

ORIGINAL INVESTIGATIONS

A Systematic Examination of the 2013 ACC/AHA Pooled Cohort Risk Assessment Tool for Atherosclerotic Cardiovascular Disease



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ABSTRACT

BACKGROUND The 2013 American College of Cardiology/American Heart Association updated cholesterol guidelines recommend the use of Pooled Cohort Equations to estimate 10-year absolute risk for atherosclerotic cardiovascular disease (ASCVD) in primary prevention.

OBJECTIVES This study sought to systematically examine the Pooled Cohort Equations to determine risk factor levels required to exceed risk thresholds outlined in new cholesterol guidelines.

METHODS We entered continuous risk factor levels in isolation and in specified combinations with the risk tool, and we observed predicted risk output patterns. We used the 10-year ASCVD risk threshold of $\geq 7.5\%$ as a clinically relevant risk threshold.

RESULTS We demonstrated that a hypothetical man or woman can reach clinically relevant risk thresholds throughout the eligible age spectrum of 40 to 79 years of age, depending on the associated risk factor burden in all race-sex groups. Age continues to be a major determinant of 10-year ASCVD risk for both men and women. Compared with the previous risk assessment tool used in cholesterol guidelines, the inclusion of a stroke endpoint and use of race-specific coefficients permit identification of at-risk African Americans and non-Hispanic white women at much younger ages and lower risk factor levels.

CONCLUSIONS These data provide context of specific risk factor levels and groups of individuals who are likely to have 10-year ASCVD risk estimates $\geq 7.5\%$. Age continues to be a major driver of risk, which highlights the importance of the clinician-patient discussion before statin therapy is initiated. (J Am Coll Cardiol 2014;64:959-68) © 2014 by the American College of Cardiology Foundation.

In November 2013, the American College of Cardiology (ACC) and American Heart Association (AHA) released updated clinical practice guidelines for the treatment of blood cholesterol to reduce atherosclerotic cardiovascular disease (ASCVD) risk (1). The guidelines reaffirm the importance of absolute

risk estimation in guiding primary prevention treatment decisions, thereby necessitating the use of multivariable risk equations to quantify this risk. Instead of using the Adult Treatment Panel III (ATP III) risk calculator to estimate 10-year coronary heart disease (CHD) risk, the cholesterol guidelines recommend using

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ABBREVIATIONS AND ACRONYMS

ASCVD = atherosclerotic cardiovascular disease

ATP III = Adult Treatment Panel III report

CHD = coronary heart disease

CVD = cardiovascular disease

HDL-C = high-density lipoprotein cholesterol

NHANES = National Health and Nutrition Examination Surveys

SBP = systolic blood pressure

a novel risk assessment tool, developed by the ACC/AHA Risk Assessment Work Group, called the *Pooled Cohort Equations* to estimate 10-year ASCVD risk (2). In the primary prevention subset, the cholesterol guidelines provide a strong recommendation (Class I, Level of Evidence: A) for consideration of statin treatment in individuals with a 10-year ASCVD risk $\geq 7.5\%$ and a moderate recommendation (Class IIa, Level of Evidence: B) in individuals with a 10-year ASCVD risk of 5% to $< 7.5\%$. The guidelines then advise clinicians to engage in a clinician-patient discussion to individualize the decision to initiate statin

treatment on the basis of patient preferences and the potential for ASCVD risk reduction, adverse effects, and drug-drug interactions.

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Although the Pooled Cohort Equations use many of the same covariates included in the ATP III risk calculator to quantitatively assess risk, the equations represent a departure from the previous tool. On the basis of recommendations from the AHA and the American Stroke Association, the Pooled Cohort Equations expand the endpoint for prediction to ASCVD to include fatal and nonfatal stroke (3). Moreover, diabetes is added as a predictor variable to allow risk stratification in the growing diabetic population. Additionally, the equations are derived from pooled data from racially and geographically diverse community-based cohorts, which permits the creation of sex- and race-specific equations for non-Hispanic white and African-American women and men (2).

We have previously investigated the intrinsic properties of Framingham-derived risk scores used in general practice (4,5). This work highlighted inherent limitations of these risk scores and the tendency to classify younger individuals and women with high risk factor burden as having “low” 10-year predicted risk. With the recent update in the cholesterol guidelines, a revised risk threshold, and the publication of the Pooled Cohort Equations, we sought to examine the intrinsic properties of the new risk assessment tool to better understand how it may guide quantitative risk assessment in primary prevention. Therefore, the objective of this study is to systematically evaluate the Pooled Cohort Equations using a previously published algorithm to determine the risk factor combinations and risk factor levels that are required to exceed treatment consideration thresholds in different age, sex, and race groups.

METHODS

The Pooled Cohort Equations are sex- and race-specific risk prediction models that incorporate age, total and high-density lipoprotein (HDL) cholesterol levels, systolic blood pressure (SBP), use of antihypertensive medication, smoking status, and diabetes status into multivariable Cox proportional hazards regression equations to estimate the 10-year absolute risk for ASCVD (includes nonfatal myocardial infarction, nonfatal stroke, and fatal cardiovascular disease [CVD]) (2). The model is based on pooled data from several contemporary National Heart, Lung, and Blood Institute-sponsored cohort studies, such as the ARIC (Atherosclerosis Risk in Communities) study (6), the CHS (Cardiovascular Health Study) (7), and the CARDIA (Coronary Artery Risk Development in Young Adults) study (8), combined with applicable data from the Framingham Original (9) and Offspring Study (10) cohorts. In total, the equations were derived from 9,098 non-Hispanic white men (1,259 events), 1,647 African-American men (238 events), 11,240 non-Hispanic white women (902 ASCVD events), and 2,641 African-American women (290 events) between 40 and 79 years of age who were free of a previous history of myocardial infarction (recognized or unrecognized), stroke, congestive heart failure, percutaneous coronary intervention, coronary bypass surgery, or atrial fibrillation.

We downloaded an online spreadsheet of the Pooled Cohort Equations, incorporating the sex- and race-specific equations (11). We entered data directly into the spreadsheet for a hypothetical non-Hispanic white man, African-American man, non-Hispanic white woman, and African-American woman from 40 to 79 years of age in 5-year increments. This approach does not examine risks for specific individuals or a specific population; rather, it systematically varies individual risk factors and aggregate risk factor burden to examine the effect on estimated 10-year ASCVD risk. We gave special attention to estimated 10-year risk $\geq 7.5\%$ because this is the threshold delineated in the cholesterol guidelines with a Class I recommendation to mark the point at which the use of a statin is recommended, because ASCVD risk reduction with a statin exceeds the risk of adverse events as reported in clinical trials.

RISK CALCULATION PROCEDURE FOR SINGLE RISK FACTORS. We varied single risk factor levels in isolation, holding other risk factor levels constant at age-adjusted national mean values, to compare the effects of individual risk factor levels on 10-year predicted risk for a non-Hispanic white man,

African-American man, non-Hispanic white woman, and an African-American woman. Age-adjusted national mean values derived from published analyses from the National Health and Nutrition Examination Surveys (NHANES) are shown in **Table 1** (12,13). We used age-specific blood pressure values to reflect the normative aging process seen with blood pressure and different mean SBP values for those who were treated and not treated with antihypertensive medications. For these analyses, we used non-smoking and nondiabetic status, because they are normative values in the population. Using the entire range of values permitted by the risk assessment tool, we varied total cholesterol from 130 to 320 mg/dl in increments of 10 mg/dl, HDL cholesterol from 20 to 100 mg/dl in increments of 5 mg/dl, and SBP from 90 to 200 mm Hg in increments of 10 mm Hg. We also compared the estimated 10-year risks for smokers (versus nonsmokers) and diabetics (versus nondiabetics), holding all other risk factors constant at age-adjusted national mean values for each race-sex group. For all analyses, we calculated separate 10-year risk estimates for those with and without antihypertensive therapy. For example, to determine the effect of total cholesterol on 10-year ASCVD risk in a 55-year-old non-Hispanic white woman with treated hypertension, we selected appropriate demographic parameters and set HDL cholesterol at 58 mg/dl, SBP at 127 mm Hg, “yes” to antihypertensive therapy, and “no” to smoking and diabetes status. We then varied total cholesterol from 130 to 320 mg/dl and recorded 10-year predicted ASCVD risk estimates.

RISK CALCULATION PROCEDURE FOR MULTIPLE RISK FACTORS. We varied the levels of all the risk factors to values around national mean levels to examine the effects of different risk factor combinations on 10-year estimated ASCVD risk. We chose ranges to be inclusive of a low value and a modestly abnormal value at intervals roughly equal to 1 SD in the population of U.S. adults. For total cholesterol, we included values of 160 mg/dl (\approx 1 SD below the mean), 200 mg/dl (approximate national mean), and 240 mg/dl (\approx 1 SD above the mean). For each race-sex group, we used the appropriate mean HDL cholesterol level \pm 10 mg/dl. For SBP, we used 110 mm Hg, 130 mm Hg, and 150 mm Hg. We also varied smoking status, diabetes status, and antihypertensive therapy use for all risk factor combinations. We examined the results for ages 40 to 75 years in 5-year intervals but only graphically display the results for 50-year-old men and 60-year-old women. These ages were chosen because it was thought that they would offer the most representative patterns of predicted risk factor

TABLE 1 Age-Adjusted Mean National Levels for Cholesterol and SBP by Race-Sex Group

	Men		Women	
	Non-Hispanic White Men	African-American Men	Non-Hispanic White Women	African-American Women
Total cholesterol, mg/dl	193 (191-195)	191 (188-193)	200 (198-202)	192 (190-194)
HDL cholesterol, mg/dl	46.7 (45.8-47.5)	52.6 (51.6-53.6)	58.1 (56.8-59.4)	58.7 (57.2-60.2)
SBP for ages 18-39 yrs, mm Hg	118 (0.4)	121 (0.4)	109 (0.3)	114 (0.5)
SBP for ages 40-59 yrs, mm Hg	124 (0.5)	129 (0.8)	120 (0.5)	128 (0.9)
SBP for ages \geq 60 yrs, mm Hg	132 (0.6)	137 (0.9)	138 (0.6)	144 (1.2)
Treated SBP for ages 18-39 yrs, mm Hg	126 (1.7)	130 (2.7)	119 (2.4)	129 (2.9)
Treated SBP for ages 40-59 yrs, mm Hg	128 (0.9)	135 (1.6)	127 (1.1)	133 (1.3)
Treated SBP for ages \geq 60 yrs, mm Hg	134 (0.7)	138 (1.2)	141 (0.8)	144 (1.3)

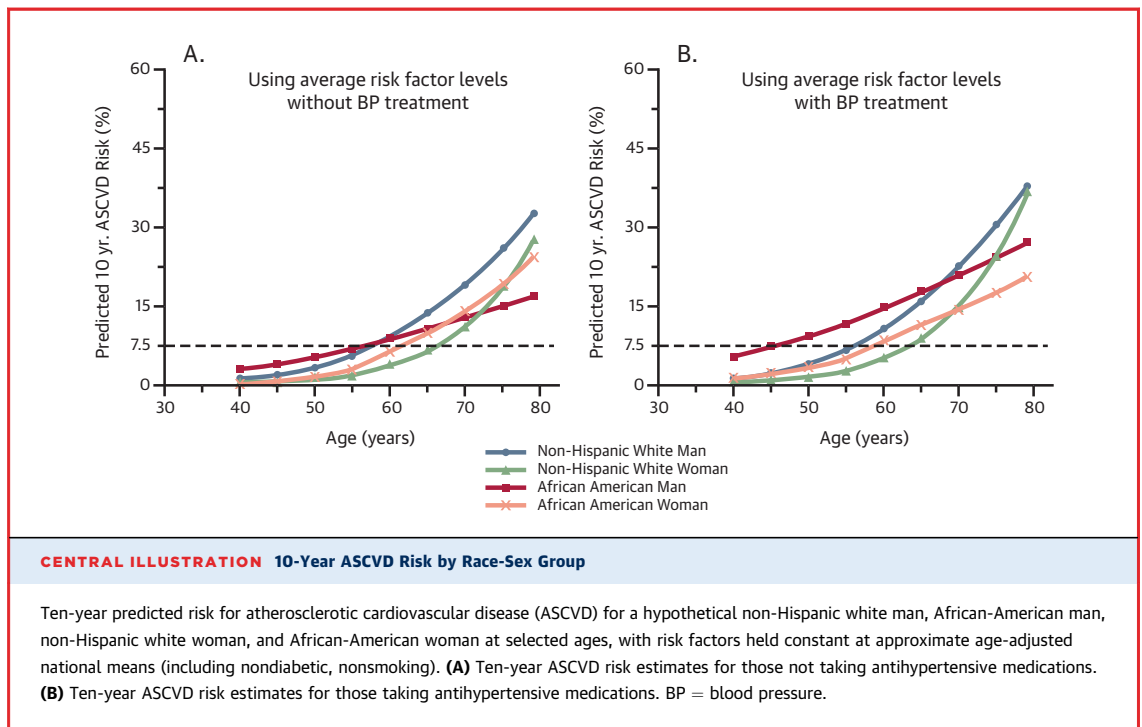
Values are mean (95% confidence interval) from Carroll et al. (13) or mean (standard error) from Wright et al. (12). HDL = high-density lipoprotein; SBP = systolic blood pressure.

combinations without an undue influence of age, with the understanding that absolute predicted risks vary directly and substantially with age.

RESULTS

EFFECT OF VARYING AGE WITH OTHER RISK FACTORS HELD CONSTANT AT NATIONAL MEAN LEVELS. When we held all risk factors constant at the age-adjusted national mean level for each race-sex group, the 10-year predicted ASCVD risk was substantially greater with increasing age (**Central Illustration**). From 40 to 55 years of age, predicted ASCVD risk was greatest in an African-American man, followed by a non-Hispanic white man, an African-American woman, and a non-Hispanic white woman. After 60 years of age, a non-Hispanic white man tended to have the highest 10-year ASCVD risk, followed by an African-American woman, a non-Hispanic white woman, and an African-American man. There was an accelerated predicted ASCVD risk after 60 years of age, which was in part an artifact explained by the use of age-specific SBP values in our model.

A non-Hispanic white man with average risk factor levels exceeded the 7.5% 10-year ASCVD risk threshold after 60 years of age, regardless of hypertension treatment status. An African-American man with average risk factor levels exceeded the 7.5% 10-year ASCVD risk threshold after 50 years of age, if his blood pressure was treated, and after 60 years of age if not treated. A non-Hispanic white woman with average risk factor levels exceeded the 7.5% ASCVD



risk threshold after 65 years of age if she had treated blood pressure and after 70 years of age if not treated. An African-American woman with average risk factor levels exceeded the 7.5% 10-year ASCVD risk threshold after 60 years of age if she had treated blood pressure and 65 years of age if not treated.

EFFECT OF VARYING SINGLE RISK FACTORS WITH OTHERS HELD CONSTANT AT NATIONAL MEAN LEVELS FOR DIFFERENT AGES. Ten-year ASCVD risks estimated after we individually varied total cholesterol, HDL cholesterol, untreated SBP, or treated SBP with all other risk factors held at age-adjusted mean levels for selected ages are shown in [Figures 1 and 2](#) (all ages entered are included in [Online Figures 1 and 2](#)). Ten-year risk varied linearly with total cholesterol, untreated SBP, and treated SBP variations in all race-sex groups. Linear variation was modest for total cholesterol and more prominent for untreated and treated SBP. Risk varied curvilinearly with HDL cholesterol for all ages in a non-Hispanic white man and an African-American man ([Figures 1B and 1F](#)) but only up to 70 years of age for a non-Hispanic white woman and 60 years of age for an African-American woman ([Figures 2B and 2F](#)). After these ages, risk estimates in women appeared to converge, which reflects interaction terms within the model or lack of data at the extremes of age and HDL cholesterol levels. In a hypothetical man who was a nonsmoker and did not have diabetes, 10-year

estimated ASCVD risk exceeded 7.5% at every level entered for total cholesterol, HDL cholesterol, and treated SBP after 65 years of age regardless of race. In a similar hypothetical woman, this occurred at 75 years of age regardless of race.

EFFECT OF SMOKING OR DIABETES STATUS ON ESTIMATED 10-YEAR ASCVD RISK. Smoking and diabetes both had prominent effects on 10-year risk of ASCVD in all race-sex groups. In a hypothetical man with average risk factor levels and untreated SBP, the presence of smoking or diabetes led to a 10-year estimated ASCVD risk $\geq 7.5\%$ at 55 years of age for a non-Hispanic white man or 45 years of age for an African-American man (50 years of age and 40 years of age, respectively, if there was treated SBP). In a hypothetical woman with average risk factor levels, the presence of smoking or diabetes led to a 10-year predicted risk $\geq 7.5\%$ at 60 years of age for a non-Hispanic white woman and 60 years of age for an African-American woman (60 years of age and 50 years of age, respectively, if there was treated SBP). In all 4 race-sex groups, the presence of diabetes appeared to have a slightly more prominent effect on predicted risk than smoking. The effect of diabetes status on 10-year predicted risk is demonstrated in [Figure 3](#).

EFFECT OF VARYING MULTIPLE RISK FACTORS SIMULTANEOUSLY. Ten-year ASCVD risk with varying levels of risk factors (but no antihypertensive use)

is demonstrated for a hypothetical 50-year-old man in **Figure 4** and a 60-year-old woman in **Figure 5** for each race category. For the risk factor levels we entered, the range of estimated risk for a hypothetical 50-year-old non-Hispanic white man was 1.7% to 30.5% in a diabetic smoker (reaching 34.9% if SBP was treated and uncontrolled) and 3.5% to 23.3% (reaching 36.4% if SBP was treated and uncontrolled) for an African-American man. For a hypothetical 60-year-old non-Hispanic white woman, estimated 10-year risk was 1.8% to 21.3% (reaching 27.9% if SBP was treated and uncontrolled) and 2.4% to 39.7% (reaching 49.4% if SBP was treated and uncontrolled) for an African-American woman.

If all “low” risk factors were entered (indicated by total cholesterol of 160 mg/dl; HDL cholesterol of 57 mg/dl for a non-Hispanic white man, 63 mg/dl for an African-American man, 68 mg/dl for a non-Hispanic white woman, or 69 mg/dl for an African-American woman; and untreated SBP of 110 mm Hg) and there was no smoking or diabetes, the 10-year ASCVD risk threshold of $\geq 7.5\%$ was reached at 65 years of age in a non-Hispanic white man, 70 years of age in an African-American man, 75 years of age in a non-Hispanic white woman, and 70 years of age in an African-American woman. If “modestly abnormal” risk factor levels were entered (indicated by total cholesterol of 240 mg/dl; HDL cholesterol of 37 mg/dl for a non-Hispanic white man, 43 mg/dl for an African-American man, 48 mg/dl for a non-Hispanic white woman, or 49 mg/dl for an African-American woman; and untreated SBP of 150 mm Hg) and there was no smoking or diabetes, 10-year ASCVD risk $\geq 7.5\%$ was reached at 50 years of age for both a non-Hispanic white man and an African-American man, 65 years of age for a non-Hispanic white woman, and 60 years of age for an African-American woman. Because of the strong relationship between age and estimated risk, younger adults with these same abnormal values for major risk factors were estimated to be at lower 10-year ASCVD risk. With the same risk factor combinations plus the addition of diabetes or smoking, the 7.5% risk threshold was reached at younger ages for all race-sex groups.

If all “optimal” risk factor levels, as defined by the ACC/AHA Prevention Guidelines panel (total cholesterol 170 mg/dl, HDL 50 mg/dl, untreated SBP of 110 mm Hg, and no diabetes or smoking) (1), were entered into the risk calculator, the 10-year ASCVD risk threshold of 7.5% was reached at 65 years of age for a non-Hispanic white man, 70 years of age for an African-American man, 75 years of age for a

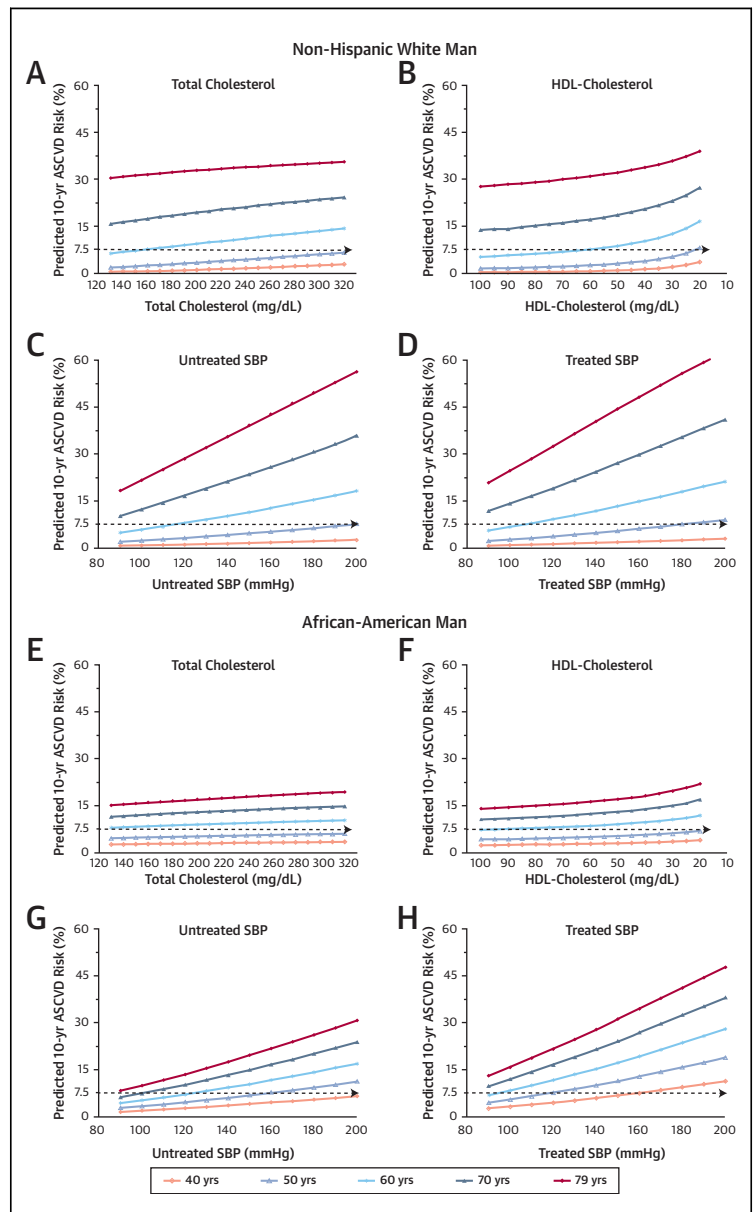
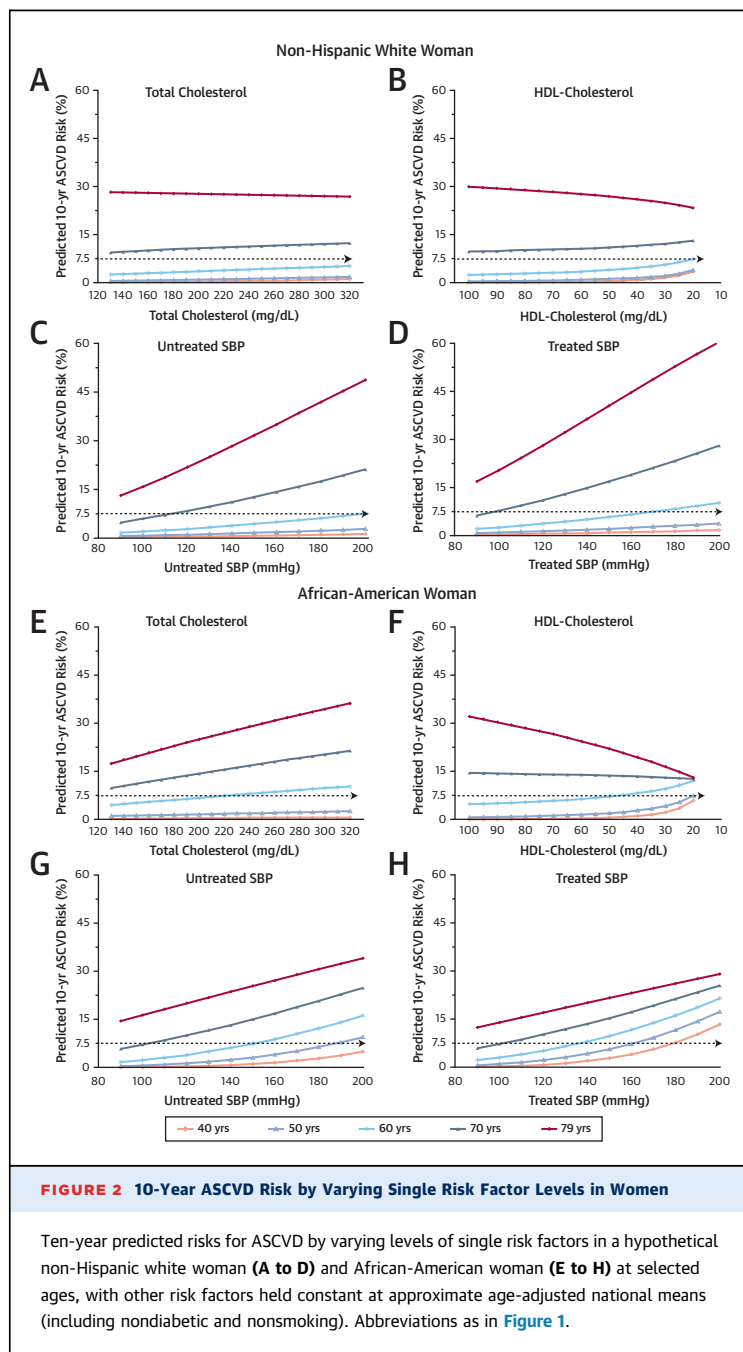


FIGURE 1 10-Year ASCVD Risk by Varying Single Risk Factor Levels in Men

Ten-year predicted risks for atherosclerotic cardiovascular disease (ASCVD) by varying levels of single risk factors in a hypothetical non-Hispanic white man (**A to D**) and African-American man (**E to H**) at selected ages, with other risk factors held constant at approximate age-adjusted national means (including nondiabetic and nonsmoking). HDL = high-density lipoprotein; SBP = systolic blood pressure.

non-Hispanic white woman, and 70 years of age for an African-American woman.

For a 40-year-old, the full range of predicted 10-year ASCVD risk with the risk factor levels we entered was 0.4% to 22.5% for a non-Hispanic white man, 2.1% to 23% for an African-American man, 0.2% to 15.3% for a non-Hispanic white



woman, and 0.1% to 23.5% for an African-American woman. For a 75-year-old, the full range of predicted 10-year ASCVD risk with the risk factor levels we entered was 17.5% to 67% for a non-Hispanic white man, 9.3% to 70.9% for an African-American man, 12% to 61% for a non-Hispanic white woman, and 11.8% to 71.2% for an African-American woman.

DISCUSSION

In this study, we systematically evaluated the intrinsic properties of the 2013 ACC/AHA Pooled Cohort Equations under various risk factor combinations and levels. We demonstrated that a hypothetical man and woman could reach a clinically relevant 10-year risk threshold of $\geq 7.5\%$ throughout the eligible age spectrum of 40 to 79 years of age, depending on the associated risk factor burden. Three key observations stand out in our analyses. First, there were important race-sex interactions with risk factor levels that reflected differential risk for ASCVD events, which may be particularly notable given the inclusion of fatal and nonfatal stroke in the endpoint. Second, the inclusion of diabetes in the equations led to important differences in predicted risk that could influence decision making in younger people with diabetes. Finally, age remained a major driver of predicted 10-year risk in the new equations, which highlights the importance of the clinician-patient discussion before the initiation of statin therapy, especially for those uncommon individuals whose sole risk factor is advanced age.

The Pooled Cohort Equations share many features with the ATP III risk assessment tool used in prior cholesterol guidelines, such as use of traditional covariates (age, sex, smoking, SBP, total cholesterol, HDL cholesterol, and antihypertensive medication use) and estimation of CVD risk over a 10-year time frame. However, unlike the ATP III risk calculator, this equation also includes diabetes as a predictor variable, expands the prediction endpoint to include fatal and nonfatal stroke, and is derived from a racially and geographically diverse sample, which permits the development of sex- and race-specific equations for non-Hispanic white and African-American men and women. These changes modify quantitative risk estimation particularly in African Americans, as well as in non-Hispanic white women, for whom risk for stroke increases earlier in life than risk for CHD (14).

CLINICAL IMPLICATIONS. Our previous evaluation of the intrinsic properties of the ATP III risk calculator demonstrated that few women exceeded treatment thresholds set by ATP III guidelines when a risk calculator that predicted a CHD endpoint was used (4). For example, with ATP III, a nondiabetic man with average risk factor levels could reach the 10% intermediate-risk category over 60 years of age. A woman, however, remained in a low-risk category at all eligible ages. Moreover, unlike a man, who could exceed the 10% intermediate-risk threshold with modestly elevated risk factors at 45 years of

age, a woman could only reach this risk threshold with extreme risk factor levels after 70 years of age (4). Thus, per ATP III guidelines, few women qualified for intensive CVD prevention when ATP III treatment thresholds were imposed on the ATP III risk calculator to guide treatment. The inclusion of stroke in the new Pooled Cohort Equations and the emphasis on absolute risk, independent of low-density lipoprotein cholesterol targets, results in the identification of many more women who may benefit from consideration of statin treatment. Because stroke constitutes a much greater proportion of CVD events in women (many of whom are younger than 75 years of age) (14), these changes in risk assessment may hold important public health implications.

Racial disparities in CVD risk between African Americans and non-Hispanic whites are well established. In nearly every age group, but particularly among those <65 years of age, incident risk for CHD and stroke is higher among African Americans than among non-Hispanic whites (15). Moreover, incident CVD events are more likely to be fatal in African Americans than in non-Hispanic whites (16,17). In the REGARDS (Reasons for Geographic and Racial Differences in Stroke) study, the black/white mortality ratio for stroke was 3.7 in men 45 to 54 years of age (16). The creation of race-specific risk equations now allows recognition and quantification of the different risk profiles and potential for benefit in African-American individuals compared with non-Hispanic whites, particularly at younger ages.

Among those with risk factor levels at national mean values, our results revealed that estimated 10-year ASCVD risk was greater in an African-American man than in other race-sex groups from 40 to 55 years of age, regardless of blood pressure treatment, presence of diabetes, or smoking status. As has been demonstrated previously, a portion of this increased risk is due to a higher prevalence of traditional risk factors, such as hypertension (as reflected by the mean SBP levels used in our calculations) and diabetes (18-20). However, it also highlights the potential benefit of identifying this higher-risk group and controlling these elevated risk factors in primary prevention to reduce the incidence of future CVD events.

The incorporation of diabetes into quantitative risk assessment is another shift from ATP III, in which diabetes was considered a "risk equivalent" condition. Subsequent studies, including a systematic review, have demonstrated that CHD risk for people with diabetes in primary prevention is not

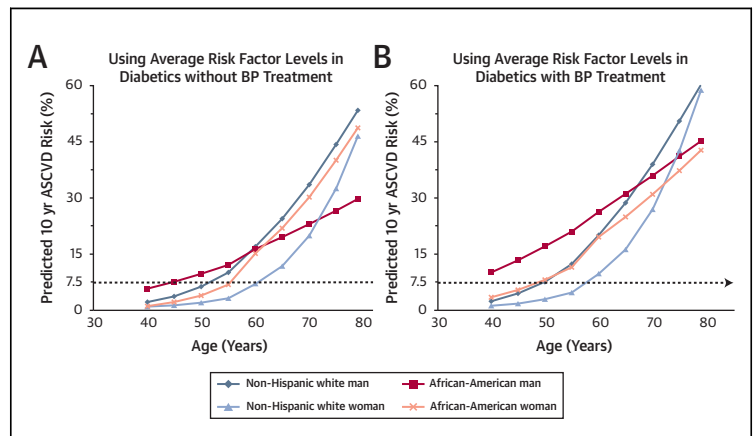
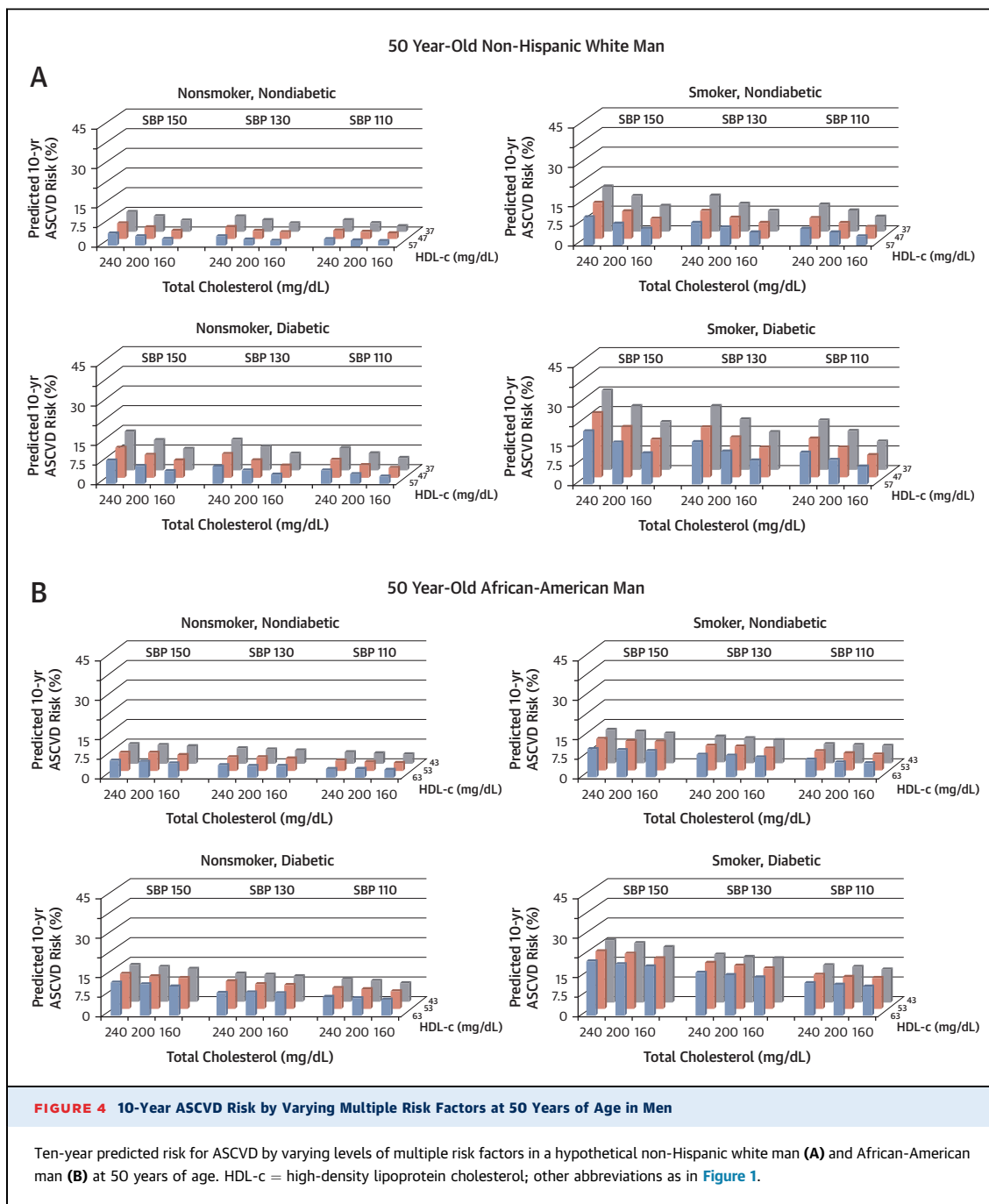


FIGURE 3 10-Year ASCVD Risk in Diabetic Patients by Race-Sex Group

Ten-year predicted risk for atherosclerotic cardiovascular disease (ASCVD) for a hypothetical non-Hispanic white man, African-American man, non-Hispanic white woman, and African-American woman with diabetes at selected ages, with risk factors held constant at approximate age-adjusted national means (including nonsmoking). (A) Ten-year ASCVD risk estimates for those not taking antihypertensive medications. (B) Ten-year ASCVD risk estimates for those taking antihypertensive medications. BP = blood pressure.

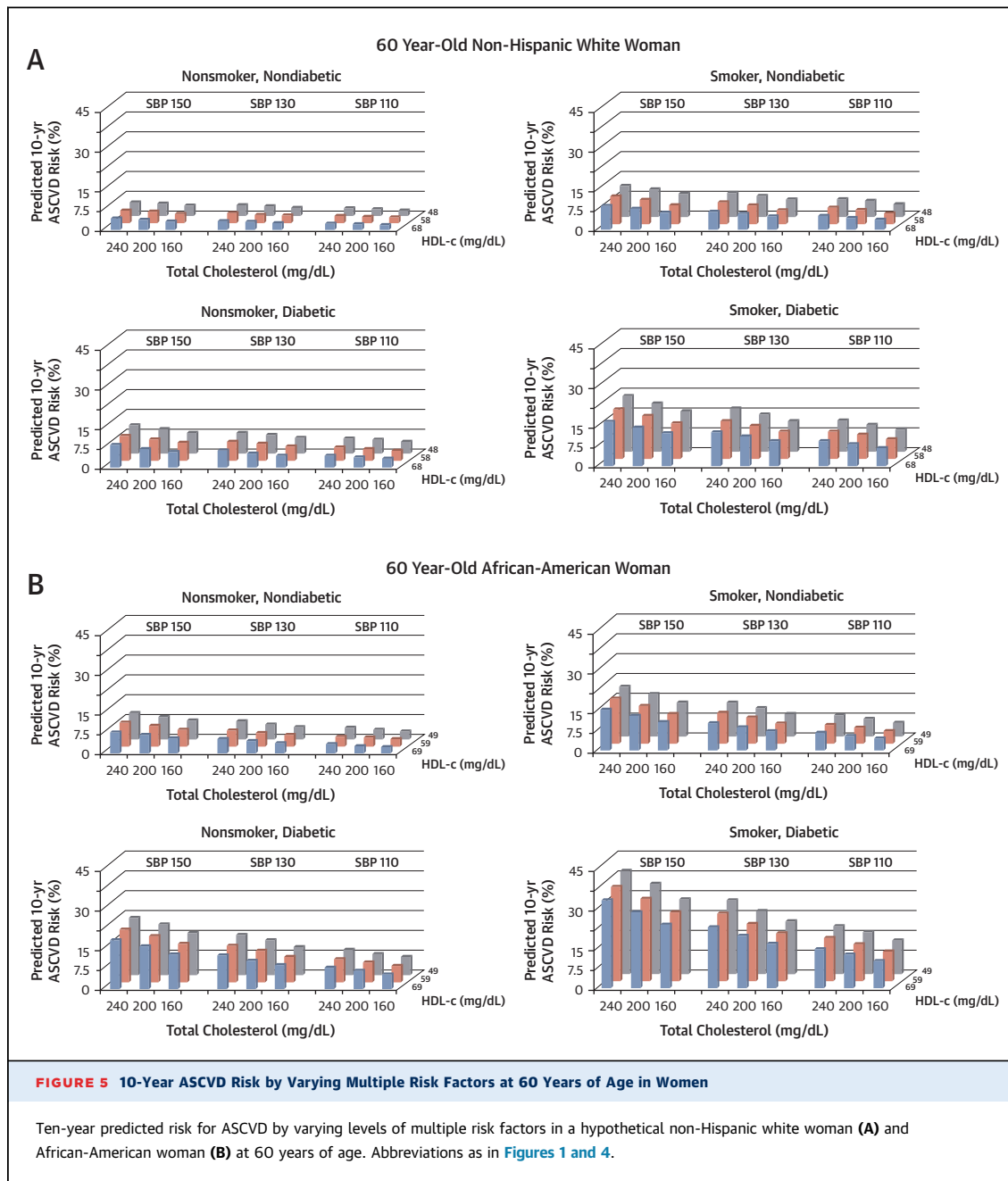
equivalent to the risk seen for individuals with prior CHD events and have suggested that the diabetic population may benefit from further risk stratification (21). In our evaluation of people with diabetes, a nonsmoking, non-Hispanic white man ≤ 50 years of age, an African-American man ≤ 40 years of age, a non-Hispanic white woman ≤ 60 years of age, and an African-American woman ≤ 55 years of age with otherwise average risk factor levels could have an estimated 10-year ASCVD risk <7.5%. This means clinicians can discuss the relative merits of statin treatment on an individual basis with younger people who have diabetes. Nevertheless, diabetes remains a major risk factor for CVD, and the presence of diabetes increases predicted 10-year ASCVD risk in all race-sex groups. For example, 60 years of age in a non-Hispanic white man, 55 years of age in an African-American man, or 70 years of age in a woman (regardless of race), nearly all people with diabetes, even those with the low risk factor levels, exceed the 7.5% 10-year risk threshold.

The strong age effect on 10-year multivariable risk assessment was once again demonstrated. Even among individuals with optimal risk factors, 10-year ASCVD risk $\geq 7.5\%$ was reached by 65 years of age in a non-Hispanic white man, 70 years of age in an African-American man, 75 years of age in a non-Hispanic white woman, and 70 years of age in an African-American woman. Unfortunately, very few individuals with all optimal risk factors actually exist



in the United States, as data from National Health and Nutrition Examination Surveys (NHANES) estimate a prevalence of 2.4% of all optimal risk factors in U.S. adults ≥ 60 years of age (15). A brief analysis of NHANES from 2007 to 2010 among non-pregnant participants 40 to 79 years of age without prevalent CVD revealed a prevalence of optimal risk factors of only 4.9% in all adults 40 to 79 years of age. Among non-Hispanic white men ≥ 65 years of age, the

prevalence of all optimal risk factors was 5.8%, and among non-Hispanic white women ≥ 75 years of age, the prevalence of all optimal risk factors was 2.4%. Within the NHANES dataset, there were no African-American men or women who had all optimal risk factors. Thus, the clinical and public health significance of this feature of the equations is minimal. From a clinical perspective, the recommended clinician-patient discussion should facilitate shared



decision making regarding the potential use of statins in these individuals with optimal risk factors. Conversely, young individuals 40 to 50 years of age may not reach a 10-year predicted ASCVD risk of 7.5% or even the moderately recommended risk threshold of 5% to <7.5% 10-year ASCVD risk in spite of significant risk factor burden. These findings highlight the importance of engaging in a clinician-patient discussion before statin prescription to review the specific components that contribute to the patient's CVD risk and potential modifiable factors

that could mitigate that risk. They also underscore the importance of the recommendation to assess longer-term risk in younger individuals (age ≤ 50 years of age) who may have substantial risk factor burden but low short-term risk, primarily because of their age.

STUDY LIMITATIONS. The precision of our findings is limited by the increments of age and risk factor levels that were used. We also varied a single risk factor at a time to illustrate the impact of the particular risk factor on predicted 10-year ASCVD risk. However, we

acknowledge that many risk factors are correlated and that some of our combinations would be rare in the general population. Although the Pooled Cohort Equations were derived from a more contemporary and diverse population than the previous Framingham-derived ATP III risk tool, the accuracy of current estimates is still limited by the relatively small numbers of African Americans included in the cohorts and secular trends of declining ASCVD incidence, which may lead to overestimation of risk.

CONCLUSIONS

The updated ACC/AHA cholesterol guidelines recommend the use of newly derived Pooled Cohort Equations to estimate 10-year ASCVD risk. The present study provides context of specific risk factor levels and groups of individuals who are likely to have 10-year ASCVD risk estimates exceeding 7.5%. Compared with the ATP III risk assessment tool, the inclusion of stroke endpoints and use of race-specific coefficients permits identification of at-risk women and African Americans at much younger ages and at lower risk factor levels. Age continues to be a major

driver of 10-year ASCVD risk, which highlights the importance of the clinician-patient discussion before initiation of statin therapy.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: The 2013 American College of Cardiology/American Heart Association guidelines on management of blood cholesterol recommend new Pooled Cohort Equations to estimate a patient's 10-year risk of atherosclerotic cardiovascular disease for primary prevention.

TRANSLATIONAL OUTLOOK: The effectiveness of guiding cardiovascular disease prevention on the basis of estimated absolute risk needs verification in prospective studies.

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APPENDIX For supplemental figures, please see the online version of this article.