, 0.45, and 0.53, respectively; [eFigure 2 in Supplement 1](#)). Most US adults would be assigned lower risk by PREVENT than the PCEs ([Figure 2A](#)), resulting in discordant treatment recommendations ([Figure 2B, 2C, and 2D](#)). Of US adults aged 40 to 79 years with no history of myocardial infarction, stroke, or heart failure, 53.0% (95% CI, 51.2%-54.8%) would be assigned to lower risk categories, although 0.41% (95% CI, 0.25%-0.62%) would be assigned to higher risk categories.

Eligibility for Statin Therapy

The ASCVD risk threshold of 7.5% or above is used to determine ACC/AHA recommendations for statin therapy. Among those recommended for but not receiving statin therapy, the most common indication was predicted risk as calculated using the PCEs ([eFigure 3B in Supplement 1](#)); less common indications included diabetes, prior ASCVD, and LDL cholesterol level of 190 mg/dL or above. The number of US adults receiving or recommended for statin therapy would be 67.5 million when using PREVENT compared with 81.8 million when using the PCEs (difference, -14.3 million [95% CI, -15.9 million to

Table. Demographic and Risk Profiles by Statin Eligibility Among US Adults Without Atherosclerotic Cardiovascular Disease (ASCVD), Diabetes, or Statin Use and Among the Total Sample^a

Characteristic ^b	Eligible with PCEs (n = 909)	Eligible with PREVENT (n = 277)	Newly eligible (n = 4)	No longer eligible (n = 636)	Total sample (N = 7765)
2020 US population equivalent, No. ^c	19 293 410	5 020 612	36 968	14 309 766	187 185 493
Gender, %					
Women	33.5	42.3	81.0	30.5	51.4
Men	66.5	57.7	19.0	69.5	48.6
Median age (SD), y	64 (7.8)	70 (5.6)	68 (13.0)	63 (7.5)	52 (13.1)
Age, %					
30-39 y					22.4
40-49 y	6.7	0.4	33.8	9.0	22.6
50-59 y	23.4	6.3		29.4	23.7
60-69 y	48.7	41.0	19.6	51.4	21.0
70-75 y	21.1	52.2	46.6	10.2	7.2
76-79 y					3.2
Race and ethnicity, % ^d					
Asian	4.7	4.4		4.7	5.5
Black	14.1	13.3	80.4	14.5	11.1
Hispanic	10.0	11.5	19.6	9.4	14.0
White	69.3	69.3		69.1	66.0
Other race	2.0	1.5		2.2	3.4
Median 10-y ASCVD risk (SD), %					
PCEs	12.0 (5.6)	18.8 (6.4)	6.8 (1.8)	10.4 (2.9)	5.4 (10.3)
PREVENT	6.1 (2.5)	9.4 (2.1)	10.2 (2.5)	5.3 (1.3)	2.2 (4.0)

Abbreviations: LDL, low-density lipoprotein; PCEs, pooled cohort equations; PREVENT, Predicting Risk of cardiovascular disease EVENTS.

^a Eligibility for statin therapy was determined based on 10-year ASCVD risk $\geq 7.5\%$, as calculated using the PCEs or PREVENT equations, among those aged 40-75 years with LDL cholesterol levels between 70 and 189 mg/dL.

^b Additional characteristics are provided in eTable 1 in Supplement 1, including presence of obesity, chronic kidney disease, hypertension, or diabetes; median values for body mass index, serum creatinine, estimated glomerular filtration rate, systolic blood pressure, hemoglobin A_{1c}, and LDL cholesterol; smoking status; and medications for blood pressure and cholesterol.

^c Data from the National Health and Nutrition Examination Survey 2011-2020 were survey adjusted to represent the 2020 US population (total sample column) or the population of US adults not receiving statins and without indications for statin therapy (remaining columns).

^d Categories for race and ethnicity are mutually exclusive and were derived from self-reported survey responses. Respondents who self-identified as Hispanic were categorized as Hispanic American. The remaining participants were categorized as non-Hispanic Asian, non-Hispanic Black, non-Hispanic White, or other race, including multiracial. The non-Hispanic descriptor was omitted for brevity.

–12.6 million]; **Figure 3A**). Most of this decline would occur among men and adults aged 50 to 69 years. Black adults would become ineligible at higher rates than White adults (–9.9% vs –8.0%, respectively). Cross-stratifications of statin eligibility by age, gender, and eGFR stage are shown in eFigure 4A-4C in Supplement 1.

The number of US adults receiving statins or recommended for high-intensity statin therapy would be 51.1 million when using PREVENT compared with 55.9 million when using the PCEs. As a result, 4.77 million (95% CI, 3.99 million–5.54 million) US adults would be recommended for initiation of moderate-intensity rather than high-intensity statins (eFigure 5 in Supplement 1). This difference encompasses 92.8% (95% CI, 90.0%–95.7%) of instances where high-intensity statin initiation would have been recommended based on ASCVD risk as calculated using the PCEs.

Eligibility for Antihypertensive Therapy

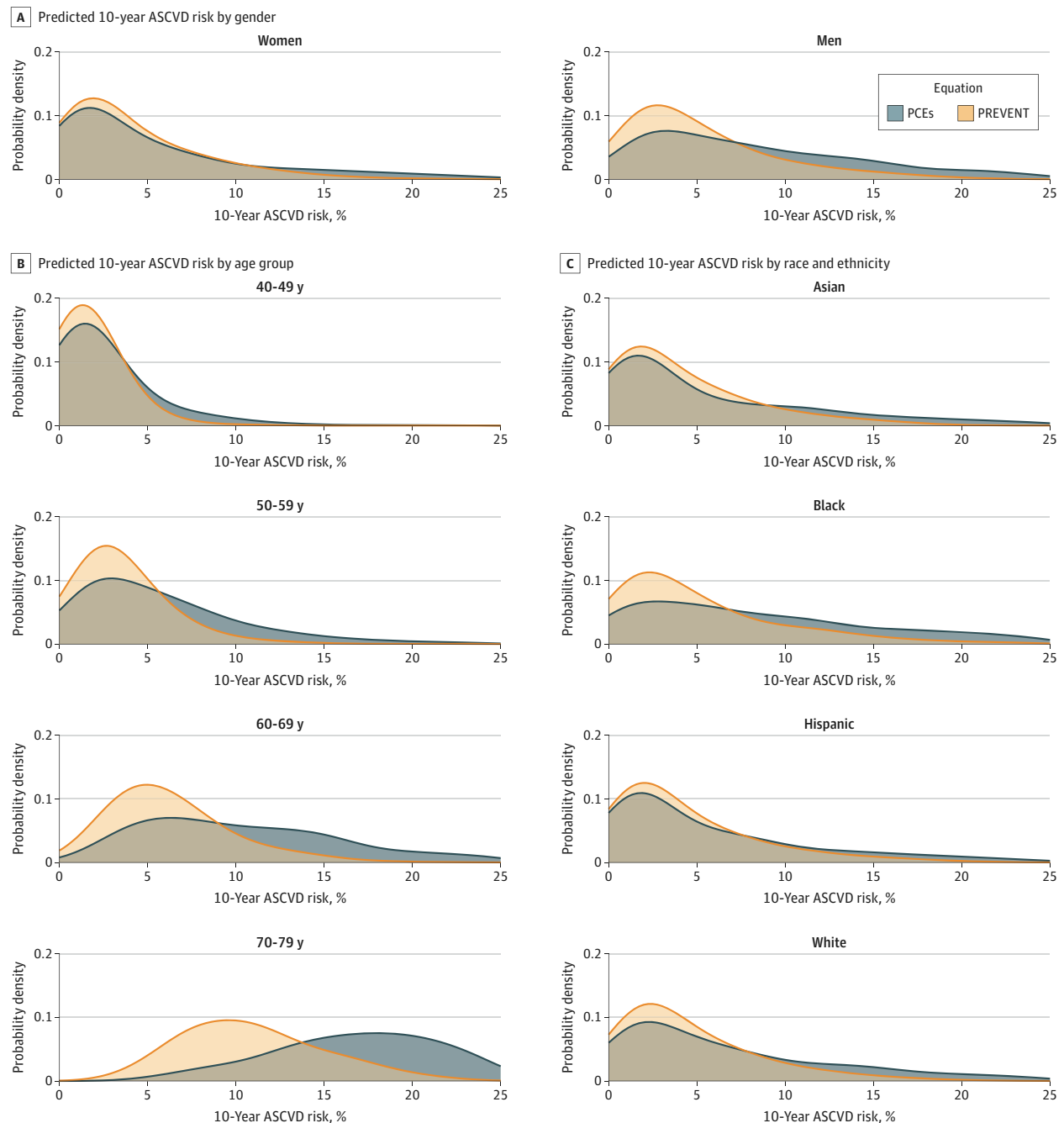
Of US adults recommended for but not receiving antihypertensive therapy, many more qualified due to blood pressure alone than due to predicted ASCVD risk of 10% or above (eFig-

ure 3C in Supplement 1). The number of US adults receiving or recommended for antihypertensive therapy would be 72.7 million when using PREVENT compared with 75.3 million when using the PCEs (difference, –2.62 million [95% CI, –3.21 million to –2.02 million]; **Figure 3B**). As with statin eligibility, most of this decline in antihypertensive therapy eligibility would occur among men and adults aged 50 to 69 years, and a greater proportion of Black adults would become ineligible compared with White adults (–2.0% vs –1.4%). The number of US adults with loss of recommended eligibility for either statin therapy or antihypertensive therapy was estimated as 15.8 million (95% CI, 14.2 million–17.6 million). Sensitivity analyses that excluded participants with out-of-range laboratory values showed similar eligibility differences for both statin and antihypertensive therapy (eFigure 6 in Supplement 1).

Implications for New ASCVD Events and New-Onset Diabetes

It was estimated that 40.5% of US adults recommended for primary prevention with statin therapy were receiving statins. If this guideline adherence rate were to remain unchanged, then

Figure 1. Marginal Distributions for Predicted 10-Year ASCVD Risk by Gender, Age, and Race and Ethnicity Among US Adults Aged 40-79 Years With No History of Myocardial Infarction, Stroke, or Heart Failure



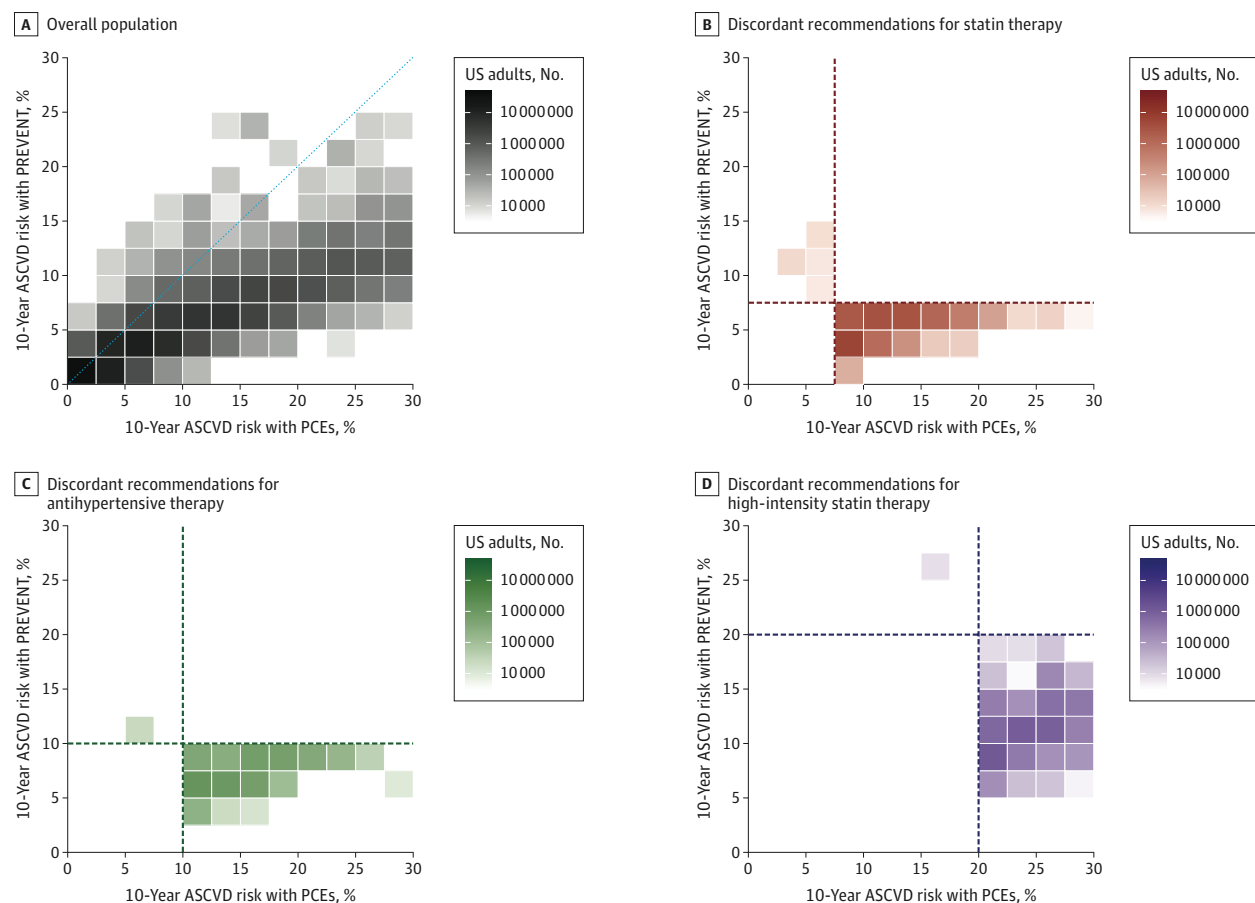
A, Probability density distributions for 10-year atherosclerotic cardiovascular disease (ASCVD) risk as calculated using the pooled cohort equations (PCEs) and Predicting Risk of cardiovascular disease EVENTS (PREVENT) equations among men and women aged 40-79 years with no history of myocardial infarction, stroke, or heart failure. Data from National Health and Nutrition Examination Survey 2011-2020 were survey adjusted to represent the 2020 US population. B, Same as A, but stratified by age group. C, Same as A, but

stratified by race and ethnicity. Categories for race and ethnicity are mutually exclusive and were derived from self-reported survey responses. Respondents who self-identified as Hispanic were categorized as Hispanic American. The remaining participants were categorized as non-Hispanic Asian, non-Hispanic Black, non-Hispanic White, or other race, including multiracial. The non-Hispanic descriptor was omitted for brevity.

the 14.3 million fewer recommendations for statin therapy associated with using PREVENT would translate to 5.78 million fewer US adults receiving statins and benefiting from the 25%

relative risk reduction for ASCVD (eTable 3 in Supplement 1). It was estimated that, over 10 years, this decrease in statin use would result in 77 000 additional ASCVD events and 57 800

Figure 2. Joint Distribution of Predicted 10-Year Atherosclerotic Cardiovascular Disease (ASCVD) Risk and Discordance in ACC/AHA Treatment Recommendations for Primary Prevention Among US Adults Aged 40-79 Years With No History of Myocardial Infarction, Stroke, or Heart Failure



A, Cross-tabulation of US adults according to 10-year predicted ASCVD risk as calculated using the pooled cohort equations (PCEs) or Predicting Risk of cardiovascular disease EVENTS (PREVENT) equations among US adults aged 40-79 years with no history of myocardial infarction, stroke, or heart failure. Cells are shaded according to total projected population count. The dotted blue line represents concordance between the 2 equations. B, Same as A, but only showing US adults with discordant recommendations for statin therapy between the PCEs and PREVENT equations. Recommendations from the American College of Cardiology (ACC) and American Heart Association (AHA) were determined based on prior myocardial infarction (MI) or stroke, low-density lipoprotein (LDL) cholesterol levels ≥ 190 mg/dL, diabetes among adults aged 40-75 years with LDL cholesterol levels between 70 and 189 mg/dL, or predicted ASCVD risk $\geq 7.5\%$ among adults aged 40-75 years with LDL cholesterol levels between 70 and 189 mg/dL. Dashed lines indicate treatment thresholds of $\geq 7.5\%$. Cholesterol values were adjusted among

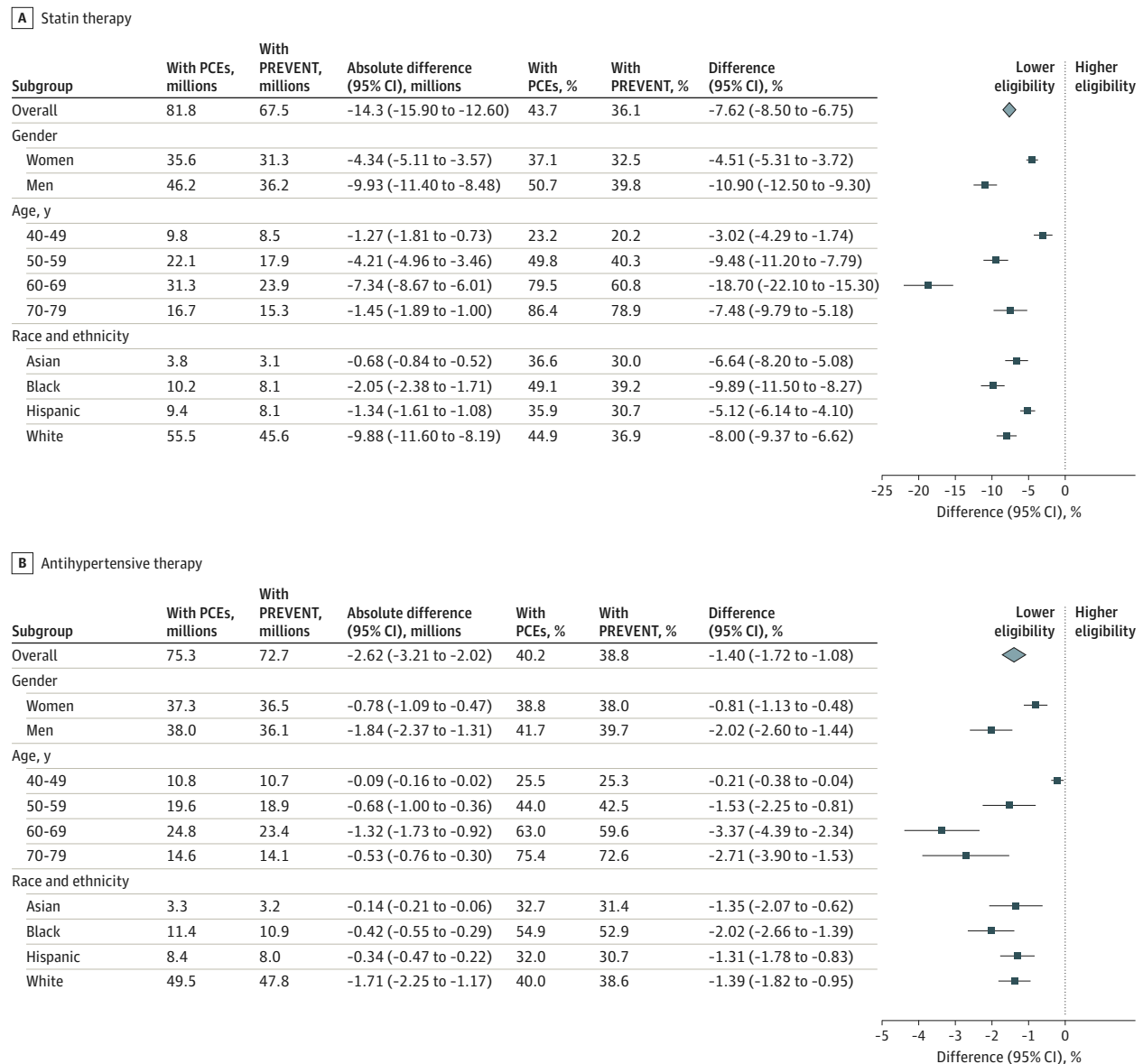
participants receiving lipid-lowering therapies to model baseline untreated values. C, Same as B, but showing US adults with discordant ACC/AHA recommendations for blood pressure (BP)-lowering medication based on stage 2 hypertension ($\geq 140/90$ mm Hg) or stage 1 hypertension ($\geq 130/80$ mm Hg) with either prior MI or stroke or predicted risk $\geq 10\%$. Dashed lines indicate treatment thresholds of $\geq 10\%$. BP values were adjusted among participants receiving antihypertensive therapy to model baseline untreated values. D, Same as B, but showing US adults with discordant ACC/AHA recommendations for high-intensity statin therapy based on prior MI or stroke, LDL cholesterol ≥ 190 mg/dL, or predicted ASCVD risk $\geq 20\%$ among adults aged 40-75 years with LDL cholesterol levels between 70 and 189 mg/dL. Dashed lines indicate treatment thresholds of $\geq 20\%$. Cholesterol values were adjusted among participants receiving lipid-lowering therapies to model baseline untreated values.

fewer occurrences of new-onset diabetes. Similarly, it was estimated that 2.62 million fewer recommendations for antihypertensive therapy would result in 1.74 million fewer US adults (66.6%) receiving blood pressure medications and 31 600 additional ASCVD events (eTable 3 in Supplement 1). After accounting for the multiplicative nature of successive risk reduction, eligibility changes to both statin and antihypertensive therapies would result in an estimated 107 000 additional ASCVD events, affecting more men than women (0.077% vs 0.039%), but similar proportions of Black and White adults (0.062% vs 0.065%).

Treatment Eligibility With Adjustments for Treated Persons

When applying adjustments among treated persons to model their baseline untreated values, additional instances of discordant treatment recommendations were identified. Based on this sensitivity analysis, decreases in statin eligibility were estimated to affect 19.4 million US adults, reflecting an additional 5.1 million individuals who are receiving statins but would not have been eligible for initiation of statin therapy based on their projected pretreatment risk (eFigure 7A in Supplement 1). Similarly, decreases in eligibility for antihypertensive medications were estimated to affect 6.39 million

Figure 3. Projected Differences in Number and Proportion of US Adults Receiving or Recommended for Statin or Antihypertensive Therapies



A, Estimated number, proportion, absolute difference, and proportion difference in US adults receiving or recommended for statin therapy when 10-year atherosclerotic cardiovascular disease (ASCVD) risk is calculated using the Predicting Risk of cardiovascular disease EVENTS (PREVENT) equations as compared with the pooled cohort equations (PCEs). Data from National Health and Nutrition Examination Survey 2011-2020 were survey adjusted to represent

the 2020 US population. B, Same as A, but for US adults receiving or recommended for antihypertensive therapy. Data showing differences for high-intensity statin therapy, with exclusion of out-of-range laboratory values or with adjustments for treated persons, are shown in eFigures 5-7 in Supplement 1.

US adults, reflecting an additional 3.77 million individuals who are receiving blood pressure medications but would not have been eligible for initiation of antihypertensive therapy based on their projected pretreatment risk (eFigure 7B in Supplement 1). Compared with the main analysis, this represents an additional 7.93 million individuals with eligibility changes for either statin or antihypertensive therapy and 77 500 additional ASCVD events over 10 years (eTable 3 in Supplement 1).

Risk Profiles by Eligibility

The Table shows the demographic and risk profiles of US adults who would be recommended for risk-based statin initiation among those not taking statins and with no other indications for statin therapy. Only 4 participants in the sample, representing 37 000 US adults, became newly eligible for statin therapy when switching from the PCEs to PREVENT; all 4 had reduced kidney function with a median eGFR of 23 mL/min/1.73 m².

By contrast, 636 participants, representing 14.3 million US adults, would no longer be recommended statin therapy due to differences in predicted risk between PREVENT and the PCEs (median risks of 5.3% and 10.4%; Table). Newly ineligible persons had fewer risk factors compared with those who remained eligible, including decreased prevalence of obesity, hypertension, and chronic kidney disease (eTable 1 in Supplement 1).

Eligibility Counts by Choice of Risk Threshold

As the simulated risk threshold for statin therapy was increased from 0% toward 100%, eligibility counts decreased from 142 million eligible individuals toward 62.5 million, with the steepest changes occurring between risk thresholds of 0% and 10% (Figure 4A). The maximum eligibility difference was observed at a risk threshold of 5.0%, with 15.6 million individuals eligible under the PCEs but not PREVENT. A similar pattern was observed when analyzing eligibility counts for antihypertensive therapy, with the maximum eligibility difference of 3.80 million individuals observed at a risk threshold of 5.5% (Figure 4B). Sensitivity analyses that analyzed treatment recommendations with adjustments for treated persons (Figure 4C and 4D) showed similar trends with wider eligibility differences between PREVENT and the PCEs.

Discussion

US guidelines for the primary prevention of ASCVD have evolved considerably over the past decade. Between 2013 and 2019, the ACC and AHA recommended several new strategies based on absolute risk³⁻⁵ that expanded treatment indications beyond prior strategies based on cholesterol and blood pressure targets alone.²⁶ By moving individuals below existing treatment thresholds, PREVENT could reduce the number of US adults receiving or recommended for statin therapy by an estimated 14.3 million compared with the PCEs. This decrease would effectively reverse the expansion in statin eligibility introduced by the 2013 ACC/AHA guidelines, which affected an estimated 12.8 million US adults.¹⁸ It was also estimated that 4.77 million US adults would be recommended for initiation of statin therapy with moderate-intensity rather than high-intensity statins, including nearly all instances (92.8%) where high-intensity statins would have been recommended based on the PCEs. A smaller reduction of 2.62 million was estimated for the number receiving or recommended for antihypertensive therapy, likely owing to the narrow blood pressure range at which risk-based criteria are applied.

Changes in eligibility for preventive therapies carry the potential for both benefit and harm. On the one hand, reduction of LDL cholesterol levels results in decreased cardiovascular risk at all baseline levels of LDL cholesterol,²⁷⁻³¹ and recent data suggest that these low-cost³² and highly effective drugs³³ remain underprescribed in the US population.^{34,35} Reduced eligibility for and dosages of statin therapy therefore raise concerns about decreased lipid control contributing to greater ASCVD burden. On the other hand, overtreatment in low-risk populations may result in adverse effects, such as increased diabetes risk,³⁶ which

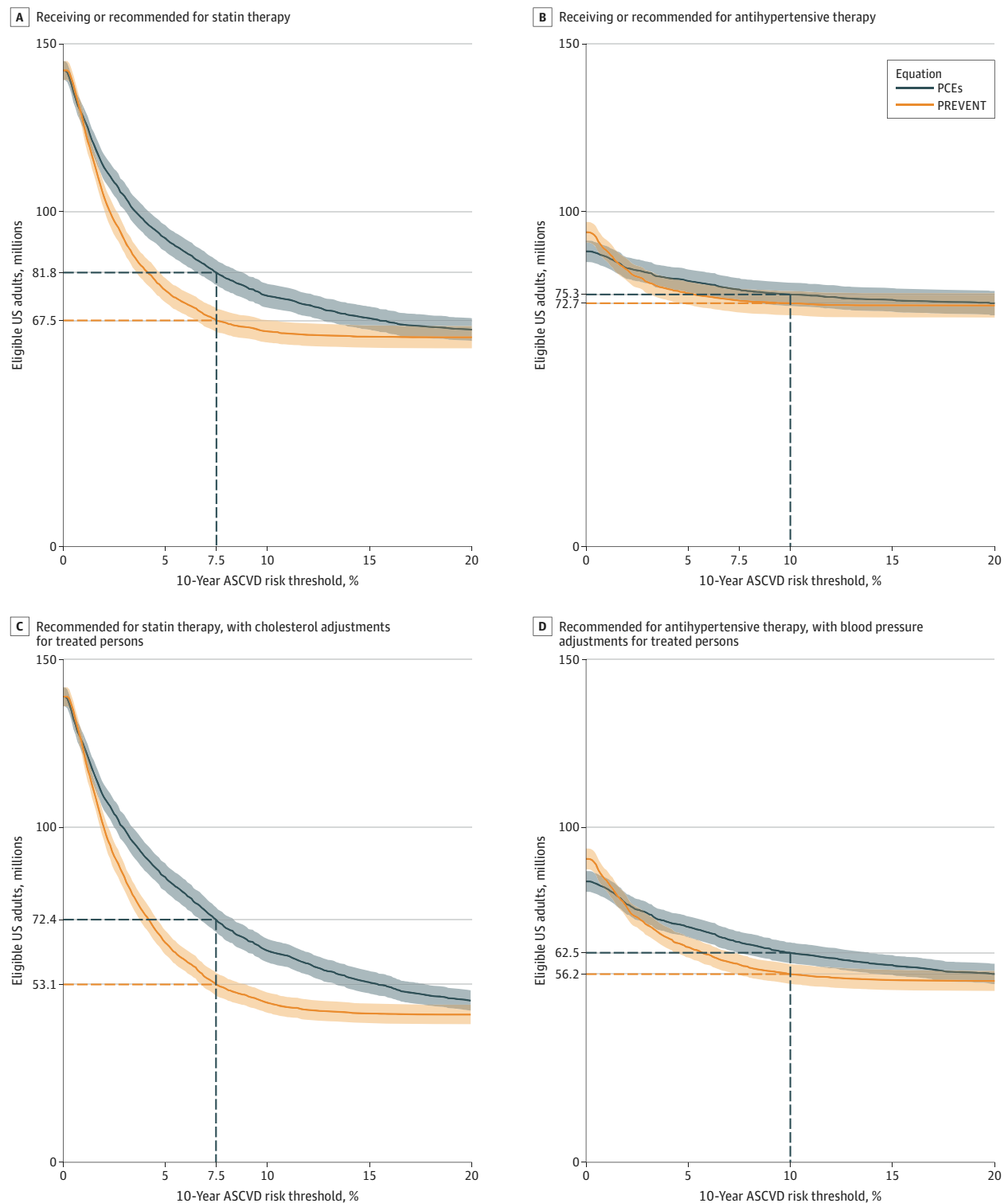
is part of the justification for more conservative risk thresholds recommended by some organizations.^{36,37} Similar trade-offs exist when considering the pharmacologic treatment of hypertension, which targets the modifiable risk factor contributing most to ASCVD deaths,³⁸ but may also cause orthostatic hypotension, organ ischemia, or sexual dysfunction.³⁹ The study estimated that, over 10 years, decreases in statin and antihypertensive therapy eligibility could result in 107 000 additional cases of myocardial infarction or stroke and 57 800 fewer cases of new-onset diabetes.

These results did not include young adults aged 30 to 39 years, who are not recommended for primary prevention regardless of ASCVD risk. However, the inclusion of these younger ages as acceptable age inputs for the PREVENT equations is noteworthy, especially in light of growing evidence that long-term achievement of lower LDL cholesterol levels is associated with improved cardiovascular outcomes.^{40,41} The study found that young adults would mostly be assigned low risk by PREVENT, with almost none aged 30 to 39 years exceeding a risk threshold of 7.5%. Although risk estimates earlier in life may still provide valuable information for counseling patients, our results suggest that very few young adults would be recommended for pharmacologic intervention.

The implications of removing race as an input also warrant discussion. The PCEs were developed using a gender- and race-stratified design to reflect differences in risk that persisted after controlling for other inputs.⁴² Race was removed because it is a social construct and an imprecise proxy for genetics, behaviors, or the effects of racism.^{9,10} Still, some were concerned that removal of race could degrade predictive performance and worsen disparities in statin prescribing.⁴³ Validation data for PREVENT showed greater underestimation of ASCVD risk among Black adults compared with White adults (calibration slopes of 1.26 and 1.06), a difference that was less pronounced for the race-calibrated PCEs (calibration slopes of 0.56 and 0.52).¹¹ These data are consistent with study findings of greater decreases in predicted risk and treatment eligibility for Black adults compared with White adults when using PREVENT. Differences by race were smaller than differences by age and gender, and the study did not find a significant difference in the proportions of Black and White adults who may experience additional myocardial infarction or stroke. Still, eligibility differences by race are concerning given longstanding disparities in cardiovascular disease treatment⁴⁴ and outcomes.⁴⁵ Future efforts are therefore needed to investigate and monitor for differential effects of new risk equations on medication prescribing and access.

Study estimates of eligibility changes and associated clinical outcomes are likely conservative. First, the main analysis did not consider eligibility changes among individuals currently receiving treatment. This may undercount individuals who were initiated on the basis of predicted risk with the PCEs, but would not have been initiated with PREVENT. Beyond the 15.8 million US adults with decreased eligibility and 107 000 ASCVD events projected in the main analysis, the study's sensitivity analysis estimated an additional 7.93 million adults who are currently receiving statins or blood pressure medications would not have been eligible for these treatments when

Figure 4. Estimated Number of US Adults Eligible for Statin or Antihypertensive Therapy by Choice of Risk Threshold



A, y-Axis shows number of US adults receiving or recommended for statin therapy when evaluated using ACC/AHA criteria, including predicted 10-year ASCVD risk higher than the corresponding risk threshold on the x-axis when calculated using the PCEs or PREVENT. Shading represents 95% CIs. Data from NHANES 2011-2020 were survey adjusted to represent the 2020 US population. B, Same as A, but for US adults receiving or recommended for antihypertensive therapy based

on ACC/AHA criteria, including predicted 10-year ASCVD risk. C, Same as A, but for US adults recommended for statin therapy. Cholesterol values were adjusted among participants receiving lipid-lowering therapies to model baseline untreated measurements. D, Same as B, but for US adults recommended for antihypertensive therapy. BP values were adjusted among participants receiving antihypertensive therapies to model baseline untreated measurements.

applying PREVENT to their pretreatment values, translating to a further increase of 77 500 ASCVD events. Second, this study did not consider the clinical implications of decreased eligibility for high-intensity statins, which would confer additional risk reductions for ASCVD and risk increases for new-onset diabetes. Third, this study only evaluated ACC/AHA Class I recommendations. Further changes could also be associated with application of PREVENT to ACC/AHA Class IIa/IIb recommendations (eg, for persons at borderline risk with risk-enhancing factors)⁵ and recommendations issued by other organizations (eg, for aspirin therapy).⁴⁶

Limitations

This study has limitations. First, PREVENT is not currently recommended to replace the PCEs, although the AHA has proposed its inclusion in future guidelines with potentially revised risk thresholds.¹² Current ACC/AHA risk thresholds are based on randomized trial data and therefore do not depend on the choice of risk equation,⁴⁷ but they may still be revised in light of new data on risks and benefits.⁴² Earlier analyses have also indicated that statin therapy may be associated with positive net benefit⁴⁷ and favorable cost-effectiveness⁴⁸ at ASCVD risk thresholds below 7.5% or even 5%. Second, this study did not evaluate the PREVENT equations using additional optional predictors, such as hemoglobin A_{1c}, urine albumin-to-creatinine ratio, and zip code. However, since all variations of the PREVENT equations were similarly calibrated,¹¹ they would likely yield similar results. Third,

ACC/AHA guidelines recommend risk discussion involving shared decision-making with patients, which does not always result in initiation of therapy. Relatedly, treatment decisions may be based directly on risk-enhancing factors⁵ or clinical trial findings²⁹ rather than guideline-recommended risk thresholds. Fourth, estimates of clinical outcomes are contingent on several assumptions, including accurate estimates of relative risk reductions and consistent adherence rates to treatment guidelines. Fifth, prescription medication data from NHANES did not include indications or dosages, limiting our analyses of participants receiving preventive therapies. Lastly, the study relied on prepandemic data from NHANES, which may not be accurate or representative of the current US population.

Conclusions

With no change to current risk-based treatment thresholds, widespread adoption of the PREVENT equations for ASCVD risk could reduce eligibility for statin and antihypertensive therapies among an estimated 15.8 million US adults and thereby increase the rate of major adverse cardiovascular events. Although PREVENT advances the important goal of more accurate and precise cardiovascular risk prediction, the magnitude of these projected changes warrants careful reconsideration of current treatment thresholds using decision-analytic or cost-effectiveness frameworks.⁴⁷⁻⁵⁰

ARTICLE INFORMATION

Accepted for Publication: June 7, 2024.

Published Online: July 29, 2024.
doi:10.1001/jama.2024.12537

Author Affiliations: Department of Biomedical Informatics, Harvard Medical School, Boston, Massachusetts (Diao, Shi, Buckley, Patel, Manrai); Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts (Diao); Department of Medicine, Beth Israel Deaconess Medical Center, Boston, Massachusetts (Shi); Division of Cardiovascular Medicine, University of Michigan, Ann Arbor (Murthy); Department of Computer Science, Cornell University, New York, New York (Pierson); Department of Population Health Sciences, Weill Cornell Medical College, New York, New York (Pierson); Division of Cardiology, Beth Israel Deaconess Medical Center, Boston, Massachusetts (Yeh, Kazi, Wadhera); Richard A. and Susan F. Smith Center for Outcomes Research, Beth Israel Deaconess Medical Center, Boston, Massachusetts (Yeh, Kazi, Wadhera).

Author Contributions: Drs Diao and Manrai had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Concept and design: Diao, Murthy, Wadhera, Manrai.

Acquisition, analysis, or interpretation of data: Diao, Shi, Buckley, Patel, Pierson, Yeh, Dhruv, Manrai.

Drafting of the manuscript: Diao, Manrai.

Critical review of the manuscript for important intellectual content: All authors.

Statistical analysis: Diao, Buckley, Patel, Manrai.

Obtained funding: Patel, Manrai.

Administrative, technical, or material support: Shi.

Supervision: Shi, Wadhera, Manrai.

Conflict of Interest Disclosures: Dr Murthy reported receiving personal fees from Ionetix, INVIA Medical Imaging Solutions, and Siemens Healthineers; grants from National Institutes of Health (NIH) and American Heart Association outside the submitted work; owning stock in General Electric, Cardinal Health, Pfizer, Amgen, Merck, and Johnson & Johnson; having stock options in Ionetix; being a paid consultant for INVIA Medical Imaging Solutions and Siemens Healthineers; receiving research support through his institution from Siemens Healthineers; and being supported by the Melvyn Rubenfire Professorship in Preventive Cardiology. Dr Dhruv reported receiving grants from National Heart, Lung, and Blood Institute (NHLBI) outside the submitted work. Dr Wadhera reported receiving grants from NHLBI and personal fees from Abbott and Chamber Cardio outside the submitted work. Dr Manrai reported receiving grants from NIH/NHLBI during the conduct of the study. No other disclosures were reported.

Funding/Support: This project was funded in part by the National Heart, Lung, and Blood Institute award K01HL138259.

Role of the Funder/Sponsor: The National Heart, Lung, and Blood Institute had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Data Sharing Statement: See Supplement 2.

REFERENCES

- Magnussen C, Ojeda FM, Leong DP, et al; Global Cardiovascular Risk Consortium. Global effect of modifiable risk factors on cardiovascular disease and mortality. *N Engl J Med*. 2023;389(14):1273-1285. doi:10.1056/NEJMoa2206916
- Goff DC Jr, Lloyd-Jones DM, Bennett G, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol*. 2014;63(25 pt B):2935-2959. doi:10.1016/j.jacc.2013.11.005
- Grundy SM, Stone NJ, Bailey AL, et al 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APHA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2019;139(25):e1082-e1143. doi:10.1161/CIR.0000000000000625
- Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APHA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2018;138(17):e426-e483. doi:10.1161/CIR.0000000000000597
- Arnett DK, Blumenthal RS, Albert MA, et al. 2019 ACC/AHA guideline on the primary prevention of

- cardiovascular disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation*. 2019;140(11):e596-e646. doi:10.1161/CIR.0000000000000678
6. Yadlowsky S, Hayward RA, Sussman JB, McClelland RL, Min YI, Basu S. Clinical implications of revised pooled cohort equations for estimating atherosclerotic cardiovascular disease risk. *Ann Intern Med*. 2018;169(1):20-29. doi:10.7326/M17-3011
7. Ndumele CE, Neeland IJ, Tuttle KR, et al; American Heart Association. A synopsis of the evidence for the science and clinical management of cardiovascular-kidney-metabolic (CKM) syndrome: a scientific statement from the American Heart Association. *Circulation*. 2023;148(20):1636-1664. doi:10.1161/CIR.0000000000001186
8. Ndumele CE, Rangaswami J, Chow SL, et al; American Heart Association. Cardiovascular-kidney-metabolic health: a presidential advisory from the American Heart Association. *Circulation*. 2023;148(20):1606-1635. doi:10.1161/CIR.0000000000001184
9. Vyas DA, Eisenstein LG, Jones DS. Hidden in plain sight—reconsidering the use of race correction in clinical algorithms. *N Engl J Med*. 2020;383(9):874-882. doi:10.1056/NEJMms2004740
10. Vasan RS, van den Heuvel E. Differences in estimates for 10-year risk of cardiovascular disease in Black versus White individuals with identical risk factor profiles using pooled cohort equations: an in silico cohort study. *Lancet Digit Health*. 2022;4(1):e55-e63. doi:10.1016/S2589-7500(21)00236-3
11. Khan SS, Matsushita K, Sang Y, et al. Development and validation of the American Heart Association's PREVENT equations. *Circulation*. 2024;149(6):430-449. doi:10.1161/CIRCULATIONAHA.123.067626
12. Khan SS, Coresh J, Pencina MJ, et al; American Heart Association. Novel prediction equations for absolute risk assessment of total cardiovascular disease incorporating cardiovascular-kidney-metabolic health: a scientific statement from the American Heart Association. *Circulation*. 2023;148(24):1982-2004. doi:10.1161/CIR.0000000000001191
13. Goldstein BA, Navar AM, Pencina MJ, Ioannidis JPA. Opportunities and challenges in developing risk prediction models with electronic health records data: a systematic review. *J Am Med Inform Assoc*. 2017;24(1):198-208. doi:10.1093/jamia/ocw042
14. Kohane IS, Aronow BJ, Avillach P, et al; Consortium For Clinical Characterization Of COVID-19 By EHR (4CE). What every reader should know about studies using electronic health record data but may be afraid to ask. *J Med Internet Res*. 2021;23(3):e22219. doi:10.2196/22219
15. Woodruff RC, Tong X, Khan SS, et al. Trends in cardiovascular disease mortality rates and excess deaths, 2010-2022. *Am J Prev Med*. 2024;66(4):582-589. doi:10.1016/j.amepre.2023.11.009
16. Akinbami LJ, Chen TC, Davy O, et al. National Health and Nutrition Examination Survey, 2017-March 2020 prepandemic file: sample design, estimation, and analytic guidelines. *Vital Health Stat*. 2022;(190):1-36. doi:10.15620/cdc:115434
17. Martin SS, Blaha MJ, Elshazly MB, et al. Comparison of a novel method vs the Friedewald equation for estimating low-density lipoprotein cholesterol levels from the standard lipid profile. *JAMA*. 2013;310(19):2061-2068. doi:10.1001/jama.2013.280532
18. Pencina MJ, Navar-Boggan AM, D'Agostino RB Sr, et al. Application of new cholesterol guidelines to a population-based sample. *N Engl J Med*. 2014;370(15):1422-1431. doi:10.1056/NEJMoa1315665
19. Wu J, Kraja AT, Oberman A, et al. A summary of the effects of antihypertensive medications on measured blood pressure. *Am J Hypertens*. 2005;18(7):935-942. doi:10.1016/j.amjhyper.2005.01.011
20. Patel AP, Wang M, Fahed AC, et al. Association of rare pathogenic DNA variants for familial hypercholesterolemia, hereditary breast and ovarian cancer syndrome, and Lynch syndrome with disease risk in adults according to family history. *JAMA Netw Open*. 2020;3(4):e203959. doi:10.1001/jamanetworkopen.2020.3959
21. Baigent C, Blackwell L, Emberson J, et al; Cholesterol Treatment Trialists' (CTT) Collaboration. Efficacy and safety of more intensive lowering of LDL cholesterol: a meta-analysis of data from 170,000 participants in 26 randomised trials. *Lancet*. 2010;376(9753):1670-1681. doi:10.1016/S0140-6736(10)61350-5
22. Birjmohun RS, Hutten BA, Kastelein JJP, Stroes ESG. Efficacy and safety of high-density lipoprotein cholesterol-increasing compounds: a meta-analysis of randomized controlled trials. *J Am Coll Cardiol*. 2005;45(2):185-197. doi:10.1016/j.jacc.2004.10.031
23. Lloyd-Jones DM, Huffman MD, Karmali KN, et al. Estimating longitudinal risks and benefits from cardiovascular preventive therapies among Medicare patients: The Million Hearts Longitudinal ASCVD Risk Assessment tool: a special report from the American Heart Association and American College of Cardiology. *Circulation*. 2017;135(13):e793-e813. doi:10.1161/CIR.0000000000000467
24. Downs JR, Clearfield M, Weis S, et al. Primary prevention of acute coronary events with lovastatin in men and women with average cholesterol levels: results of AFCAPS/TexCAPS. *JAMA*. 1998;279(20):1615-1622. doi:10.1001/jama.279.20.1615
25. Nakamura H, Arakawa K, Itakura H, et al; MEGA Study Group. Primary prevention of cardiovascular disease with pravastatin in Japan (MEGA Study): a prospective randomised controlled trial. *Lancet*. 2006;368(9542):1155-1163. doi:10.1016/S0140-6736(06)69472-5
26. National Cholesterol Education Program. Third report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATP III final report). 2002. Accessed June 14, 2024. <https://www.nhlbi.nih.gov/resources/third-report-expert-panel-detection-evaluation-and-treatment-high-blood-cholesterol-0>
27. Collins R, Armitage J, Parish S, Sleight P, Peto R; Heart Protection Study Collaborative Group. Effects of cholesterol-lowering with simvastatin on stroke and other major vascular events in 20 536 people with cerebrovascular disease or other high-risk conditions. *Lancet*. 2004;363(9411):757-767. doi:10.1016/S0140-6736(04)15690-0
28. Baigent C, Keech A, Kearney PM, et al; Cholesterol Treatment Trialists' (CTT) Collaborators. Efficacy and safety of cholesterol-lowering treatment: prospective meta-analysis of data from 90,056 participants in 14 randomised trials of statins. *Lancet*. 2005;366(9493):1267-1278. doi:10.1016/S0140-6736(05)67394-1
29. Ridker PM, Danielson E, Fonseca FAH, et al; JUPITER Study Group. Rosuvastatin to prevent vascular events in men and women with elevated C-reactive protein. *N Engl J Med*. 2008;359(21):2195-2207. doi:10.1056/NEJMoa0807646
30. Baigent C, Landray MJ, Reith C, et al; SHARP Investigators. The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection): a randomised placebo-controlled trial. *Lancet*. 2011;377(9784):2181-2192. doi:10.1016/S0140-6736(11)60739-3
31. Giugliano RP, Pedersen TR, Park JG, et al; FOURIER Investigators. Clinical efficacy and safety of achieving very low LDL-cholesterol concentrations with the PCSK9 inhibitor evolocumab: a prespecified secondary analysis of the FOURIER trial. *Lancet*. 2017;390(10106):1962-1971. doi:10.1016/S0140-6736(17)32290-0
32. Heller DJ, Coxson PG, Penko J, et al. Evaluating the impact and cost-effectiveness of statin use guidelines for primary prevention of coronary heart disease and stroke. *Circulation*. 2017;136(12):1087-1098. doi:10.1161/CIRCULATIONAHA.117.027067
33. Taylor F, Ward K, Moore TH, et al. Statins for the primary prevention of cardiovascular disease. *Cochrane Database Syst Rev*. 2011;(1):CD004816. doi:10.1002/14651858.CD004816.pub4
34. Kim CJ, Sussman JB, Mukamal KJ, Eades M, Anderson TS. Trends in primary prevention statin use by cardiovascular risk score from 1999 to 2018: a repeated cross-sectional study. *Ann Intern Med*. 2023;176(12):1684-1688. doi:10.7326/M23-1915
35. Lu Y, Liu Y, Dhingra LS, et al. National trends in racial and ethnic disparities in use of recommended therapies in adults with atherosclerotic cardiovascular disease, 1999-2020. *JAMA Netw Open*. 2023;6(12):e2345964. doi:10.1001/jamanetworkopen.2023.45964
36. Chou R, Cantor A, Dana T, et al. Statin use for the primary prevention of cardiovascular disease in adults: updated evidence report and systematic review for the US Preventive Services Task Force. *JAMA*. 2022;328(8):754-771. doi:10.1001/jama.2022.12138
37. Mangione CM, Barry MJ, Nicholson WK, et al; US Preventive Services Task Force. Statin use for the primary prevention of cardiovascular disease in adults: US Preventive Services Task Force recommendation statement. *JAMA*. 2022;328(8):746-753. doi:10.1001/jama.2022.13044
38. Danaei G, Ding EL, Mozaffarian D, et al. The preventable causes of death in the United States: comparative risk assessment of dietary, lifestyle, and metabolic risk factors. *PLoS Med*. 2009;6(4):e1000058. doi:10.1371/journal.pmed.1000058
39. Curb JD, Borhani NO, Blazekowski TP, Zimbaldi N, Fotiu S, Williams W. Long-term surveillance for adverse effects of antihypertensive drugs. *JAMA*. 1985;253(22):3263-3268. doi:10.1001/jama.1985.03350460063022
40. Domanski MJ, Tian X, Wu CO, et al. Time course of LDL cholesterol exposure and cardiovascular disease event risk. *J Am Coll Cardiol*.

2020;76(13):1507-1516. doi:10.1016/j.jacc.2020.07.059

41. Gaba P, O'Donoghue ML, Park JG, et al. Association between achieved low-density lipoprotein cholesterol levels and long-term cardiovascular and safety outcomes: an analysis of FOURIER-OLE. *Circulation*. 2023;147(16):1192-1203. doi:10.1161/CIRCULATIONAHA.122.063399

42. Tsao CW, Aday AW, Almarazq ZI, et al; American Heart Association Council on Epidemiology and Prevention Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2023 update: a report from the American Heart Association. *Circulation*. 2023;147(8):e93-e621. doi:10.1161/CIR.0000000000001123

43. Frank DA, Johnson AE, Hausmann LRM, Gellad WF, Roberts ET, Vajravelu RK. Disparities in guideline-recommended statin use for prevention of atherosclerotic cardiovascular disease by race, ethnicity, and gender: a nationally representative cross-sectional analysis of adults in the United States. *Ann Intern Med*. 2023;176(8):1057-1066. doi:10.7326/M23-0720

44. Dorsch MP, Lester CA, Ding Y, Joseph M, Brook RD. Effects of race on statin prescribing for primary prevention with high atherosclerotic cardiovascular disease risk in a large healthcare system. *J Am Heart Assoc*. 2019;8(22):e014709. doi:10.1161/JAHA.119.014709

45. Heart disease deaths—health, United States. Published June 26, 2023. Accessed May 18, 2024. <https://www.cdc.gov/nchs/health-topics/heart-disease-deaths.htm>

46. US Preventive Services Task Force. Aspirin use to prevent cardiovascular disease: preventive medication. Published April 26, 2022. Accessed December 20, 2023. <https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/aspirin-to-prevent-cardiovascular-disease-preventive-medication>

47. Stone NJ, Robinson JG, Lichtenstein AH, et al; American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular

risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation*. 2014;129(25)(suppl 2):S1-S45. doi:10.1161/01.cir.0000437738.63853.7a

48. Pandya A, Sy S, Cho S, Weinstein MC, Gaziano TA. Cost-effectiveness of 10-year risk thresholds for initiation of statin therapy for primary prevention of cardiovascular disease. *JAMA*. 2015;314(2):142-150. doi:10.1001/jama.2015.6822

49. Kazi DS, Moran AE, Coxson PG, et al. Cost-effectiveness of PCSK9 inhibitor therapy in patients with heterozygous familial hypercholesterolemia or atherosclerotic cardiovascular disease. *JAMA*. 2016;316(7):743-753. doi:10.1001/jama.2016.11004

50. Spahillari A, Zhu J, Ferket BS, et al. Cost-effectiveness of contemporary statin use guidelines with or without coronary artery calcium assessment in African American individuals. *JAMA Cardiol*. 2020;5(8):871-880. doi:10.1001/jamacardio.2020.1240