JACC: ADVANCES VOL. 3, NO. 12, 2024

ORIGINAL RESEARCH

OUTCOMES AND QUALITY

PREVENT and Pooled Cohort Equations in Mortality Risk Prediction

National Health and Nutrition Examination Survey

Naman S. Shetty, MD,[a,b] Mokshad Gaonkar, MS,[c] Nirav Patel, MD, MSPH,[c] Nehal Vekariya, MS,[c] Peng Li, PhD,[d] Garima Arora, MD,[c] Pankaj Arora, MD[c,e]

ABSTRACT

BACKGROUND The Predicting Risk of CVD Events (PREVENT) equations were developed to address limitations of the Pooled Cohort Equations (PCEs) in predicting atherosclerotic cardiovascular disease (ASCVD) risk. The comparative effectiveness of the PREVENT equations versus the PCEs in predicting mortality risk remains unknown.

OBJECTIVES The purpose of this study was to compare the risk discrimination value of the PREVENT equations with the PCEs for predicting mortality.

METHODS This retrospective cohort study included individuals aged 40 to 79 years, free of cardiovascular disease, from the National Health and Nutrition Examination Survey (1999-2004). The outcomes of interest were all-cause and cardiovascular mortality. Harrell's C-statistics was used to examine risk discrimination.

RESULTS In this study, including 4,342 individuals (median age: 50.3 [IQR: 44.3-59.6] years, 51.5% females, and 77.0% non-Hispanic White), the median 10-year ASCVD risk was 4.0% (IQR: 1.5%-9.9%) using the PCEs and 2.4% (IQR: 1.2%-5.3%) using the PREVENT equations. The PREVENT equations generated lower ASCVD risk estimates in 81.0% (79.4%-82.6%) of individuals relative to the PCEs, with the lower estimates disproportionately affecting males (97.7% [96.6%-98.8%]) and Black individuals (89.6% [87.3%-91.8%]). Using a 5.0% risk threshold, PREVENT and PCEs classified 26.7% (~16.9 million U.S. individuals) and 43.4% (~27.5 million U.S. individuals), respectively, as having a 10-year ASCVD risk >5%. Among the 10.2% classified as high risk by the PCEs, 96.2% were reclassified to a lower risk by PREVENT. The risk discrimination value for all-cause and cardiovascular mortality was similar using the PREVENT equations and the PCEs.

CONCLUSIONS The PREVENT equations provide similar risk discrimination values for mortality compared to the PCEs but estimate lower 10-year ASCVD risk. Replacing PCEs with the PREVENT equations could reduce statin eligibility in a significant number of individuals. (JACC Adv. 2024;3:101372) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

From the [a]Department of Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, Boston, Massachusetts, USA; [b]Harvard Medical School, Boston, Massachusetts, USA; [c]Division of Cardiovascular Disease, University of Alabama at Birmingham, Birmingham, Alabama, USA; [d]School of Nursing, University of Alabama at Birmingham, Birmingham, Alabama, USA; and the [e]Section of Cardiology, Birmingham Veterans Affairs Medical Center, Birmingham, Alabama, USA.

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

Manuscript received June 25, 2024; revised manuscript received September 5, 2024, accepted September 10, 2024.

ISSN 2772-963X https://doi.org/10.1016/j.jacadv.2024.101372

ABBREVIATIONS AND ACRONYMS

ASCVD = atherosclerotic cardiovascular disease

NHANES = National Health and Nutrition Examination Survey

NT-proBNP = N-terminal ProB-type natriuretic peptide

PCE = Pooled Cohort Equations

PREVENT Equations = Predicting Risk of CVD Events Equations

The Pooled Cohort Equations (PCEs) were introduced in 2013 as an atherosclerotic cardiovascular disease (ASCVD) risk stratification tool to guide the initiation of antihypertensive and statin therapy.[1-3] Nonetheless, several limitations of the PCEs on predicting ASCVD risk have been identified, including the inclusion of race, the exclusion of individuals below 40 years of age, and the overestimation of risk.[4] To overcome the abovementioned limitations of the PCEs, the American Heart Association introduced the Predicting Risk of CVD Events (PREVENT) equations as a new risk prediction tool for ASCVD.[4,5] The PREVENT equations not only overcome the limitations of the PCEs but also incorporate markers of renal function, focus on reducing overestimation of risk, and include younger individuals aged 30 to 79 years.[4,5] During the development and validation of the PREVENT equations, the PREVENT equations have been shown to have marginally better risk discrimination for ASCVD compared with the PCEs.[4,5] Considering the pivotal role of the ASCVD risk in guiding preventive efforts, it is important to assess the comparative efficacy of the PREVENT equations and PCEs in risk estimation prior to the widespread clinical implementation of the PREVENT equations. Additionally, since the PREVENT equations do not incorporate cardiac biomarkers, it is necessary to determine if the inclusion of cardiac biomarkers in the PREVENT equations improves risk discrimination for mortality. This study leverages nationwide population-level data from the National Health and Nutrition Examination Survey (NHANES) to: 1) compare the 10-year ASCVD risk estimated by the PCEs and PREVENT equations at baseline; 2) compare the risk stratification of the PCEs and PREVENT equations for mortality; and 3) evaluate whether the incorporation of N-terminal proB-type natriuretic peptide (NT-proBNP) and cardiac troponin I (cTnI) enhances the risk stratification value of the PREVENT equations for mortality.

METHODS

This study utilized data from the NHANES cycles between 1999 and 2004. The study design and survey characteristics of the NHANES have been described previously.[6-9] In brief, the NHANES is a program that assesses the health and nutritional status of the civilian noninstitutionalized population in the United States. The NHANES is conducted every 2 years by the National Center for Health Statistics, part of the Centers for Disease Control and Prevention. Each NHANES cycle collects data of population health and well-being through interviews, physical examinations, and collection of biological specimens. The NHANES also provides crucial data on the risk factors and prevalence for major diseases. Participants with self-reported prevalent cardiovascular disease, pregnant or breastfeeding females, and those with missing data to compute the PCEs and PREVENT equations were excluded. Ethical oversight was provided by the University of Alabama at Birmingham Institutional Review Board.

The analysis comparing the PCEs and PREVENT equations was conducted in individuals aged between 40 and 79 years. The PCEs were developed to predict the 10-year risk of ASCVD (ie, a composite of nonfatal myocardial infarction, coronary heart disease death, and stroke). The PREVENT equations were developed to predict 10- and 30-year risk of ASCVD, CVD (ASCVD and heart failure), and heart failure. To allow comparison with the PCEs, the 10-year PREVENT equation for ASCVD was used in this study. The parameters included in the PREVENT equations and PCEs have been previously published.[3,5] In brief, PCEs included age, sex, race, total cholesterol, high-density lipoprotein, systolic blood pressure, diabetes, smoking, and the base PREVENT equations for ASCVD had age, sex, total cholesterol, high-density lipoprotein, systolic blood pressure, diabetes, smoking, estimated glomerular filtration rate, use of antihypertensive and lipid-lowering medications.[3,5] For this study, we excluded additional measures, such as glycosylated hemoglobin A1C levels, social determinants of health, and urine albumin creatinine ratio, in the PREVENT equations. Considering that the PCEs were designed for individuals who were not on statins, participants on self-reported lipid-lowering therapy were excluded. The PREVENT equations and PCEs were developed and validated for parameters within a specific range.[3,5] Participants who had parameters outside the specified range of the PCEs and PREVENT equations were excluded, as outlined previously.[3,5]

The analysis examining the value of incorporating cardiac biomarkers to the PREVENT equations included participants aged 30 to 79 years and individuals on statins, as the PREVENT equations account for statin use. NT-proBNP and cTnI levels were analyzed on the Roche Cobas e601 analyzer and Abbott ARCHITECT i2000SR analyzer, respectively.[9,10] Elevated NT-proBNP levels were defined as ≥125 pg/mL and elevated cTnI levels were defined as ≥6 ng/L in males and ≥4 ng/L in females.[11] Furthermore, a sensitivity analysis was conducted,

including participants who were currently taking lipid-lowering therapy.

The outcome of interest for this study was all-cause and cardiovascular mortality. Mortality data for the participants were ascertained using the NHANES Linked Mortality File. This file links participants with mortality data from the National Death Index through December 31, 2019. International Classification of Diseases codes I00-I99 were used to identify cardiovascular causes as the cause of death.[12] Follow-up was censored at 10 years considering the use of the PCEs and the 10-year ASCVD PREVENT equation, which were developed and validated to predict the ASCVD risk over a 10-year period.

To account for the complex multistage sampling of the NHANES, the SURVEY procedures utilizing the biomarker subsample weights were used.[6-8,13] The weights were adjusted based on the number of survey cycles combined for the analysis. In this study, we applied domain statements in the survey procedures of SAS, following the National Center for Health Statistics analytical guidelines, to perform precise subgroup analysis.[14] The estimates of the PREVENT equations and PCEs in each individual were calculated and graphically presented. Based on the 10-year ASCVD risk, the cohort was categorized into standard risk groups (low [<5%], intermediate [5% to 20%], and high [≥20%]) using both the PREVENT equations and the PCEs. Risk reclassification across these groups was examined by replacing the PREVENT equations with the PCEs. Harrell's C-statistics was used to examine the risk discrimination value of models using the PREVENT equations and PCEs. Furthermore, a sensitivity analysis was conducted, including participants who were currently taking lipid-lowering therapy. For the analysis examining the additional risk stratification value of biomarkers in the PREVENT equation, the cohort was stratified based on the 10-year PREVENT ASCVD risk estimates (<10%, ≥10%) and biomarker levels (no elevation in cTnI and NT-proBNP, elevation in cTnI or NT-proBNP, and elevation in both cTnI and NT-proBNP). Cumulative incidence curves were used to assess the risk of mortality in each group. A 2-tailed P value <0.05 was considered statistically significant. All analyses were conducted on SAS, 9.4 and R, 4.2.2.

RESULTS

Among the 4,342 participants representing 63.3 million U.S. individuals (weighted median age: 50.3 [IQR: 44.3-59.6] years, 51.5% females, and 77.0% non-Hispanic White), the weighted median 10-year ASCVD risk estimated by the PCEs and PREVENT equations was 4.0% (IQR: 1.5%-9.9%) and 2.4% (IQR: 1.2%-5.3%), respectively (Table 1). Compared with the PCEs, the PREVENT equations estimated a lower 10-year ASCVD risk for 81.0% (95% CI: 79.4% to 82.6%) of participants (Figure 1). In the sex-stratified analysis, the proportion of individuals with lower 10-year ASCVD risk estimates using the PREVENT equations in place of the PCEs was higher among males (97.7% [95% CI: 96.6%-98.8%]) compared with females (65.4% [95% CI: 62.1%-68.6%]). Race-stratified analysis demonstrated that non-Hispanic Black individuals (89.6% [95% CI: 87.3%-91.9%]) had relatively higher 10-year ASCVD risk estimates using the PREVENT equations instead of the PCEs compared with non-Hispanic White individuals (80.4% [95% CI: 78.4%-82.4%]) and Mexican

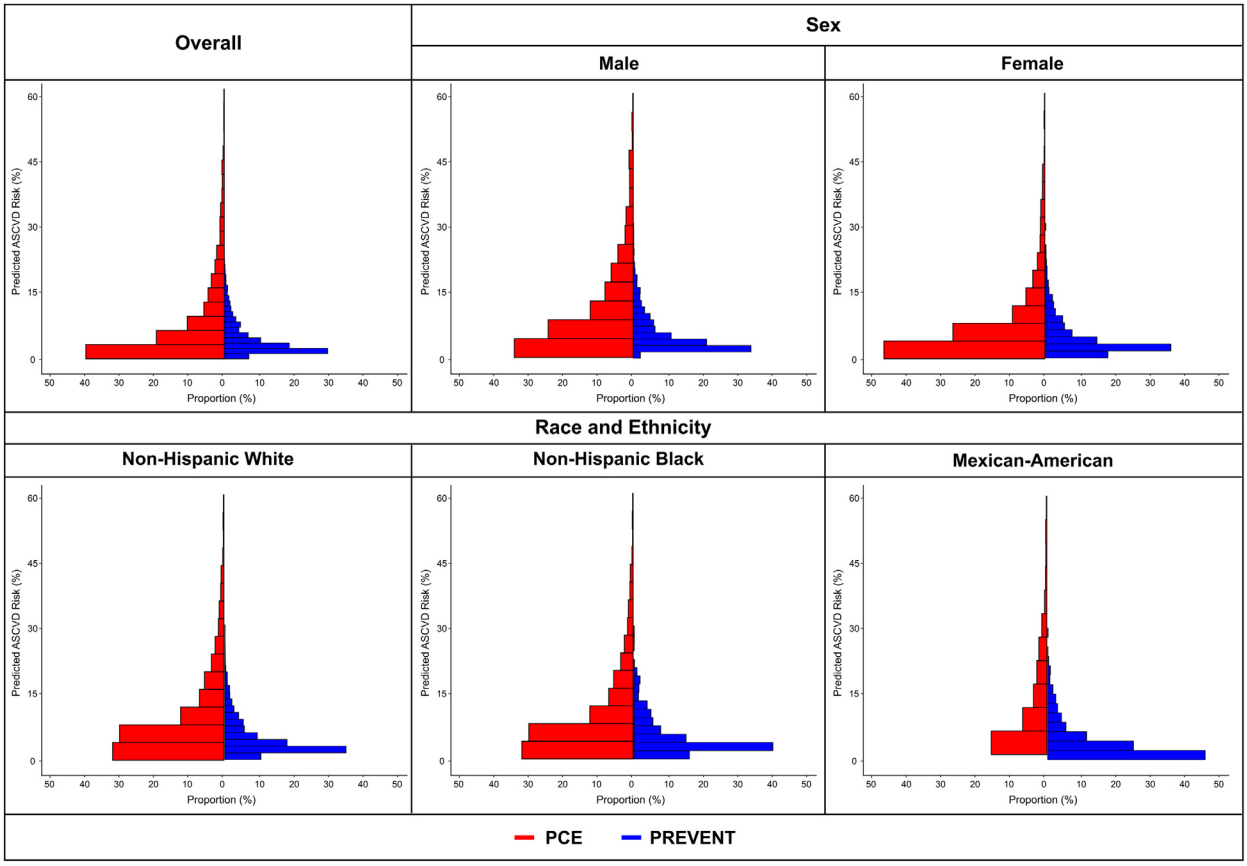
TABLE 1 Baseline Characteristics in the Analytical Population Comparing the Pooled Cohort Equations and PREVENT Equations in the National Health and Nutrition Examination Survey Cycles 1999-2004 (n/N = 4,342/63,337,093)

Age, y	50.3 (44.3-59.6)
Female	51.5 (50.0-53.0)[a]
Race and ethnicity	
Non-Hispanic White	77.0 (73.6-80.5)[a]
Non-Hispanic Black	8.6 (7.0-10.3)[a]
Other[b]	9.0 (6.6-11.5)[a]
Mexican American	5.3 (3.6-7.0)[a]
Education level	
High school or less	43.6 (40.7-46.6)[a]
More than high school	56.4 (53.4-59.3)[a]
Insurance status	
Insured	87.2 (85.6-88.8)[a]
Uninsured	12.8 (11.2-14.4)[a]
Family poverty income ratio	
≥1.30	85.3 (83.1-87.4)[a]
<1.30	14.7 (12.6-16.9)[a]
Systolic blood pressure, mm Hg	123 (113-135)
Diastolic blood pressure, mm Hg	74 (68-81)
Body mass index, kg/m^2	27.4 (24.2-30.8)
Statin use	NA[a]
Current smoker	21.8 (20.0-23.5)[a]
Total cholesterol, mg/dL	209 (186-234)
HDL, mg/dL	51 (41-62)
GFR, mL/min per 1.73 m^2	96 (84-108)
Troponin I, ng/L	1.8 (1.2-2.8)
NT-proBNP, pg/mL	51.4 (26.3-96.9)
PCE ASCVD risk, (%)	4.0 (1.5-9.9)
PREVENT ASCVD risk, (%)	2.4 (1.2-5.3)

Values are median (IQR). [a]Values are % (95% CI). [b]Race reported as self-identified Hispanic or non-Hispanic other than Black, White, or Asian.

ASCVD = atherosclerotic cardiovascular disease; HDL = high-density lipoprotein; GFR = glomerular filtration rate; NT-proBNP = N-terminal pro-B-type natriuretic peptide; PCE = Pooled Cohort Equation; PREVENT Equations = Predicting Risk of CVD Events Equations.

FIGURE 1 10-Year Atherosclerotic Cardiovascular Disease Risk Determined Using the Pooled Cohort Equations and the PREVENT Equations

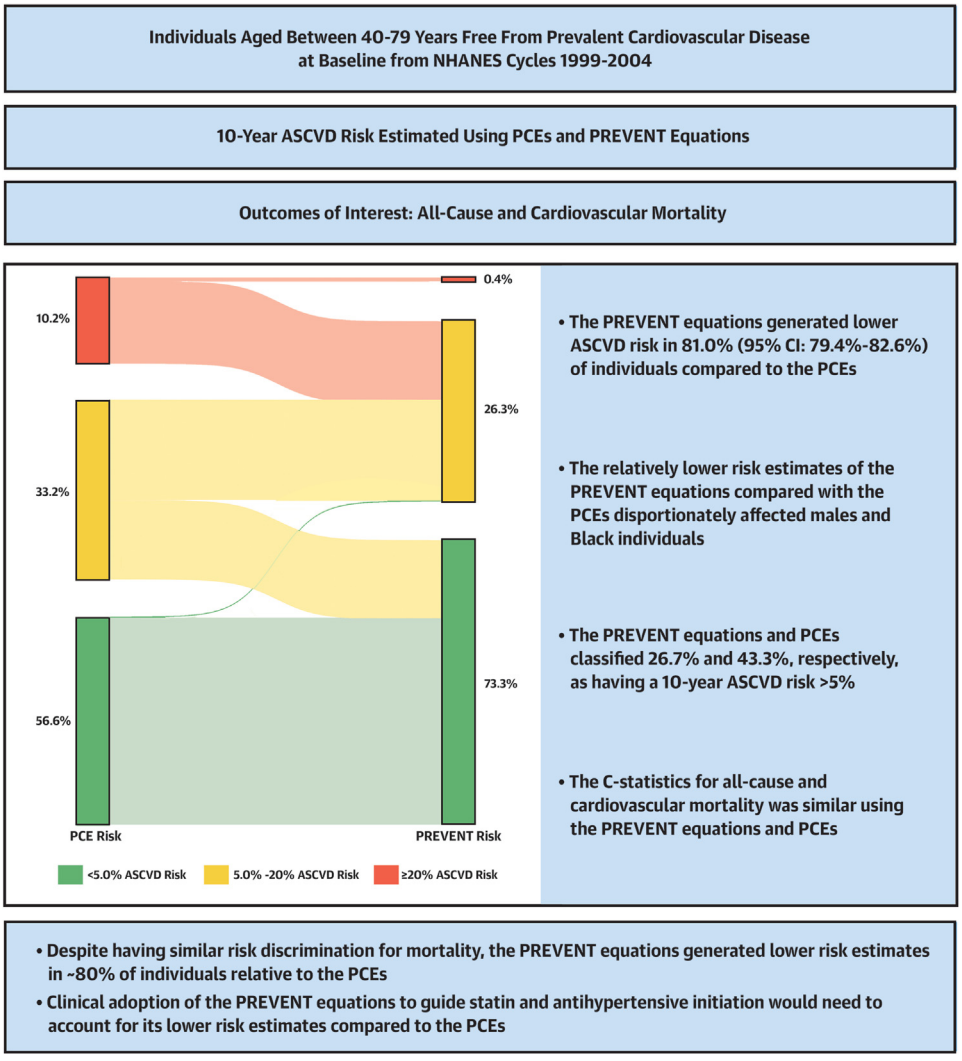


The 10-year atherosclerotic cardiovascular disease risk estimated by the PREVENT equations and the Pooled Cohort Equations (PCEs) has been depicted in the overall population and stratified by race and sex. The 10-year ASCVD risk estimated by the PREVENT equations and the PCEs have been depicted in red and blue, respectively. The x-axis represents the proportion of individuals, and the y-axis represents the ASCVD risk. ASCVD = atherosclerotic cardiovascular disease; PREVENT Equations = Predicting Risk of CVD Events Equations.

American (78.3% [95% CI: 75.4%-81.2%]). Using the PCEs, 56.6%, 33.2%, and 10.2% were classified as low, intermediate, and high risk, respectively. Utilizing the PREVENT equations, 73.3%, 26.3%, and 0.4% were categorized as low, intermediate, and high risk, respectively. Using the ASCVD risk threshold for statin initiation, 43.4% using PCEs and 26.7% using PREVENT equations of the study population were classified as having a 10-year ASCVD risk of >5.0%. Among the participants classified as high risk by the PCEs, the PREVENT equations classified 96.2% as intermediate risk. Within participants with intermediate ASCVD risk by the PCEs, the PREVENT equations classified 0.006% and 50.7% as high and low risk, respectively. Among the participants with low ASCVD risk determined by the PCEs, the PREVENT equations classified 0.2% of individuals as having intermediate ASCVD risk (**Central Illustration**).

For all-cause mortality, the C-statistics for models with the PREVENT equations was 0.795 (SE: 0.014) and the PCEs was 0.788 (SE: 0.014) (**Table 2**). For cardiovascular mortality, the C-statistics for models with the PREVENT equations was 0.796 (SE: 0.037) and the PCEs were 0.779 (SE: 0.038) for the outcome of cardiovascular mortality (**Table 2**). Based on the C-statistics, the PREVENT equations and the PCEs demonstrated good risk discrimination for the

CENTRAL ILLUSTRATION **PREVENT and Pooled Cohort Equations in Mortality Risk Prediction: National Health and Nutrition Examination Survey**



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Sankey diagram showing reclassification of 10-year atherosclerotic cardiovascular disease risk categories using the pooled cohort equations and PREVENT equations. The low-, intermediate-, and high-risk groups have been defined as <5%, 5% to 20%, and 20% risk of ASCVD. The low-, intermediate-, and high-risk groups are depicted in green, yellow, and red, respectively. NHANES = National Health and Nutrition Examination Survey; PCEs = Pooled Cohort Equations; other abbreviations as in Figure 1.

outcomes of all-cause and cardiovascular mortality. However, the PREVENT equations and PCEs had comparable risk discrimination (Table 2). The results of the sensitivity analysis including individuals on lipid-lowering therapy have been depicted in Supplemental Figure 1 and Supplemental Tables 1 to 3.

The biomarker-based analysis included 6,482 individuals, representing 116 million U.S. individuals (Table 3). Among the participants included, 81.1%, 15.8%, and 3.1% of individuals had nonelevated biomarkers, elevation in a single biomarker, and elevations in both biomarkers, respectively. Among those

TABLE 2 Risk Discrimination Value of the Pooled Cohort Equations and the PREVENT Equations for Predicting the Risk of All-Cause and Cardiovascular Mortality in the National Health and Nutrition Examination Survey Cycles 1999-2004

	Unadjusted		Adjusted[a]	
	All-Cause Mortality	Cardiovascular Mortality	All-Cause Mortality	Cardiovascular Mortality
PREVENT	0.777 (0.014)	0.791 (0.036)	0.795 (0.014)	0.796 (0.037)
PCE	0.777 (0.014)	0.784 (0.036)	0.788 (0.014)	0.779 (0.038)

[a]Models adjusted for income, insurance status, education level, and number of health care visits/year.
Abbreviations as in Table 1.

with PREVENT ASCVD risk <10%, the cumulative incidence of all-cause mortality was 4.8%, 8.9%, and 19.2% in the nonelevated biomarkers, elevation in a single biomarker, and elevation in both biomarkers groups, respectively. Similarly, among individuals with a PREVENT ASCVD risk ≥10%, those without any biomarker elevation, those with elevation in 1 biomarker, and those with elevations in both biomarkers had a cumulative incidence of all-cause mortality of 3.1%, 4.8%, and 21.8%, respectively. Among those with PREVENT ASCVD risk <10%, the cumulative incidence of cardiovascular mortality was 0.8%, 1.5%, and 3.2% in the nonelevated biomarkers, elevation in a single biomarker, and elevation in both biomarkers groups, respectively. Similarly, among individuals with a PREVENT ASCVD risk ≥10%, those without any biomarker elevation, those with elevation in 1 biomarker, and those with elevations in both biomarkers had a cumulative incidence of cardiovascular mortality of 3.1%, 4.8%, and 21.8%, respectively (Figure 2). The C-statistics were 0.818 (SE: 0.012) and 0.811 (SE: 0.013) in the PREVENT model for all-cause mortality without and with biomarkers, respectively. For the outcome of cardiovascular mortality, the C-statistics of the PREVENT models without and with biomarkers were 0.828 (SE: 0.030) and 0.838 (SE: 0.033), respectively (Table 4). However, there were no significant changes in C-statistics in the PREVENT equations for all-cause and cardiovascular mortality after the addition of biomarkers (Table 5).

TABLE 3 Baseline Characteristics of the Cardiac Biomarker-Based Analytical Population in the National Health and Nutrition Examination Survey Cycles 1999-2004 (n/N = 6,482/15,898,740)

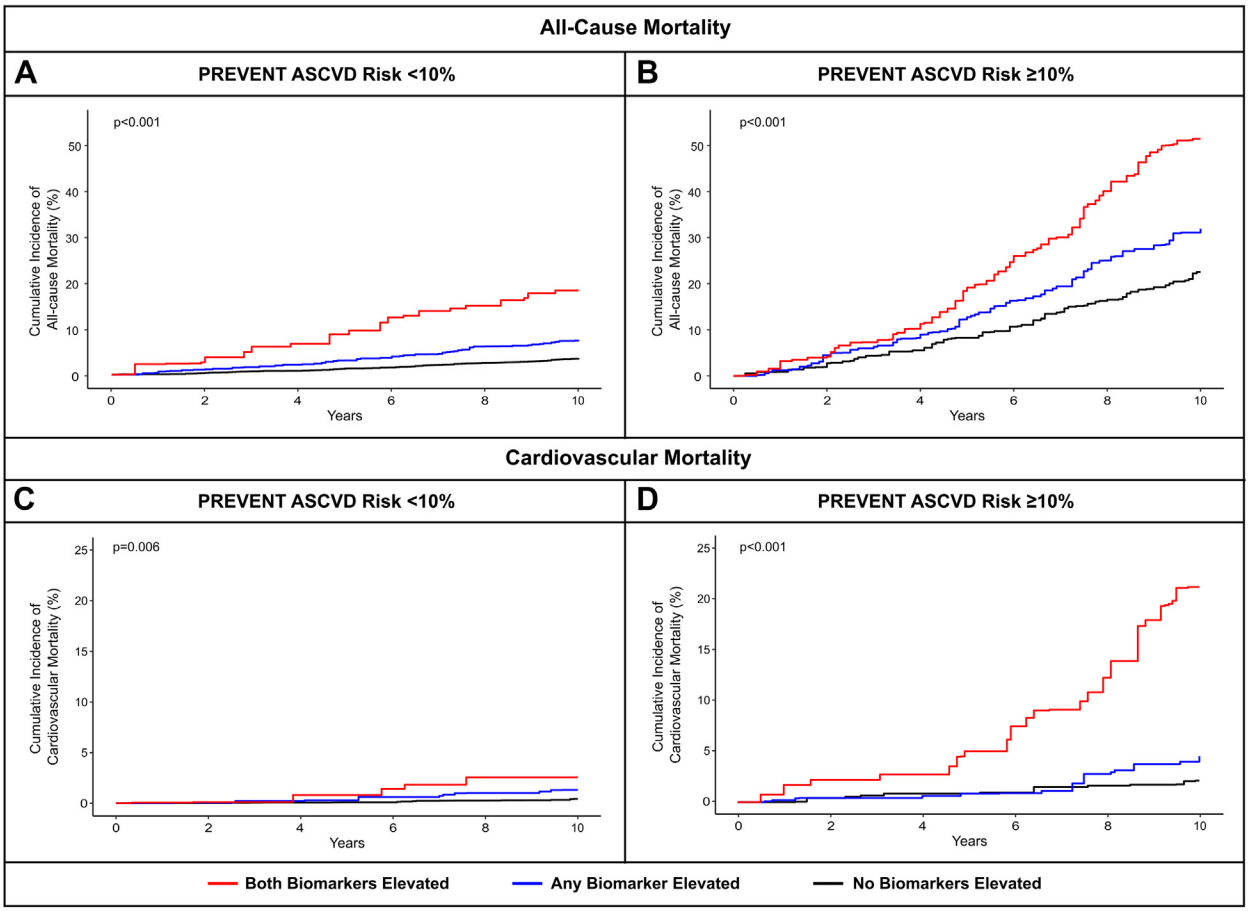
Age, y	46.1 (38.1-56.2)
Female	50.4 (49.1-51.7)[a]
Race and ethnicity	
Non-Hispanic White	74.0 (70.5-77.5)[a]
Non-Hispanic Black	9.7 (7.9-11.6)[a]
Other[b]	9.7 (7.1-12.4)[a]
Mexican American	6.5 (4.8-8.1)[a]
Education level	
High school or less	43.8 (41.4-46.3)[a]
More than high school	56.2 (53.7-58.6)[a]
Insurance status	
Insured	84.7 (83.0-86.5)[a]
Uninsured	15.3 (13.5-17.0)[a]
Family poverty income ratio	
≥1.30	84.0 (82.1-86.0)[a]
<1.30	16.0 (14.0-17.9)[a]
Systolic blood pressure, mm Hg	120 (111-132)
Diastolic blood pressure, mm Hg	73 (67-80)
Body mass index, kg/m^2	27.3 (24.1-30.8)
Statin use	9.5 (8.4-10.5)[a]
Current smoker	23.8 (22.1-25.4)[a]
Total cholesterol, mg/dL	204 (181-230)
HDL, mg/dL	50 (41-61)
GFR, mL/min per 1.73 m^2	100 (87-112)
Troponin I, ng/L	1.7 (1.1-2.6)
NT-proBNP, pg/mL	44.5 (22.8-85.4)
PCE ASCVD risk, (%)	2.8 (0.9-8.0)
PREVENT ASCVD risk, (%)	1.7 (0.8-4.3)

Values are median (IQR). [a]Values are % (95% CI). [b]Race reported as self-identified Hispanic or non-Hispanic other than Black, White, or Asian.
Abbreviations as in Table 1.

DISCUSSION

The current population-level analysis demonstrates that the PREVENT equations estimate a lower 10-year ASCVD risk than the PCEs. The lower estimation of risk by the PREVENT equations disproportionately affected non-Black individuals and males compared with their respective counterparts. Compared with the 1 in 10 individuals classified as high risk by the PCEs, the PREVENT equations categorized only 1 in 250 individuals as high risk. Among the individuals classified as high risk by the PCEs, the PREVENT equations reclassified 96.2% of individuals to a low/borderline risk category. The current article demonstrates that the discriminative ability for mortality was similar using the PREVENT equations and the PCEs. Addition of biomarkers to the PREVENT equations did not improve the risk stratification value for mortality.

FIGURE 2 Cumulative Incidence of All-Cause and Cardiovascular Mortality Stratified by 10-Year ASCVD Risk Estimated by the PREVENT Equations and Cardiac Biomarkers



This figure depicts the cumulative incidence of all-cause (Panels A and B) and cardiovascular (Panels C and D) mortality stratified by the 10-year ASCVD and cardiac biomarkers. Using the PREVENT equations, the cohort was stratified into high risk (≥10%) and low risk (<10%). Further stratification was done based on the N-terminal pro-B-type natriuretic peptide (NT-proBNP) and cardiac troponin I (cTnI) levels. Elevated NT-proBNP levels were defined as ≥125 pg/mL and elevated cTnI was defined as ≥6 ng/L in males and ≥4 ng/L in Females. Based on the biomarkers, the cohort was stratified into no biomarker elevations, elevations in either NT-proBNP or cTnI, and elevations in both NT-proBNP and cTnI. The log-rank test was used to compare the cumulative incidence of mortality across the groups. Abbreviations as in Figure 1.

While prior research demonstrated that the PREVENT equations had marginally better risk discrimination compared with the PCEs for the outcome of ASCVD,[4,5] the current article focused on comparing the risk prediction values of the PCEs and PREVENT equations for the outcome of all-cause and cardiovascular mortality. However, it should be noted that the calibration of PREVENT was significantly better than that of PCE for predicting outcomes such as ASCVD, total CVD, and heart failure. [4]

Despite the similar risk discrimination value of the PREVENT equations and the PCEs, the widespread clinical adoption of the PREVENT equations would need to account for the relatively lower risk estimates of the PREVENT equations as compared with PCEs. Current cholesterol and hypertension guidelines recommend using the 10-year ASCVD risk estimated by the PCEs to guide the initiation of therapy.[1,2] Therefore, replacing the PCEs with PREVENT equations may reduce the statin and antihypertensive

TABLE 4 Risk Discrimination of the PREVENT Equations on Including Cardiac Biomarkers for Predicting the Risk of All-Cause and Cardiovascular Mortality in the National Health and Nutrition Examination Survey Cycles 1999-2004

	Unadjusted		Adjusted[a]	
	All-Cause Mortality	Cardiovascular Mortality	All-Cause Mortality	Cardiovascular Mortality
PREVENT equations	0.808 (0.011)	0.838 (0.024)	0.818 (0.012)	0.828 (0.030)
PREVENT equations + NT-proBNP	0.795 (0.014)	0.825 (0.032)	0.806 (0.014)	0.830 (0.035)
PREVENT equations + troponin I	0.799 (0.012)	0.831 (0.025)	0.812 (0.012)	0.831 (0.030)
PREVENT equations + NT-proBNP + troponin I	0.799 (0.012)	0.833 (0.030)	0.811 (0.013)	0.838 (0.033)

[a]Models adjusted for income, insurance status, education level, and number of health care visits/year.
Abbreviations as in Table 1.

eligibility in the general population. Based on the 10-year ASCVD risk threshold of 5%, direct replacement of the PCEs with the PREVENT equations would reduce the statin-eligible population by ~11 million U.S. adults. Considering the recent reversal of the decline in cardiovascular mortality,[15,16] a reduction in the eligibility of statins and antihypertensives secondary to the implementation of the PREVENT equations may further intensify the increase in cardiovascular mortality. Furthermore, the relatively lower estimates of risk by the PREVENT equations compared with the PCEs disproportionately affects Black individuals. Black individuals have a higher burden of hypertension and cardiovascular mortality compared with other racial groups.[6,13,17] Hence, utilization of the PREVENT equations may further increase the racial disparities in CVD. Any attempt at clinical implementation of the PREVENT equation must be accompanied by an appropriate modification of the risk threshold to guide the initiation of statins and antihypertensives. Nonetheless, it important to note that the direct implementation of PREVENT equations may be beneficial in reducing statin over treatment among individuals in whom the PCEs overestimate ASCVD risk.

STUDY LIMITATIONS. The current study has several limitations. First, the study is limited by the measurement of the ASCVD risk at a single time point, while ASCVD risk is dynamic and changes over time. The change in the parameters included in the risk prediction equations over time could not be accounted for in the current study. Second, the PCEs and PREVENT equations were developed and validated for the outcome of ASCVD. However, the PREVENT equations can also estimate risk among individuals aged 30 to 79 years and account for lipid-lowering medication use. The PCEs are limited to individuals aged 40 to 79 years and not on statin therapy. The current study utilized mortality as the outcome of interest due to the unavailability of data on the outcome of ASCVD. Third, the study used data from the NHANES cycles between 1999 and 2004 as cardiac biomarkers were only available in these cycles. Fourth, it should be noted that smaller unweighted sample sizes, particularly for cardiovascular mortality, may impact the accuracy of our study results, warranting careful interpretation. Moreover, the equations used were not initially developed for the specific subgroups, especially within older age ranges, which may have been underrepresented. As a result, further research is needed to validate these findings in larger and more appropriately stratified populations. Fifth, the PREVENT equations incorporating additional measures glycosylated hemoglobin A1C levels, social determinants of

TABLE 5 Change in Discrimination of the PREVENT Equations on Including Cardiac Biomarkers for Predicting the Risk of All-Cause and Cardiovascular Mortality in the National Health and Nutrition Examination Survey Cycles 1999-2004

	Unadjusted		Adjusted[a]	
	All-Cause Mortality	Cardiovascular Mortality	All-Cause Mortality	Cardiovascular Mortality
PREVENT equations	Referent	Referent	Referent	Referent
PREVENT equations + NT-proBNP	−0.013 (−0.048 to 0.022)	−0.013 (−0.091 to 0.065)	−0.012 (−0.048 to 0.024)	0.002 (−0.088 to 0.092)
PREVENT equations + troponin I	−0.009 (−0.041 to 0.023)	−0.007 (−0.075 to 0.061)	−0.006 (−0.039 to 0.027)	0.003 (−0.08 to 0.086)
PREVENT equations + NT-proBNP + troponin I	−0.009 (−0.041 to 0.023)	−0.005 (−0.08 to 0.07)	−0.007 (−0.042 to 0.028)	0.010 (−0.077 to 0.097)

[a]Models adjusted for income, insurance status, education level, and number of health care visits/year.
Abbreviations as in Table 1.

health, and urine albumin creatinine ratio were not assessed.

CONCLUSIONS

This population-level analysis shows that the PREVENT equations estimate a lower 10-year ASCVD risk compared with PCEs. The relatively lower risk estimates of the PREVENT equation disproportionately affect males and Black individuals compared with their respective counterparts. The PREVENT equations and PCEs have similar risk prediction values for mortality. The inclusion of cardiac biomarkers did not improve the mortality risk prediction value of the PREVENT equations.

FUNDING SUPPORT AND AUTHOR DISCLOSURES

Dr Arora is supported by the National Heart, Lung, and Blood Institute of the National Institutes of Health (NIH) awards (R01HL160982, R01HL163852, and R01HL163081); and has received grant support from Merck Sharp & Dohme LLC and Bristol Myers Squibb and consulting income from Bristol Myers Squibb, which are all unrelated to this work. Dr Patel is supported by the National Institutes of Health grant T32HL007457. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose.

ADDRESS FOR CORRESPONDENCE: Dr Pankaj Arora, Division of Cardiovascular Disease, The University of Alabama at Birmingham, 1670 University Boulevard, Volker Hall B140, Birmingham, Alabama 35294-0019 USA. E-mail: parora@uabmc.edu.

PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: The PREVENT Equations generate lower ASCVD risk estimates compared with the PCEs. The relative estimation of ASCVD risk by the PREVENT Equations compared with the PCEs disproportionately affects males and non-Hispanic Black individuals compared with their respective counterparts. The risk discrimination values of the PREVENT Equations and PCEs for all-cause and cardiovascular mortality were similar. The addition of cardiac biomarkers does not improve the mortality risk discrimination value of the PREVENT Equations.

TRANSLATIONAL OUTLOOK: Considering the use of ASCVD risk to guide initiation of antihypertensive and statin therapy, the replacement of the PCEs with the PREVENT Equations should be accompanied by modifications in the ASCVD thresholds for initiation of antihypertensive and statin therapy to account for the lower ASCVD risk estimates of the PREVENT Equations compared with the PCEs. Direct replacement of the PCEs with the PREVENT Equations may lead to the widening of racial disparities in cardiovascular disease as the relatively lower ASCVD risk estimates of the PREVENT Equations compared with the PCEs disproportionately affect Black individuals compared with their counterparts. Given that cardiac biomarkers do not improve the mortality risk prediction value of the PREVENT Equations, further research should focus on delineating a targeted population that would benefit from cardiac biomarker testing above and beyond the PREVENT Equations.

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KEY WORDS cardiac biomarkers, mortality, Pooled Cohort Equations, PREVENT equations, risk reclassification

APPENDIX For supplemental tables and a figure, please see the online version of this paper.