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Accuracy of the Atherosclerotic Cardiovascular Risk Equation in a Large Contemporary, Multiethnic Population

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ABSTRACT

BACKGROUND The accuracy of the 2013 American College of Cardiology/American Heart Association (ACC/AHA) Pooled Cohort Risk Equation for atherosclerotic cardiovascular disease (ASCVD) events in contemporary and ethnically diverse populations is not well understood.

OBJECTIVES The goal of this study was to evaluate the accuracy of the 2013 ACC/AHA Pooled Cohort Risk Equation within a large, multiethnic population in clinical care.

METHODS The target population for consideration of cholesterol-lowering therapy in a large, integrated health care delivery system population was identified in 2008 and followed up through 2013. The main analyses excluded those with known ASCVD, diabetes mellitus, low-density lipoprotein cholesterol levels <70 or ≥190 mg/dl, prior lipid-lowering therapy use, or incomplete 5-year follow-up. Patient characteristics were obtained from electronic medical records, and ASCVD events were ascertained by using validated algorithms for hospitalization databases and death certificates. We compared predicted versus observed 5-year ASCVD risk, overall and according to sex and race/ethnicity. We additionally examined predicted versus observed risk in patients with diabetes mellitus.

RESULTS Among 307,591 eligible adults without diabetes between 40 and 75 years of age, 22,283 were black, 52,917 were Asian/Pacific Islander, and 18,745 were Hispanic. We observed 2,061 ASCVD events during 1,515,142 person-years. In each 5-year predicted ASCVD risk category, observed 5-year ASCVD risk was substantially lower: 0.20% for predicted risk <2.50%; 0.65% for predicted risk 2.50% to <3.75%; 0.90% for predicted risk 3.75% to <5.00%; and 1.85% for predicted risk ≥5.00% (C statistic: 0.74). Similar ASCVD risk overestimation and poor calibration with moderate discrimination (C statistic: 0.68 to 0.74) were observed in sex, racial/ethnic, and socioeconomic status subgroups, and in sensitivity analyses among patients receiving statins for primary prevention. Calibration among 4,242 eligible adults with diabetes was improved, but discrimination was worse (C statistic: 0.64).

CONCLUSIONS In a large, contemporary "real-world" population, the ACC/AHA Pooled Cohort Risk Equation substantially overestimated actual 5-year risk in adults without diabetes, overall and across sociodemographic subgroups. (J Am Coll Cardiol 2016;67:2118–30) © 2016 by the American College of Cardiology Foundation. Published by Elsevier. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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Publication of the 2013 American College of Cardiology (ACC)/American Heart Association (AHA) Pooled Cohort Risk Equation for estimating atherosclerotic cardiovascular disease (ASCVD) risk is considered an important step forward, as it estimates risk for both heart disease and stroke, and provides estimates applicable to black/African-American subjects (1,2). This equation was developed from several prospective U.S.-based cohorts of enrolled volunteers, primarily conducted in the 1990s, with limited ethnic diversity and age range. Predicted ASCVD risk using the equation was reported to be systematically higher than the observed risk in some highly selected cohorts (3,4) but not in others (5). Importantly, however, these studies included persons screened for participation or enrolled in clinical trials, or in much earlier time periods, with limited generalizability to contemporary and diverse populations that are more representative of eligible patients treated in typical clinical practice (6,7). Validation efforts in more contemporary cohorts have further been limited due to inclusion of analyzed participants treated with statin therapy or having a high likelihood of initiating statins during follow-up (4,6,8). Lack of comprehensive surveillance in some studies is another possible reason for overestimation by the Pooled Cohort Risk Equation due to under-ascertainment of ASCVD events (3,9).

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Another major knowledge gap is the lack of accurate ASCVD risk estimation specific to persons of Asian/Pacific Islander and Hispanic ethnicities, who are currently combined with the white population in the Pooled Cohort Risk Equation (10). Furthermore, patterns of risk in more contemporary, community-based populations may be significantly different from the older cohorts used to derive the Pooled Cohort Risk Equation, which does not reflect the recent treatment era and risk factor levels (11,12). Estimates suggest that nearly one-half of U.S. adults and up to 65% of European adults would be eligible for statins on the basis of new ACC/AHA cholesterol guidelines using the Pooled Cohort Risk Equation (13,14). Thus, evaluating the accuracy of ASCVD risk prediction is essential if it is being used as a decision-making tool to determine which persons should receive statin therapy for primary prevention (13,15), and it could have a far-reaching impact if applied at a population level.

To address these knowledge gaps, we examined a very large, contemporary, multiethnic, community-based "real-world" population whose clinical characteristics would typically trigger a discussion of initiation of cholesterol-lowering therapy per risk assessment according to the Pooled Cohort Risk Equation (i.e., patients 40 to 75 years of age, without known ASCVD or diabetes, who have low-density lipoprotein cholesterol [LDL-C] levels between 70 and 189 mg/dl). The study compared predicted versus observed 5-year risks of ASCVD events, overall and within sex and multiple ethnic subgroups, along with measures of calibration and discrimination. The analyses were repeated among a cohort of eligible adults with diabetes mellitus.

ABBREVIATIONS AND ACRONYMS

ACC = American College of Cardiology

AHA = American Heart Association

ASCVD = atherosclerotic cardiovascular disease

CHD = coronary heart disease

HDL-C = high-density lipoprotein cholesterol

LDL-C = low-density lipoprotein cholesterol

METHODS

SOURCE POPULATION. Kaiser Permanente Northern California is a large integrated health care delivery system providing comprehensive inpatient and outpatient care to approximately 4 million ethnically diverse persons who are highly representative of the local and statewide population (16).

STUDY SAMPLE. Using outpatient laboratory databases, we initially identified all members of the Kaiser Permanente Northern California system between January 1, 2008, and December 31, 2008, who were ≥21 years of age and had LDL-C levels between 70 and 189 mg/dl within 5 years before study entry. The earliest LDL-C measurement in the year 2008 was used as the index date or, if the patient's last available LDL-C measurement was before 2008, the index date used was January 1, 2008. We excluded those who met any of the following criteria: sex or race/ethnicity was unknown; prescribed statins or other lipid-lowering therapies within 5 years before

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