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ORIGINAL RESEARCH

Improving Cardiovascular Disease Primary Prevention Treatment Thresholds in a New England Health Care System

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ABSTRACT

BACKGROUND Atherosclerotic cardiovascular disease (ASCVD) risk estimation based on the pooled cohort equation (PCE) overestimates in population-based cohorts. Whether it performs equally across disaggregated demographics in health care populations is less known.

OBJECTIVES The purpose of the study was to recalibrate PCE and rederive prevention thresholds in a contemporary health care system and evaluate its performance across sociodemographics.

METHODS We retrospectively inspected electronic health records between 2010 to 2012 and 2020 to 2022 within Mass General Brigham health care in New England region. We compared performance of the original vs recalibrated PCE measured by calibration, discrimination, reclassification rate, and net benefit among 160,926 patients aged 40 to 79 years and without prior ASCVD or lipid-lowering medication.

RESULTS Of the 160,926 patients (mean age: 54.6 ± 8.6 years; 61.4% female), 20,373 (12.7%) developed ASCVD over 10 years. The original PCE globally underestimated ASCVD risk (observed vs predicted incidence rate: 0.13 vs 0.05). Recalibration upclassified risk primarily among individuals with low-to-borderline risk by the original PCE and additionally identified 40% of patients who had undergone ASCVD events yet deemed statin-ineligible based on the original PCE. Treatment thresholds yielding the greatest net benefit were ≥24.0% for women (+23.3%) vs ≥26.0% for men (+18.7%), whereas ≥26.0% for White or other race (+24.7%) vs ≥14.0% Black or African American (+12.5%), respectively. Specifically, Hispanic or Latino and non-Hispanic Black patients conferred the greatest sensitivity improvement at ≥12.3% threshold compared to higher ≥23.6% among non-Hispanic Asian or Pacific Islanders. Generally, lower thresholds earlier in life were optimal.

CONCLUSIONS Recalibration and personalized treatment thresholds derived within a health system may improve prevention treatment allocation efficiency. (JACC Adv. 2024;3:101257) © 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/).

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ABBREVIATIONS AND ACRONYMS

AA = African American

ASCVD = atherosclerotic cardiovascular disease

MGB = Mass General Brigham

PCE = pooled cohort equations

Accurate estimation of future risk is the cornerstone of primary prevention of atherosclerotic cardiovascular disease (ASCVD).[1,2] Since the implementation of the pooled cohort equations (PCEs) prediction framework of 10-year ASCVD risk[2] in the 2013 American College of Cardiology and the American Heart Association prevention guidelines,[3-5] efforts have been made to validate its generalizability across multiethnic cohorts.[6-8] Evidence suggested that PCE often overestimates risk, potentially due to temporal and demographic differences in risk factors distributions, nontraditional risk factors, and discrepancies in data collection across studies.[9-11] To address this, subsequent guidelines have underscored shared decision-making and incorporated additional risk-enhancing factors while retaining the PCE in its original form.[5]

Prior studies[6,12,13] have recalibrated PCE to reflect target population-specific underlying risk and discovered modest improvement in calibration and discrimination ability. Nevertheless, whether PCE appropriately estimates ASCVD risk in health care populations with greater prevalence of risk factors, ASCVD events, and comorbidities is less known. Additionally, the effect of recalibration on disaggregated sociodemographic subgroups is not well known. Furthermore, current ubiquitous treatment threshold is agnostic to systemic risk differences and novel nonphenotyped risk drivers.

In this regard, tailoring prediction to local health care settings may better estimate population burden, guide clinicians in determining statin therapy eligibility, and achieve timely primary prevention.[14] Furthermore, considering that age is the most dominant driver of absolute risk, determining whether prediction frameworks have age-differential transportability may inform individualized prevention opportunities. Here, we evaluated the predictive performance of existing vs recalibrated PCE in a large, multisite contemporary health care population and compared their performance across sociodemographics.

METHODS

The present study protocols complied with the tenets of the Declaration of Helsinki and were approved by the Massachusetts General Hospital Institutional Review Board (2018P001236). Informed consent was waived as this was a retrospective study of routinely collected data. The present study followed the Strengthening the Reporting of Observational Studies in Epidemiology guidelines.

DATA SOURCE AND STUDY POPULATION. The Mass General Brigham (MGB) is the largest health care network in the New England region of the United States. Briefly, MGB comprises tertiary hospitals and affiliated community care sites serving ≥1.5 million patients annually.[15] Based on electronic health records available as of August 10, 2023, we retrospectively identified 221,984 patients aged 40 to 79 years with at least 1 MGB outpatient health care encounter spanning primary and specialty care between January 1, 2010 and December 31, 2012 (Supplemental Figure 1) to capture 10-year risk. Consistent with PCE specifications, participants were included if they had at least 5 years of follow-up for the 95th percentile of time to ASCVD events.[2] We excluded patients with prior ASCVD, those prescribed lipid-lowering medications, or without cardiovascular risk factor measurements required for PCE, leaving a final analytical sample of 160,926 patients.

DEMOGRAPHICS, LIFESTYLE, AND CLINICAL RISK FACTORS. Risk factors were pooled from nonemergency outpatient records within 1 year and the most proximate to the index date. Self-identified race and ethnicity were classified into: 1) White or other, given the same effects in PCE; or 2) Black or African American (AA). Current smoker was defined as ever responding "yes" to tobacco smoking and without records of cessation. Diabetes mellitus was identified as glycated hemoglobin ≥6.5%, diagnosis records containing the term "diabetes" but excluding non-type 1·2 diabetes indications, or use of insulin or/and oral glucose-lowering medications excluding isolated prescription of metformin. Use of blood pressure- and

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.

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lipid-lowering medications were determined in adherence to the United States Adopted Names nomenclature classifications.[16,17]

OUTCOMES. The primary outcome was a first composite ASCVD, defined as nonfatal myocardial infarction, coronary heart disease death, or fatal or nonfatal stroke ascertained by diagnostic and procedural codes, hospitalization records, and All Patient Refined Diagnostic Related Groups classifications (Supplemental Table 1). Death identified within the MGB network was verified by the United States Social Security Death Index; out-of-network death was collected by the participant's next of kin and deposited into the health record, whenever possible. We retrospectively followed patients through review of the electronic health records until the first ASCVD event within 10 years from the index date or the end of 10-year follow-up, whichever came first (Supplemental Methods).

STATISTICAL ANALYSIS. Baseline characteristics were summarized as mean ± SD, median (IQR), or count (percent). We first compared the empirical vs predicted risk based on the original PCE. The PCEs are sex- and race-specific Cox proportional hazards regression model integrating: 1) mean baseline survival function denoting ASCVD-free state at a given time; and 2) regression coefficients corresponding to individual cardiovascular risk factor. The Kaplan-Meier method was adopted to estimate MGB population's 10-year cumulative incidence rate by sex and race strata. The original PCE score was calculated using the identical sex- and race-specific baseline survival at year 10 and beta coefficients for each risk factor as applied in its original derivation cohorts.[2]

We then recalibrated the PCE to improve prediction among MGB patients. The study population was randomly split into 80% for derivation of recalibrated risk scores and 20% for internal validation. Recalibration involved replacing the MGB study population-specific baseline survival and risk factors mean/proportion but without rederiving regression coefficients (Supplemental Figure 2).[6] For example, for a given Hispanic or Latino male patient, the recalibrated PCE replaces baseline survival of the original PCE's male "White or other" (0.91) with 10-year ASCVD-free survival rate of male Hispanic or Latino MGB population (0.89). For each original and recalibrated PCE score, patients were subsequently categorized as low (<5.0%), borderline (5.0%-<7.5%), intermediate (7.5%-<20.0%), and high (≥20%) predicted 10-year risk, respectively.[3]

Calibration was assessed based on: 1) Hosmer-Lemeshow and Greenwood-Nam-D'Agostino chi-square test statistics for goodness-of-fit; 2) the receiver operating characteristic curve; and 3) calibration bar plots comparing the predicted and Kaplan-Meier-adjusted observed risk across deciles of predicted risk. Hosmer-Lemeshow chi-square statistic of <20 or a $P \geq 0.05$ indicates good calibration. Greenwood-Nam-D'Agostino chi-square $P \geq 0.05$ indicates nominal goodness-of-fit. To ensure that the scores accurately distinguish low- vs high-risk patients, discrimination was assessed using Harrell's C-index based on Cox proportional hazards model. Model performance was evaluated among total MGB patients as well as separately by sex and binary race category.

To demonstrate clinical utility of the original and recalibrated PCE, we constructed 4 × 4 reclassification tables to determine the extent of risk down- or up-classification resultant from recalibration. We then quantified the net change in sensitivity at a clinical guideline-endorsed treatment threshold of ≥7.5%.[3] Net sensitivity change refers to proportion of individuals with low/borderline risk based on the original PCE and intermediate/high risk based on the recalibrated PCE among patients who had undergone ASCVD event. Conversely, net specificity change refers to proportion of individuals without ASCVD events with low/borderline risk based on the original PCE who were incorrectly upclassified to intermediate/high risk category based on the recalibrated PCE. Net benefit was defined as the sum of net gain in sensitivity and loss in specificity.

Four secondary analyses were performed. First, we determined the optimal treatment thresholds yielding the greatest net benefit based on the recalibrated PCE, both globally and separately by age. Second, we further explored the implications of PCE recalibration across disaggregated racial and ethnic populations, including Hispanic or Latino, non-Hispanic Asian, non-Hispanic Black or AA, non-Hispanic White, and uncategorized or those reporting multiple categories. Third, we compared the performance of PCEs by health care encounter type at index date to account for potential differences in underlying risk and health care utilization pattern between patients receiving routine primary care vs specialty care. Fourth, as structural and physical environments associate with cardiovascular health, we mapped 10-year ASCVD incidence rate across the 2020 Census Bureau designated area among 151,310 Massachusetts-residing patients. We also performed geospatial-based PCE recalibration by re-estimating baseline survival and risk factor distributions across quartile of geospatial-based ASCVD rate in addendum to the usual sex by binary race stratification. We

TABLE 1 Baseline Characteristics of Mass General Brigham Patients (N = 160,926)

Annualized within-network health care visit	7.7 (3.3-14.4)
Age at index date, y	54.57 ± 8.63
Women	98,782 (61.38%)
Self-reported race and ethnicity	
Hispanic or Latino	5,005 (3.11%)
Non-Hispanic Asian or Pacific Islander	6,745 (4.19%)
Non-Hispanic Black or African American	10,799 (6.71%)
Non-Hispanic White	133,038 (82.67%)
Uncategorized or multiracial	5,339 (3.32%)
Total cholesterol, mg/dL	197.36 ± 31.52
High-density lipoprotein cholesterol, mg/dL	58.20 ± 17.19
Systolic blood pressure, mm Hg	125.96 ± 16.71
Current smoker	2,900 (1.80%)
Diabetes mellitus	14,085 (8.75%)
Antihypertensives prescription	25,417 (15.79%)
10-y ASCVD risk, %[a]	5.37 (6.46)
Incident 10-y ASCVD	20,373 (12.66%)
Incident 10-y major adverse cardiovascular events[b]	39,578 (24.59%)

[a]10-year ASCVD risk calculated from the original pooled cohort equations. [b]Composite of ischemic heart disease, stroke, heart failure, or all-cause death.
ASCVD = atherosclerotic cardiovascular disease.

evaluated whether recalibrated PCE performs consistently throughout low- and high-risk regions.

All statistical tests were 2-sided, and statistical significance was set at $P < 0.05$. All analyses were performed using R version 4.1.0 (R Foundation for Statistical Computing).

RESULTS

BASELINE CHARACTERISTICS. The study included 160,926 MGB middle-aged patients (mean age, 54.6 ± 8.6 years; 98,782 [61.4%] females) without ASCVD or prior statin prescriptions at identified baseline (**Table 1**). In total, 92,071 (57.2%) were White or other race women, 57,891 (36.0%) were White or other race men, 6,711 (4.2%) were Black or AA women, and 4,253 (2.6%) were Black or AA men (Supplemental Table 2). At index date, 65,915 (40.96%) patients had primary care encounter, whereas the most common specialty care visit included radiology (5.49%), obstetrics/gynecology (4.36%), and cardiology (4.09%), respectively (Supplemental Table 3). The mean predicted 10-year ASCVD risk was 5.4% ± 6.5% based on the original PCE and ranged from 3.4% ± 4.5% among White or other race women to 9.2% ± 6.6% among Black or AA men (Supplemental Figure 3). Recalibration and validation subcohorts had comparable demographic, lifestyle, and clinical risk factor distributions (Supplemental Table 4).

Over a 10-year follow-up, 20,373 (12.7%) ASCVD events occurred. The baseline survival rate ranged from 0.82 (95% CI: 0.82-0.82) among White or Other men to 0.90 (95% CI: 0.90-0.90) among White or Other race women (Supplemental Figure 4).

RECALIBRATION AND VALIDATION OF THE PCEs. Recalibration of PCE in the MGB patient population largely upclassified risk, culminating in a mean (SD) 10-year predicted ASCVD risk of 18.3% ± 16.9% (Supplemental Figure 5). Whereas two-thirds of MGB patients were identified as low risk based on the original PCE, the recalibrated PCE now classified 20.3% as low, 12.1% as borderline, 34.8% as intermediate, and 32.8% as high risk.

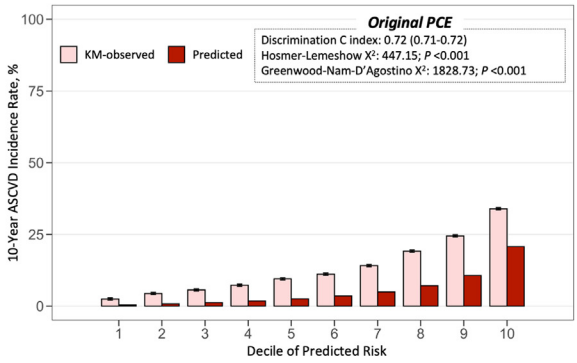
In contrast to the universal risk underestimation by the original PCE, the recalibrated predictions more closely mirrored empirical ASCVD incidence rates in low- to borderline-predicted risk patients (**Figure 1**, Supplemental Table 5). Conversely, the recalibrated PCE overestimated risk in high-risk group. As a result, recalibration improved overall calibration (Hosmer-Lemeshow chi-square from 447.2 to 242.7) but not discrimination (C-index from 0.72 [95% CI: 0.71-0.72] to 0.70 [95% CI: 0.70-0.71]) (Supplemental Figure 6). Consistent with the original PCE, the recalibrated PCE had relatively superior discrimination in women over men (0.70 [95% CI: 0.69-0.71] vs 0.68 [95% CI: 0.67-0.69]) and White or other race over Black or AA (0.71 [95% CI: 0.71-0.72] vs 0.66 [95% CI: 0.63-0.70]) (Supplemental Tables 6 to 9).

We further recalibrated PCE based on granular racial and ethnic stratification. Baseline 10-year survival rate was the lowest among non-Hispanic White men (0.82 [95% CI: 0.81-0.82]) and the highest among non-Hispanic Asian or Pacific Islander women (0.94 [95% CI: 0.93-0.95]) (Supplemental Table 10). Recalibration better approximated ASCVD incidence in low-risk groups but overestimated in high-risk patients across all racial and ethnic strata (Supplemental Table 11).

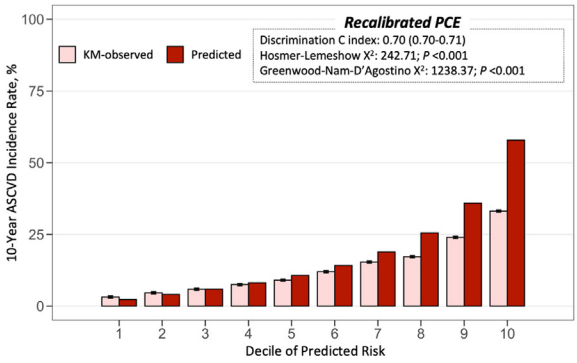
Based on the original PCE, 13,487 (20.5%) patients receiving primary care at index date had intermediate-to-high estimated risk, whereas 23,850 (25.1%) patients visiting specialty care were eligible for statin therapy (Supplemental Table 12). Irrespective of type of health care encounter, the original PCE ubiquitously underestimated risk, and recalibration recovered underestimation and most proximately mirrored the observed incidence in the borderline risk group.

The 10-year ASCVD incidence rate also varied across different regions of Massachusetts, ranging from 2.7 to 312.9 per 1,000 person-year (Supplemental Figure 7). Recalibration integrating geospatial

FIGURE 1 Performance of the Original and Recalibrated PCE



	1	2	3	4	5	6	7	8	9	10
Mean predicted risk	0.39%	0.75%	1.20%	1.77%	2.51%	3.51%	4.93%	7.11%	10.69%	20.78%
No. events	79	140	180	232	302	351	444	595	752	983
Person-Years	31813	31490	31161	30971	30500	30024	29419	28131	26591	23748



	1	2	3	4	5	6	7	8	9	10
Mean predicted risk	2.28%	4.05%	5.90%	8.08%	10.71%	14.16%	18.88%	25.54%	35.90%	57.84%
No. events	101	148	188	239	287	378	484	533	737	963
Person-Years	31719	31465	31201	30800	30585	29892	29115	28462	27027	23582

Validation of recalibration performance was assessed among 20% subset of the total study population. Observed ASCVD incidence at 10 years was adjusted for variable follow-up time using the Kaplan-Meier estimate. Predicted ASCVD incidence at 10 years of follow-up was calculated using the pooled cohort equations and ($S_0[t]$) at 10 years. Hosmer-Lemeshow chi-square statistic greater than 20 or a *P* value of <0.05 indicates poor calibration. Greenwood-Nam-D'Agostino chi-square *P* value of <0.05 indicates poor goodness-of-fit. ASCVD = atherosclerotic cardiovascular disease; PCE = pooled cohort equations.

variation did not further improve discrimination (C-index: 0.71 [95% CI: 0.70-0.72]) (Supplemental Figures 8 and 9, Supplemental Table 13).

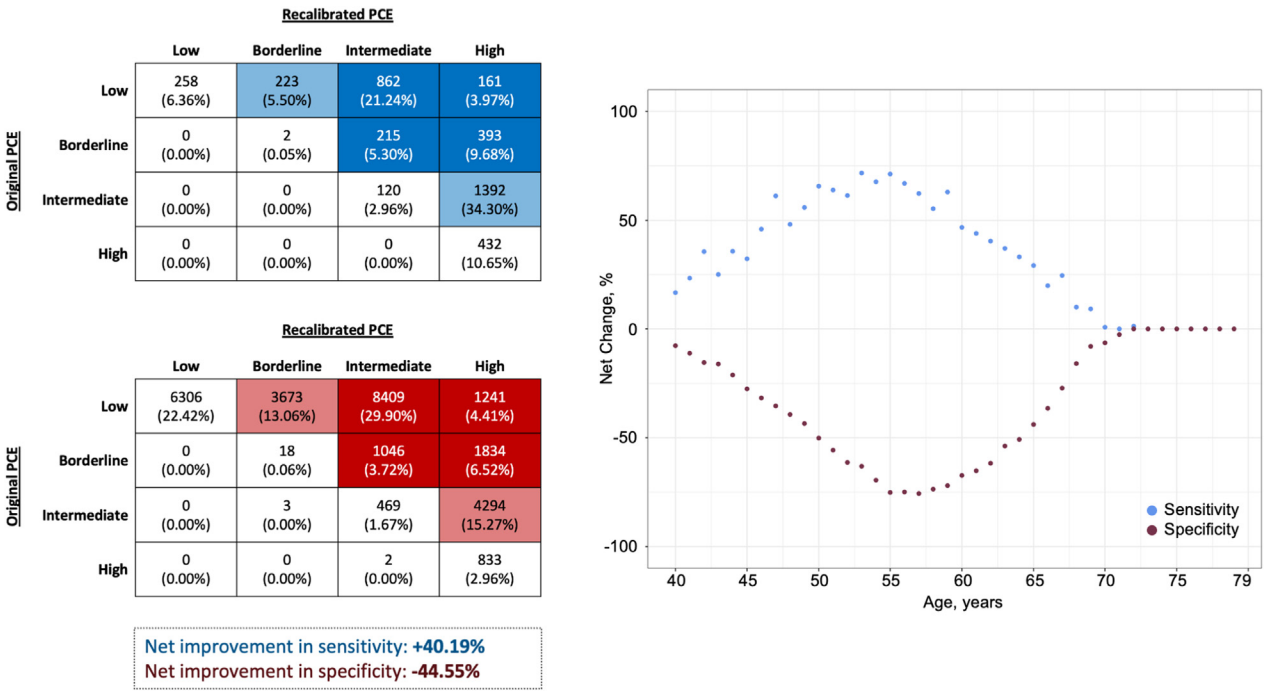
CLINICAL UTILITY OF PCE RECALIBRATION AND AGE-VARYING IMPLICATIONS. Recalibration improved sensitivity by 40.2% and simultaneously decreased specificity by 44.6% (**Figure 2**). Specifically, 1,631 of 4,058 denoted low/borderline risk individuals who underwent ASCVD were now appropriately upclassified, but 12,530 of 28,128 noncases were inappropriately upclassified. Compared to incorrectly reclassified individuals, appropriately reclassified patients were more likely to be non-Hispanic White and to have diabetes mellitus and existing antihypertensives prescription (Supplemental Table 14). The extent of benefit and loss from recalibration was principally determined by age. Individuals of age 55 years derived the greatest sensitivity improvement by 71.2% but simultaneously with specificity loss of 75.2% (Supplemental Table 15). While younger patients derived greater relative benefit from recalibration, reclassification rate plateaued by age 70 (Supplemental Figure 10).

We explored population-wide and age-specific implications of recalibration across different treatment thresholds (**Central Illustration**, **Figures 3 and 4**, Supplemental Tables 16 and 17). Patients aged 40 to 49 years conferred the greatest net benefit (+16.4%) at a treatment threshold of ≥7.4%, and patients aged 50 to 59 years benefitted from higher treatment threshold of ≥15.5% (net benefit: +18.5%). By the sixth decade in life, recalibration generally resulted in greater loss in specificity relative to an increase in sensitivity. Secondary analyses further quantified sex-, disaggregated race and ethnicity-, and region-specific optimal treatment thresholds (Supplemental Tables 18 to 21, **Figure 4**). Treatment threshold deriving maximum sensitivity gain differed between sex with women favoring lower treatment threshold of ≥9.5% compared to ≥18.0% in men. Hispanic or Latino and non-Hispanic Black patients conferred the greatest sensitivity improvement at ≥12.3% threshold compared to higher ≥23.6% among non-Hispanic Asian or Pacific Islanders. Across Massachusetts, low-risk regions conferred greater net benefit (+27.2%) at lower treatment threshold of ≥19.5% in contrast to high-risk regions (+19.0%) favoring higher cutoff of ≥29.0%.

DISCUSSION

In this large, contemporary New England health care system, the PCE universally underestimated ASCVD risk and overlooked a considerable fraction of candidates eligible for statin initiation. Recalibration improved risk estimation among low-to-borderline risk patients at the cost of overestimation in intermediate-to-high risk patients. As a result, younger patients benefitted the most from recalibration. With a vast heterogeneity of absolute risk observed across age, lower treatment thresholds

FIGURE 2 Net Change in Sensitivity and Specificity at Treatment Threshold ≥7.5%



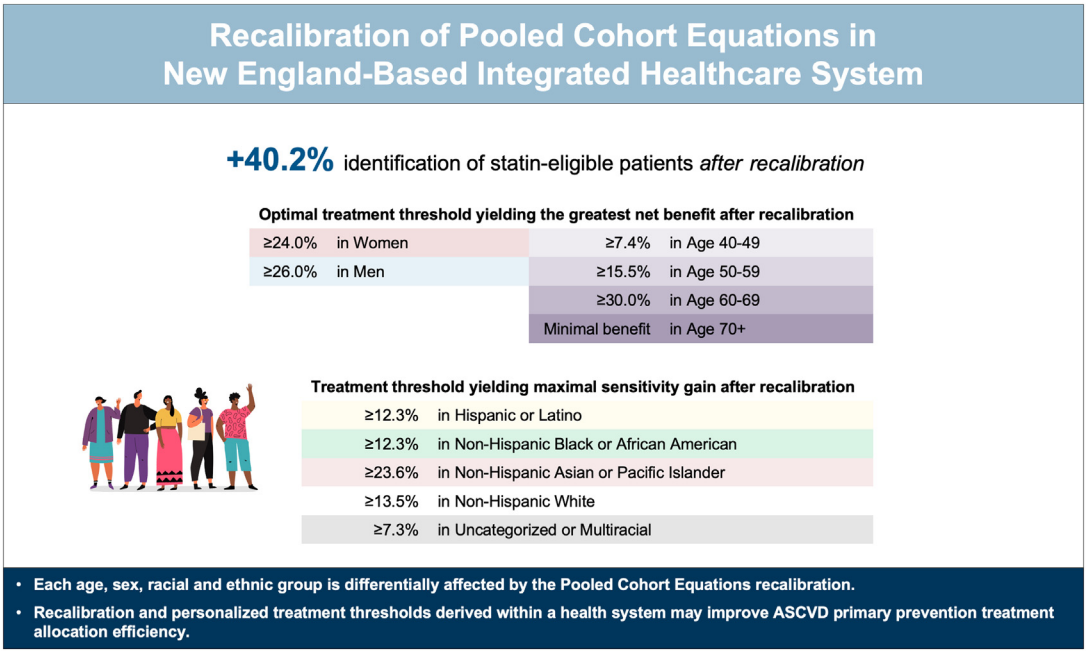
Low risk indicates 0% to <5% probability of developing the first ASCVD event within 10 years; borderline risk refers to 5% to <7.5%; intermediate risk refers to 7.5% to <20%; and high risk refers to ≥20%. Net sensitivity gain (blue) refers to proportion of individuals with low/borderline risk based on the original PCE and intermediate/high risk based on the recalibrated PCE among ASCVD cases. Net specificity loss (red) refers to proportion of individuals with low/borderline risk based on the original PCE and intermediate/high risk based on the recalibrated PCE among noncases. ASCVD = atherosclerotic cardiovascular disease; PCE = pooled cohort equation.

favorably identified younger patients requiring risk/treatment discussion, whereas higher thresholds allowed appropriate reclassification in older individuals. Disaggregation of race and ethnicity and integration of geospatial data revealed further heterogeneity of risk and benefit yielded from recalibration. These observations permit several conclusions regarding the downstream implications of a key risk prediction framework in clinical practice.

Utility of ASCVD risk estimation tool has been known to be divergent across contextual background of the target population, methodological approaches in risk factors and outcomes ascertainment, and clinical practice. In contrast to its commonplace overestimation in population-based cohorts,[7,8,18] the original PCE underestimated ASCVD risk within the New England health care system. Such observations diverge from Minnesota primary care[19] patients aged ≥30 years (mean ASCVD risk: 5.6%, 10-year ASCVD event rate: 5.2%, C-index: 0.78) demonstrating modest underestimation in low predicted risk group in contrast to stark overestimation in high-risk individuals. Our study extends beyond primary care by evaluating implications in integrated health care setting representing diverse locations, practices, and patient background. Furthermore, the apparent risk underestimation may also be attributable to temporal changes in preventive and therapeutic landscape since the PCE derivation studies era.[14,20] Enrichment of cardiovascular events among individuals seeking health care, active disease surveillance, wider array of available therapeutics, and endorsement of intensive risk factor management by the contemporary clinical guidelines may not align with epidemiology of a general population or from earlier cohort.[21] Nevertheless, systemic risk underestimation will lead to inappropriate underprescription of statins among patients with underlying elevated ASCVD risk.

The PCE recalibration conveyed opportunities to mitigate treatment gap by reflecting empirical cardiovascular burden of the New England health care users in age-, sex-, and race-differential manner. Overall, recalibration upclassified risk, thereby additionally uncovering 40% of MGB patients overlooked

CENTRAL ILLUSTRATION **Improving Cardiovascular Disease Primary Prevention Treatment Thresholds in a New England Health Care System**



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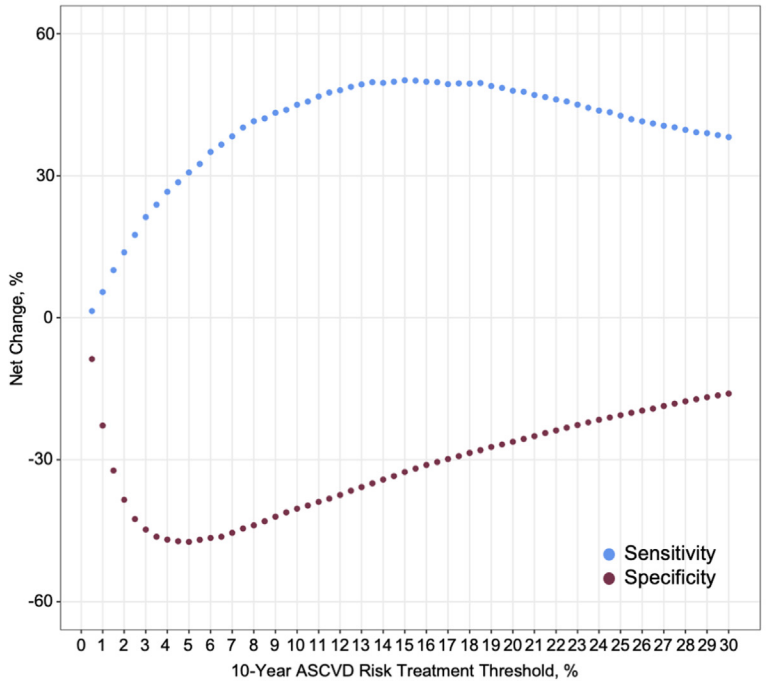
Sociodemographic-specific clinical implications of recalibrating the pooled cohort equations within the Mass General Brigham health care system. ASCVD = atherosclerotic cardiovascular disease.

by the existing algorithm for statin eligibility. Nevertheless, each age decile exhibited varying benefit-to-harm across different treatment thresholds with younger adults favoring lower cutoff at the expense of relatively lesser specificity loss. International guidelines[1,3] on the primary prevention of cardiovascular disease recommend certain preventive strategies when a threshold is reached. However, 10-year risk scores are largely age-driven, such that younger individuals are generally assigned low predicted risk and thus are prone to treatment delay until advanced ages. Nonetheless, younger individuals derive the greatest residual lifetime benefit in absolute risk reduction, gain in healthy life-years, and compression of health care cost from timely intervention.[14,22,23] Conversely, tolerance and safety implications from unwarranted statin prescription may also be age-dependent in the context of existing comorbidities or concomitant medications.[24] To address risk factors, trajectory, and life expectancy, the European Society of Cardiology therapeutic guideline[1] proposed an age-specific interpretation of 10-year ASCVD risk. With novel research infrastructure[25] tracking lifetime trajectories of atherosclerosis to capture premature alterations, our findings further endorse the adoption of age-specific treatment thresholds to inform orthogonal risk assessments and optimize windows of therapy eligibility where appropriate.

Beyond age, our results also highlight that integration of individual- or population-level characteristics may additionally augment identification of statin-eligible patients. In alignment with our previous observations[26] demonstrating sex and racial heterogeneities in optimal treatment threshold, prevention guidelines[1,3] denote population differences in pathophysiology, therapeutic response, epigenetics, and social constructs. Notably, evaluations further account for sex-specific risk modifiers/enhancers (eg, a history of preeclampsia and premature menopause) or South Asian ancestry that are intricately related to downstream determinants of health. Modifiable risk also diverges early in life, as longitudinal tracking of blood pressure from childhood to

FIGURE 3 Net Change in Sensitivity and Specificity Across Different Treatment Thresholds



Treatment threshold	Net sensitivity change	Net specificity change	Net Benefit
1.0%	+5.42%	-22.77%	-17.35%
2.0%	+13.80%	-38.48%	-24.68%
3.0%	+21.27%	-44.77%	-23.50%
4.0%	+26.61%	-46.89%	-20.28%
5.0%	+30.70%	-47.37%	-16.67%
6.0%	+35.04%	-46.53%	-11.49%
7.0%	+38.32%	-45.46%	-7.14%
8.0%	+41.52%	-43.87%	-2.35%
9.0%	+43.30%	-42.05%	+1.25%
10.0%	+45.00%	-40.36%	+4.64%
11.0%	+46.75%	-38.92%	+7.83%
12.0%	+48.05%	-37.46%	+10.59%
13.0%	+49.29%	-35.80%	+13.49%
14.0%	+49.61%	-34.22%	+15.39%
15.0%	+50.15%	-32.60%	+17.55%
16.0%	+49.85%	-31.09%	+18.76%
17.0%	+49.33%	-29.84%	+19.49%
18.0%	+49.46%	-28.56%	+20.90%
19.0%	+48.94%	-27.31%	+21.63%
20.0%	+47.95%	-26.20%	+21.75%
21.0%	+47.07%	-25.01%	+22.06%
22.0%	+46.11%	-23.80%	+22.31%
23.0%	+45.02%	-22.66%	+22.36%
24.0%	+43.77%	-21.56%	+22.21%
25.0%	+42.68%	-20.58%	+22.10%
26.0%	+41.50%	-19.61%	+21.89%
27.0%	+40.56%	-18.63%	+21.93%
28.0%	+39.70%	-17.64%	+22.06%
29.0%	+39.01%	-16.79%	+22.22%
30.0%	+38.17%	-16.02%	+22.15%

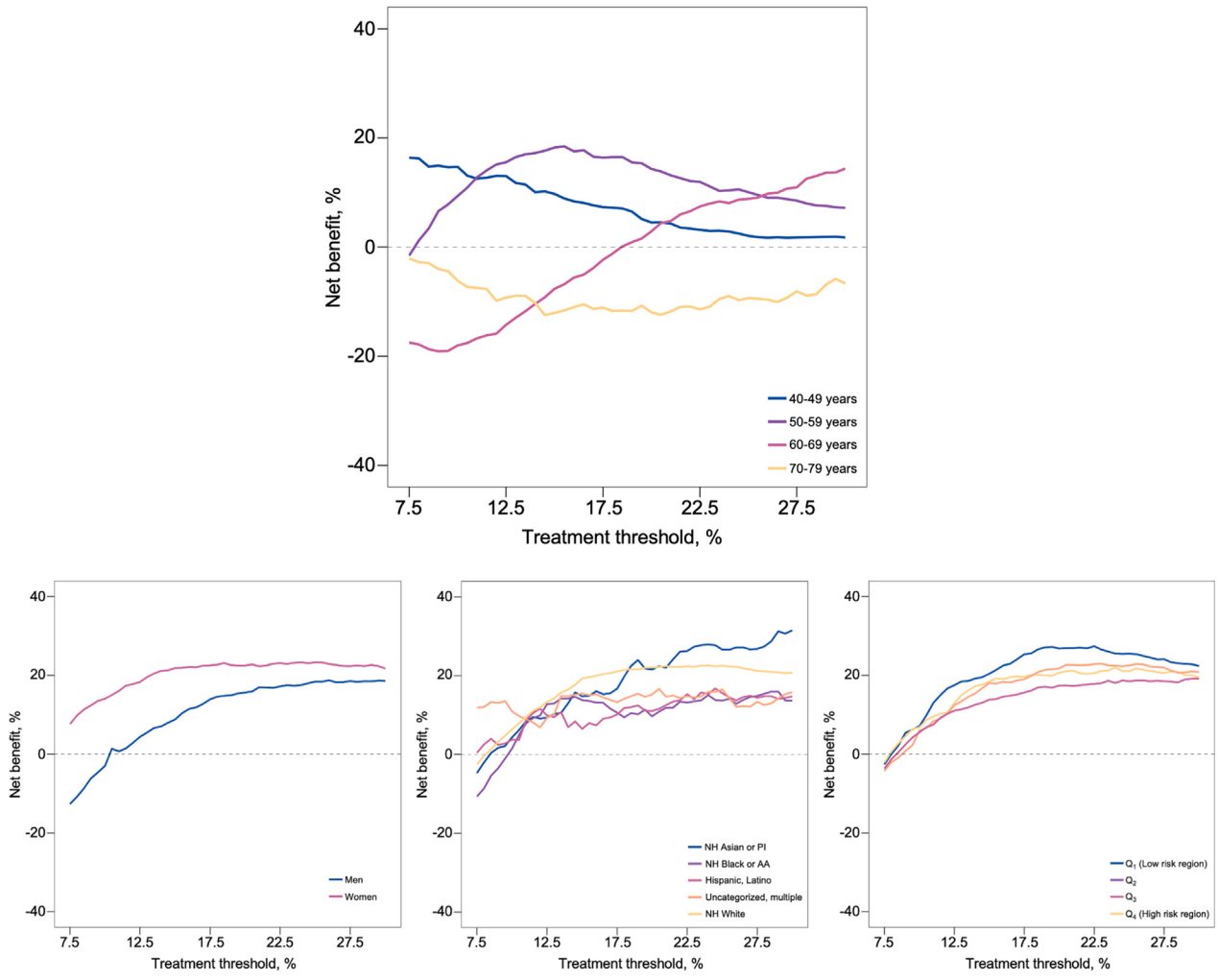
Reclassification was assessed among 20% validation subset of the total study population. Net sensitivity gain (blue) refers to proportion of individuals with low/borderline risk based on the original PCE and intermediate/high risk based on the recalibrated PCE among ASCVD cases. Net specificity loss (red) refers to proportion of individuals with low/borderline risk based on the original PCE and intermediate/high risk based on the recalibrated PCE among noncases. ASCVD = atherosclerotic cardiovascular disease; PCE = pooled cohort equation.

middle age demonstrated apparent differences in acceleration and trajectory patterns by sex and race.[27] Physical and structural environment may also serve as locally relevant predictive features, as we observed striking ASCVD event gradient even within Massachusetts. In this context, race-agnostic framework[28] has recently emerged offering to optionally integrate area-level socioeconomic deprivation[29] to better capture multilevel determinants of health. However, recent evidence[30] demonstrated that removal of race does not improve predictive performance, and the performance equity of the novel framework remains unvalidated in external populations. Comparative effectiveness of individualized treatment thresholds should be assessed in diverse demographic and contextual populations to achieve parsimonious, feasible, and equitable risk stratification and clinical actionability.

STRENGTHS AND LIMITATIONS. We leveraged contemporary health care data to evaluate the clinical performance of the mainstream ASCVD risk prediction tool. The sizable nature and diverse background of the study population allowed a granular projection of sociodemographic-specific implications from PCE recalibration.

Nevertheless, our findings should be interpreted in the context of potential limitations. First, we collected risk factor measures during routine clinical practice with varied contexts, environment, and protocols. Notably, lifestyle such as current smoking may be underreported or selectively updated.[31] Therefore, direct comparison to findings from observational cohort studies with standardized measurements may be limited. Second, the recalibrated scores based on MGB patients may differently reclassify risk and affect downstream clinical implications across geographically diverse populations or patients with differing duration and severity of existing cardiometabolic disorder.[32] The present work highlights the need for recalibration to optimize performance in target populations. Third, ASCVD ascertainment may have been underreported for patients who seek

FIGURE 4 Nomogram of Net Benefit Resultant From PCE Recalibration by Sociodemographics



Net benefit refers to the sum of net increase in sensitivity and decrease in specificity. Geospatial data were mapped for 151,310 Massachusetts-residing patients by the 2020 Census Bureau designation. Low-risk region refers to areas in Massachusetts with the lowest 10-year ASCVD incidence rate, whereas quartile 4 refers to regions with the highest ASCVD incidence rate. AA = African American; ASCVD = atherosclerotic cardiovascular disease; NH = non-Hispanic; PCE = pooled cohort equation; PI = Pacific Islanders; Q = quartile.

out-of-network care. However, MGB is the largest multi-institutional health system in New England, spanning university hospitals and local clinics, and the study participants periodically utilize within-network health care (median 8 [IQR: 3-14] visits per-year); therefore, we expect the underreporting to be minimal.

CONCLUSIONS

PCE consistently underestimated 10-year ASCVD risk in the largest New England health care network. Recalibration improved sensitivity with concurrent reduction in specificity by differing magnitude across predicted risk level and delineated different optimal treatment thresholds across sociodemographics. These results highlight the need for individualized assessment of statin allocation and support the impetus for incorporating locally relevant personalized risk estimation frameworks.

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PERSPECTIVES

COMPETENCY IN MEDICAL KNOWLEDGE: Recalibrating ASCVD risk prediction model may additionally identify patients with underlying elevated risk and inform tailored treatment thresholds enabling timely prevention.

TRANSLATIONAL OUTLOOK: Recalibrating the risk prediction framework and personalizing treatment thresholds within a health system may improve prevention treatment allocation efficiency.

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APPENDIX For supplemental methods, tables, and figures, please see the online version of this paper.