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10-Year Risk Equations for Incident Heart Failure in the General Population

Sadiya S. Khan, MD MS[a,b], **Hongyan Ning, MD MS**[b], **Sanjiv J. Shah, MD**[a], **Clyde W. Yancy, MD, SCM**[a], **Mercedes Carnethon, PhD**[b], **Jarett D. Berry, MD**[c], **Robert Mentz, MD**[d], **Emily O'Brien, PhD**[d], **Adolfo Correa, MD, MPH, PhD**[e], **Navin Suthahar, MD, MSc**[f], **Rudolf A. de Boer, MD, PhD**[f], **John T. Wilkins, MD MS**[a,b], and **Donald M. Lloyd-Jones, MD ScM**[a,b]

[a]Division of Cardiology, Department of Medicine, Northwestern University Feinberg School of Medicine; Chicago, IL [b]Department of Preventive Medicine, Northwestern University Feinberg School of Medicine; Chicago, IL [c]Division of Cardiology, University of Texas Southwestern Medical Center; Dallas, TX [d]Duke University Medical Center; Durham, NC [e]Department of Medicine, University of Mississippi Medical Center, Jackson, MS [f]Department of Cardiology, University Medical Centre Groningen, University of Groningen, Groningen, The Netherlands

Abstract

Background—Primary prevention strategies to mitigate the burden of heart failure (HF) are urgently needed. However, no validated risk prediction tools are currently in use.

Objectives—We sought to derive 10-year risk equations of developing incident HF.

Methods—Race- and sex-specific 10-year risk equations for HF were derived and validated from individual-level data from 7 community-based cohorts with at least 12 years of follow-up. Participants who were recruited between 1985-2000, between 30 to 80 years, and were free of cardiovascular disease at baseline were included to create a pooled cohort (PC) and randomly split for derivation and internal validation. Model performance was also assessed in 2 additional cohorts.

Results—In the derivation sample of the PC (n=11771), 58% were women, 22% were black with a mean age 52±12 years, and HF occurred in 1339 participants. Predictors of HF included in the

Address for Correspondence: Sadiya S. Khan, MD, MS, Assistant Professor of Medicine, Division of Cardiology, Department of Medicine and Preventive Medicine, Northwestern University Feinberg School of Medicine, 680 N. Lake Shore Drive, 14-002, Chicago, IL 60611, Telephone: 312-503-2515, Fax: 312-503-2515, s-khan-1@northwestern.edu, Twitter: @HeartDocSadiya.

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Tweet: @HeartDocSadiya "Robust tool estimating HF risk frames the patient-centered discussion. Time to shift our focus to prevention and risk reduction."

race-sex specific models were age, blood pressure (treated or untreated), fasting glucose (treated or untreated), body mass index, cholesterol, smoking status, and QRS duration. The PC equations to Prevent HF (PCP-HF) model had good discrimination and strong calibration in internal and external validation cohorts. A web-based tool was developed to facilitate clinical application of this tool.

Conclusions—We present a contemporary analysis from 33,010 men and women demonstrating the utility of the sex and race-specific 10-year PCP-HF risk score, which integrates clinical parameters readily available in primary care settings. This tool can be useful in risk-based decision making to determine who may merit intensive screening and/or targeted prevention strategies.

Condensed Abstract

There is an is urgent need to identify strategies to prevent heart failure given the substantial morbidity, mortality, and cost associated with HF. We developed the Pooled Cohort equations to Prevent HF (PCP-HF) to estimate 10-year risk of incident HF among participants aged 30-80 years from 5 population-based cohorts. We assessed model performance internally and validated it externally in 2 large cohorts. The PCP-HF risk score demonstrated good discrimination and calibration. The PCP-HF risk score is a novel tool that integrates clinical risk factor data and may be useful in individual level risk-based decision making and population-level prevention of HF.

Keywords

Heart Failure; primary prevention; risk factor; epidemiology

Introduction

Heart failure (HF) is highly prevalent, affecting more than 6 million US adults. (1,2) Over the lifetime, the risk for developing HF is estimated to range from 20 to 46% in white and black middle-aged men and women.(3) In the context of the growing aging population, the increasing burden of HF risk factors (e.g. obesity, diabetes), and advances in secondary prevention treatments for coronary heart disease, prevalence of HF has continued to increase (1,4,5). If current trends continue, HF is estimated to affect more than 8 million people by 2030 and total healthcare costs projected to exceed $70 billion.(6) The burden of HF continues to grow globally as well with a 23% increase in prevalence in the UK from 2002 to 2014.(7) Because HF is associated with significant morbidity, mortality, and cost of care, focusing on prevention is of utmost importance to address the public health and economic burden associated with HF, both nationally and globally (8).

Current guidelines emphasize the need for a standardized screening strategy to identify individuals with higher likelihood of developing HF.(9) Whereas risk prediction for atherosclerotic cardiovascular disease (ASCVD) has been widely implemented in clinical practice to guide preventive strategies for coronary heart disease and stroke, no validated race and sex-specific risk prediction tools for incident HF are available to guide similar personalized risk-based decision making.(10) Existing HF risk prediction models have limtations, including derivation in non-representative, non-contemporary or restricted higher-risk samples (e.g. history of coronary heart disease, valvular heart disease) with

limited ethnic diversity.(11) Further, many risk models lack extensive external validation, limiting their applicability and implementation in a general population without prevalent cardiovascular disease (CVD).

Thus, using pooled individual level data from five diverse population-based cohorts, we sought to develop equations to estimate the 10-year risk of incident HF utilizing routinely available clinical data in a broad general population (30-80 years) of white and black adults without prevalent CVD. The Pooled Cohort equations to Prevent HF (PCP-HF) were also assessed for external validity in an additional two large population-based cohorts.

Methods

For derivation, we included pooled individual-level data from 5 large, racially and geographically diverse, National Heart Lung and Blood Institute (NHLBI) sponsored cohort studies, including: the Atherosclerosis Risk in Communities (ARIC) Study, Coronary Artery Risk Development in Young Adults (CARDIA) Study, Cardiovascular Health Study (CHS), Framingham Heart Study Offspring Cohort (FOF), and Multi-Ethnic Study of Atherosclerosis (MESA). The study designs of each cohort have been previously described.(11–18) All cohorts represent community-based or population-based samples with direct measurement of risk factors, surveillance and adjudication for incident HF, and had at least 12 years of follow-up. Black and white participants from the pooled cohorts (PC) were included in the analysis if they were recruited between 1985-2000, were between the ages of 30 to 80 years old, and free from CVD at baseline. External validation was performed in white participants from the Prevention of REnal and Vascular ENd-stage Disease (PREVEND) cohort and in black participants from the JHS cohorts. In the JHS validation, participants who were included in the derivation or internal validation samples as part of the ARIC cohort were removed.

The protocols used to obtain data and ascertainment of vital status and HF for the Lifetime Risk Pooling Project, which includes the PC (ARIC, CARDIA, CHS, FOF, MESA), JHS, and PREVEND have been previously described.(12–19) The study protocol was approved by the Institutional Review Board at Northwestern University. Height, weight, blood pressure, and fasting glucose and cholesterol were measured directly in all participants; smoking status was self-reported. QRS duration was available from standardized automated ECG analysis. Incident HF events were adjudicated with the use of strategies selected by each cohort's investigator group with available clinical records and pre-specified criteria (Detailed descriptions are provided in the Online Appendix).

All statistical analyses were performed with the use of SAS statistical software version 9.2 (SAS institute) and R version 3.1.2. Individual participant-level data were pooled to create the PC and the dataset was randomly split into two equal samples for derivation and internal validation in distinct participants. We chose this approach as opposed to bootstrapping to determine the beta-coefficeints with the entire dataset as our sample size was large. The baseline 10-year risk equations were developed from sex and race specific proportional hazards models that included HF risk factors: age, systolic blood pressure (SBP), anti-hypertension medication usage, body mass index (BMI), total and high-density cholesterol

levels (TC; HDL-C), current smoking status, fasting glucose, diabetic medication usage, and electrocardiogram measurement of QRS duration. A variable for lipid therapy was evaluated, but did not remain in the final model, because prevalence of lipid treatment was relatively low in our cohorts (4.2%) and a statistical significant association with outcomes was lacking. Multiple Cox regression models were conducted to estimate the equation parameters. Likelihood statistics and Akaike information criterion were applied to optimize the regression model similar to the previously published methods for the Pooled Cohort Equations for ASCVD.(20) Specifically, interactions with age were tested for each risk factor and were retained in final models if the p value for the interaction term was less than .01, or the p value was .01 to .05 and the continuous net reclassification improvement for nonevents was 15 percent or greater, or the integrated discrimination improvement index was statistically significant. End points were censored at 12 years. Non-HF related death in follow-up was censored. Discrimination was assessed using Harrell's C-statistic with 95% confidence intervals (CI). Greenwood-Nam-D'Agostino statistic was applied to evaluate the calibration of the model in derivation and validation samples. In order to demonstrate the utility of HF-specific risk estimation, we also assessed the discrimination and calibration in the prediction of HF using non-HF specific CVD risk scores: Adult Treatement Panel (ATP) III Framingham Risk Score, General Cardiovascular Risk Profile CVD Score, and the Pooled Cohort Equations for ASCVD.(21–23).

Results

Baseline characteristics of white and black adults from the derivation sample of the PC and the external validation cohorts (JHS, and PREVEND) are shown in Table 1. In the derivation cohort, 58% were women, 22% black, with mean age 52±12 years. Prevalence of risk factors were similar in the derivation and validation cohorts in each sex-race group with higher mean total cholesterol and lower prevalence of diabetes in the PREVEND cohort (Online Tables 1 and 2). Mean BMI and SBP were higher among black men and women compared with white men and women. Higher prevalence of treatment for risk factors of hypertension and diabetes was also present in black adults compared with white adults.

Over a follow-up of 10 years, 1339 HF events occurred in the derivation cohort. Variables and coefficients for the risk scores are presented in Table 2 and Online Table 3. Discrimination and calibration metrics of the 10-year risk equation, PCP-HF, are shown in Table 3 for the derivation and validation cohorts. The PCP-HF risk score had good to excellent discrimination in the derivation (Online Figure 1) and internal validation cohorts (PC) as well as externally (JHS and PREVEND). Among white men and women and black men and women in the PC internal validation sample, the C-statistic (95% confidence interval [CI]) in each sex-race group was 0.79 (95% CI: 0.76, 0.81), 0.71 (0.63, 0.80), 0.85 (0.82, 0.88), and 0.78 (0.71, 0.85), respectively (Figure 1). The PCP-HF risk score was also well-calibrated as assessed by the GND chi-square statistic in the PC internal validation sample ($p>0.05$ for all). External validation performed in the JHS and PREVEND samples demonstrated good discrimination (C-statistic ranging from 0.71-0.88 in black and white men and women) and strong calibration (Figure 2). For comparison, the c-statistics for age alone in prediction of 10-year risk of HF was 0.70 (0.68, 0.74) and 0.69 (0.61, 0.76) in white

and black men and 0.74 (0.71, 0.89) and 0.65 (0.59, 0.71) in white and black women, respectively.

We also examined C-indices and GND chi-squared test for the prediction of HF in the internal validation subset of the PC when using non-HF specific CVD risk scores (Online Table 4). C-statistic for the ATP III Framingham Risk Score, General Cardiovascular Risk Score, and the ASCVD Pooled Cohort Equations were simliar (>0.70 for all sex-race groups). However, calibration was poor for all of the non-HF specific CVD risk scores (GND chi-sq $p<0.01$ for all). We were unable to specifically assess the discrimination and calibration of previously published HF-specific risk scores (Online Table 5) due to lack of available data on biomarkers or cardiovascular imaging in all participants, similar to the real-world primary care setting.

Observed and predicted mean 10-year risk of HF in sex-race groups are shown in Online Figure 2. Notably, participants in the highest group of predicted risk were at significantly higher risk compared with other strata and experienced the majority of the observed events in all groups. White men in the highest decile of predicted HF risk were more likely to be older, have hypertension, and have diabetes as shown in Online Table 6. Varying risk factor profiles and estimated risk of HF are demonstrated in Online Table 7 for white and black men and women. For example, estimated absolute 10-year HF risk is 23% and 25%, for a 55-year old white man and black man and 14% and 26% for a 55-year old white and black woman, respectively, with a high risk profile compared with <1% risk in all sex-race groups with an optimal risk factor profile (Figure 3).

To facilitate clinical application of the PCP-HF risk tool, a web-based tool was developed and provides an estimated 10-year risk of HF for adults aged 30-80 years without prevalent CVD (Central Illustration). An example of how to calculate the HF risk score for a 50-year-old individual with BMI 28kg/m^2, untreated SBP 130mm Hg, untreated fasting glucose 100 mg/dL, TC 200mg/dL, HDL-C 50 mg/dL, and QRS duration of 120 ms is shown in Online Table 8.

Discussion

In this study, we developed and validated sex- and race-specific 10-year risk prediction models for incident HF from 5 population-based cohorts using clinical variables routinely available in the primary care setting. The PCP-HF tool was derived from a sample of participants representative of the general US population without prevalent CVD. We validated this model in 2 additional population-based cohorts from the US and Europe, where it confirmed the clinical utility of the PCP-HF tool in risk assessment in a general primary prevention population. Lifetime risk of hospitalized HF has been estimated to be greater than that of incident CHD and stroke in both white and black adults in data from the ARIC cohort (24). Ample evidence supports successful prevention or postponement of HF development through modification or prevention of risk factors.(25,26) Therefore, focused efforts on prevention of HF are now of paramount importance and have been highlighted in the research priorities of the National Heart, Lung, and Blood Institute as an overarching strategic goal.(27)

While practice guidelienes for HF from national and international societies, including the American College of Cardiology (ACC)/American Heart Association (AHA), Heart Failure Society of America, and the European Society of Cardiology place continued emphasis on primary prevention of HF, identifying prevention and/or intervention strategies has been limited by well-validated risk prediction models in asymptomatic individuals without prevalent CVD. The ACC/AHA currently recommend a classification scheme to stage patients as follows: stage 0, no HF risk factors; stage A, HF risk factors; B, asymptomatic cardiac structural disease; C, symptomatic HF, and stage D, end-stage HF.(28) This construct emphasizes the progressive nature of HF and emphasizes the need for focused upstream efforts toward primordial and primary prevention and identification of individuals at risk for symptomatic HF (Stage 0/A/B). Individuals in these at-risk categories (0/A/B) represent the vast majority of the general population with estimates of 8-fold increase in mortality once Stage C/D HF develops underscoring the importance of intervening prior to this transition (29–31).

The present study confirms known individual risk factors as significant predictors of HF in at-risk participants and integrates these clinical variables into a reliable tool to provide a summary estimate of a persons' likelihood of experiencing symptomatic HF (ACC/AHA Stage C/D) over a 10-year period. The PCP-HF tool provides a framekwork to guide risk assessment on an individual level for clinician-patient risk discussions and population level to promote research to identify optimal prevention and/or intervention strategies (e.g. randomized primary prevention trials) and policy approaches (e.g. reduction of dietary sodium intake) to reduce the burden of HF. For example, individuals who achieve greater than a 5% 10-year absolute risk estimate of HF (or highest decile of risk) may benefit from more intensive blood pressure lowering, use of specific therapies (e.g. sodium-glucose co-transporter 2 inhibitors), and more frequent surveillance.(32,33)

Our findings build upon prior HF risk prediction algorithms from individual cohorts, including the FHS, ARIC, Healthy Aging and Body Composition (Health ABC) study, and MESA.(34–37) The FHS risk score is derived from a mostly white population that included participants with prevalent CVD, and likely over-estimates risk in a general healthy population (Stage 0/A).(35,38) Both the MESA and ARIC risk scores integrate the use of N-terminal pro-brain natriuretic peptide (BNP), which is not routinely obtained in asymptomatic individuals without prevalent CVD.(34,36) The Health ABC study included 5-year risk estimates in elderly participants between the ages of 70-79 limiting the generalizability in young and middle-aged adults.(35) The International Collaboration on Heart Failure Subtypes pooled 3 community based cohorts (FHS, CHS, PREVEND) and developed risk scores for HF with preserved and reduced ejection fraction with external validation in MESA.(39) However, the majority of participants in the derivation subset were white (95%) and individuals with prior coronary heart disease were included (9%). In contrast, the PCP-HF risk score derivation included a broad age range of white and black men and women free of CVD at baseline from 5 population-based cohorts to allow for robust sex- and race- specific personalized 10-year estimates of HF from young adulthood to older age.

The PCP-HF score is an appealing and inexpensive initial screening tool to identify individuals in the primary care setting who are at higher risk for development of incident HF and may benefit from additional screening measures to refine and personalize risk assessment akin to the description of “risk enhancers” in the 2018 ACC/AHA Primary Prevention of ASCVD guidelines (40). Sequential screening for HF could integrate traditional and novel biomarkers (e.g. brain natriuretic peptide, galectin-3, soluble ST2 receptor) and advanced imaging (e.g. speckle tracking echocardiography, cardiac magnetic resonance imaging) in a stepwise, individualized, and cost-effective approach.(41) Studies on generalized use of brain natriuretic peptide (BNP) biomarkers for screening in asymptomatic adults have yielded mixed results.(42,43) In participants with known HF risk factors in the St. Vincent’s Screening to prevent Heart Failure Study, 36% of individuals were identified to have a BNP of 50ng/L or higher. Use of the PCP-HF tool, which is intended for a broader population may help to identify individuals at high 10-year risk who may also benefit from targeted BNP screening.(42) In addition, while imaging tools, such as speckle tracking echocardiography may be limited in their applicability for widespread screening in the general population due to cost, sequential screening strategies following identification of high risk indivdiauls to target with more intensive screening may provide the most effective and cost-efficient approach (44).

Significant health disparities in HF risk factors and incidence of HF exist across gender and race/ethnic groups. In the Coronary Artery Risk Development in Young Adults Study, premature development of incident HF before the age of 50 years occurred more commonly among Blacks than Whites.(45) In the MESA study of participants aged 45-84 years at baseline, the highest risk of developing incident HF was in Blacks, followed by Hispanic, White, and Chinese Americans (4.6, 3.5, 2.4, and 1.0 per 1000 person-years, respectively). (46) Differences in HF risk may be related to differences in prevalence of HF risk factors of obesity, diabetes, and hypertension.(47) Therefore, sex- and race-specific 10 year risk estimates in the PCP-HF tool were derived to provide absolute risk estimates specific to black and white men and women.

Key strengths of our study include derivation in 5 large population-based cohorts with inclusion of a diverse, contemporary sample that have representative proportion of women and blacks allowing for sex- and race-specific equations, broad age range from 30 to 80 years, and systematic adjudication of HF. Our study also has several limitations to note. The present observational study design cannot predict the effect of specific antihypertensive or antidiabetic therapies on risk for incident HF. Nevertheless, our estimates of risk for HF based on these clinical covariates may help guide clinicians and patients in decision-making regarding prevention strategies and/or intensification of therapies in individuals at higher risk for HF (e.g. aggressive blood pressure lowering). The current model is not able to discriminate between HF with systolic dysfunction or preserved ejection fraction. Nevertheless, the PCP-HF tool demonstrated good discrimination and calibration for HF events of all subtypes and allows for initiation of preventive strategies for shared risk factors for HF with preserved and reduced ejection fraction (e.g. choice of sodium-glucose cotransporter 2 inhibitors for DM management). This will allow broader upstream utility and generalizability, especially in the context of equally poor outcomes observed in patients with both HF with preserved and reduced ejection fraction.(5,48) Adjudication of HF events

across cohorts differed, but all used pre-specified well-validated criteria. Finally, the PCP-HF tool is not able to provide accurate risk estimates for individuals from racial/ethnic groups other than non-Hispanic whites and non-Hispanic blacks. However, use of the equation versions for whites of the same sex can be considered and will need to be studied further.

In summary, we present a contemporary analysis from 33,010 men and women from 7 population-based cohorts describing the development and validation of novel sex- and race-specific estimates of 10-year risk of incident HF. Use of factors readily accessible in the primary care setting support implementation of the PCP-HF score in clinical practice to quantify absolute risk estimates for HF and identify individuals with higher likelihood of developing HF who may merit more intensive screening, targeted prevention, and/or enrollment in future primary prevention trials. The PCP-HF tool has excellent discrimination and calibration among a diverse group of US and European adults enhancing its broad generalizability and may be a valuable tool in risk assessment of HF on an individual and population level.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations

ACC	American College of Cardiology
AHA	American Heart Association
ARIC	Atherosclerosis Risk in Communities
ASCVD	Atherosclerotic cardiovascular disease

ATP	Adult Treatment Panel
BMI	Body mass index
CARDIA	Coronary Artery Risk Development in Young Adults
CHS	Cardiovascular Health Study
CI	Confidence Interval
FOF	Framingham Heart Study Offspring Cohort
HDL-c	High-density cholesterol
Health ABC	Healthy Aging and Body Composition
HF	Heart Failure
JHS	Jackson Heart Study
MESA	Multi-Ethnic Study of Atherosclerosis
NHLBI	National Heart Lung and Blood Institute
PC	Pooled Cohort
PCP-HF	Pooled Cohort Equations to Prevent Heart Failure
PREVEND	Prevention of REnal and Vascular ENd-stage Disease
SBP	Systolic blood pressure
TC	Total cholesterol

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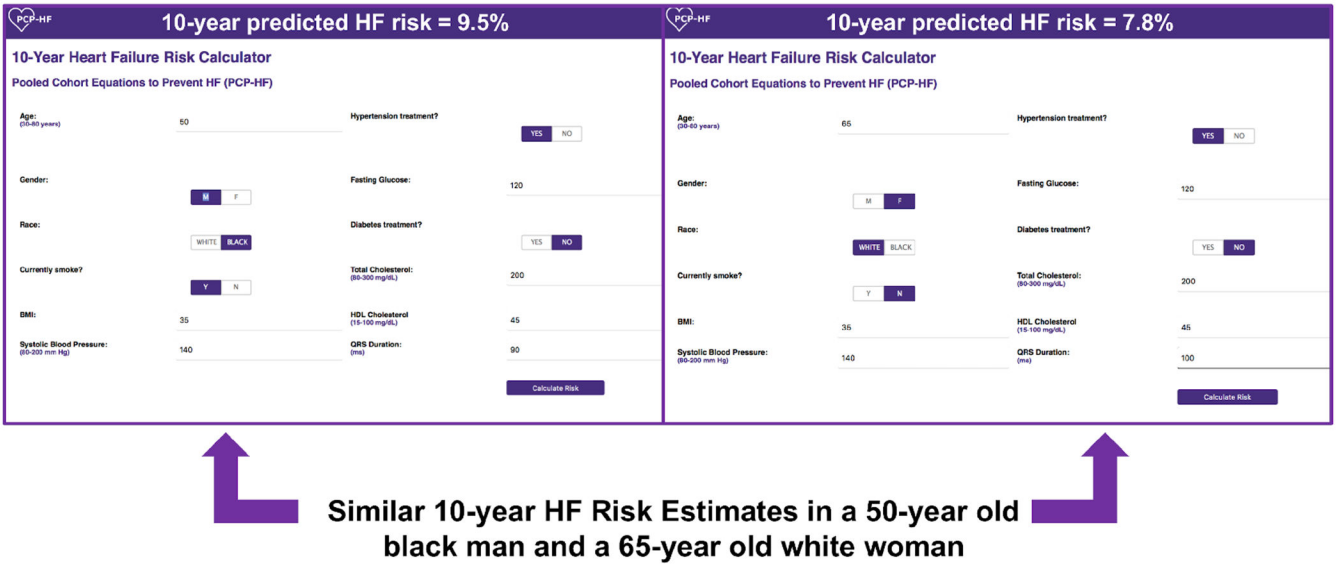
CLINICAL PERSPECTIVES

Competency in Systems-Based Practice:

Race- and sex-specific equations derived from community-based cohorts with long-term follow-up identified age, body mass index, blood pressure, fasting blood glucose and cholesterol levels, smoking status, and QRS duration as predictors of the risk of developing heart failure over 10 years.

Translational Outlook:

Prospective studies are needed to evaluate the clinical utility of specific preventive strategies in patients identified by this risk model.



Central Illustration: Examples of predicted 10-year heart failure risk using the online PCP-HF tool in a 50-year-old black man and 65-year old white woman.

Ten-year predicted HF risk is high and similar for a 50-year black man and a 65-year old white woman with the following risk profile: treated systolic blood pressure 140 mm Hg, body mass index 35 kg/m^2, untreated fasting glucose 120mg/dL, total cholesterol 200mg/dL, HDL-C 45 mg/dL, current smoker, and QRS of 90ms.

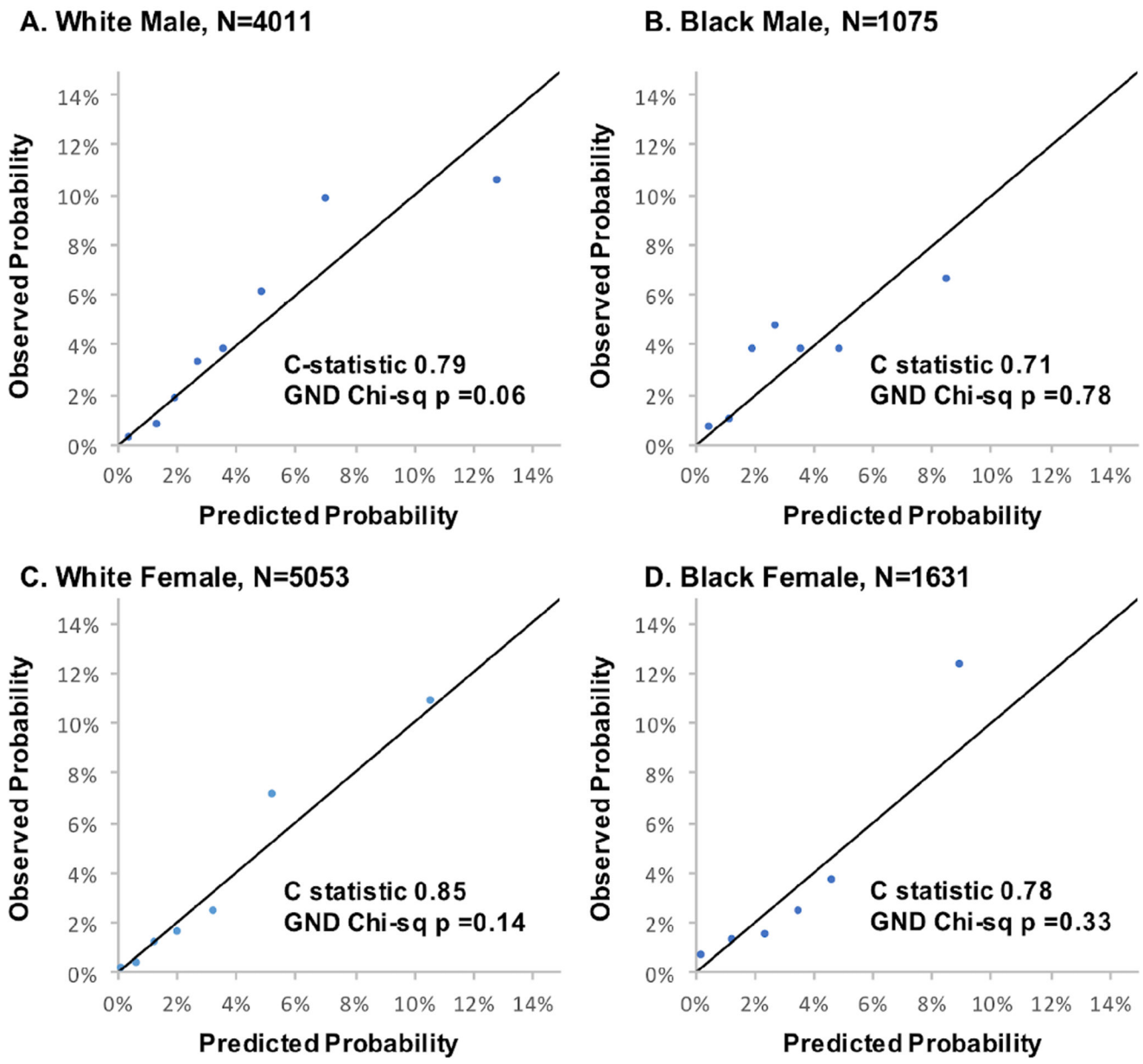


Figure 1. Sex- and Race-Specific Calibration Plots in the Validation Sample of the Pooled Cohort (n=11,770) with Discrimination and Calibration Statistics.

Calibration of the Pooled Cohort equations to Prevent Heart Failure (PCP-HF) risk score in the randomly split validation sample of the pooled cohort, which includes the ARIC, CARDIA, CHS, FOF, and MESA cohorts. Participants are grouped into deciles (collapsed when fewer than 2 events were observed in any group) according to increasing predicted risk and average predicted risk is compared with average observed risk in each category in each sex-race group. The model demonstrated good to excellent discrimination with c-statistics ranging from 0.71-0.85 and strong calibration (chi-sq p>0.05 for all sex-race groups).

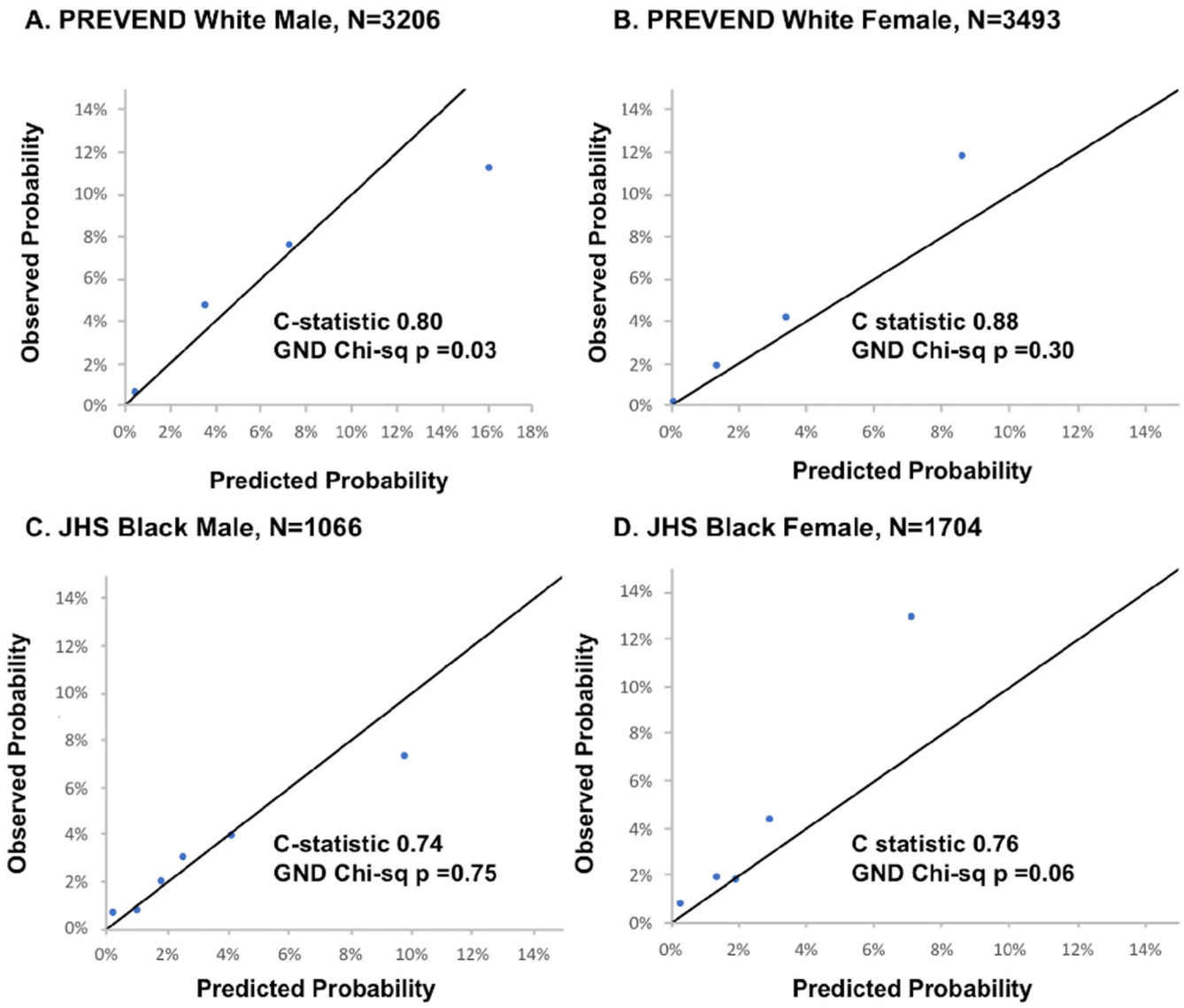


Figure 2. Calibration Plots in the Jackson Heart Study and PREVEND Validation Samples with Discrimination and Calibration Statistics.

Calibration of the Pooled Cohort equations to Prevent Heart Failure (PCP-HF) risk score in 2 large population-based cohorts of White (PREVEND) and Black (Jackson Heart Study) adults aged 30-80 years after excluding individuals with prevalent CVD. The remaining participants were grouped into deciles (collapsed when fewer than 2 events were observed in any group) according to increasing predicted risk and average predicted risk is compared with average observed risk in each sex-race group. The model demonstrated good discrimination with c-statistics ranging from 0.74-0.79 and strong calibration (chi-sq <20 with p>0.05 for all sex-race groups except white men p=0.03).

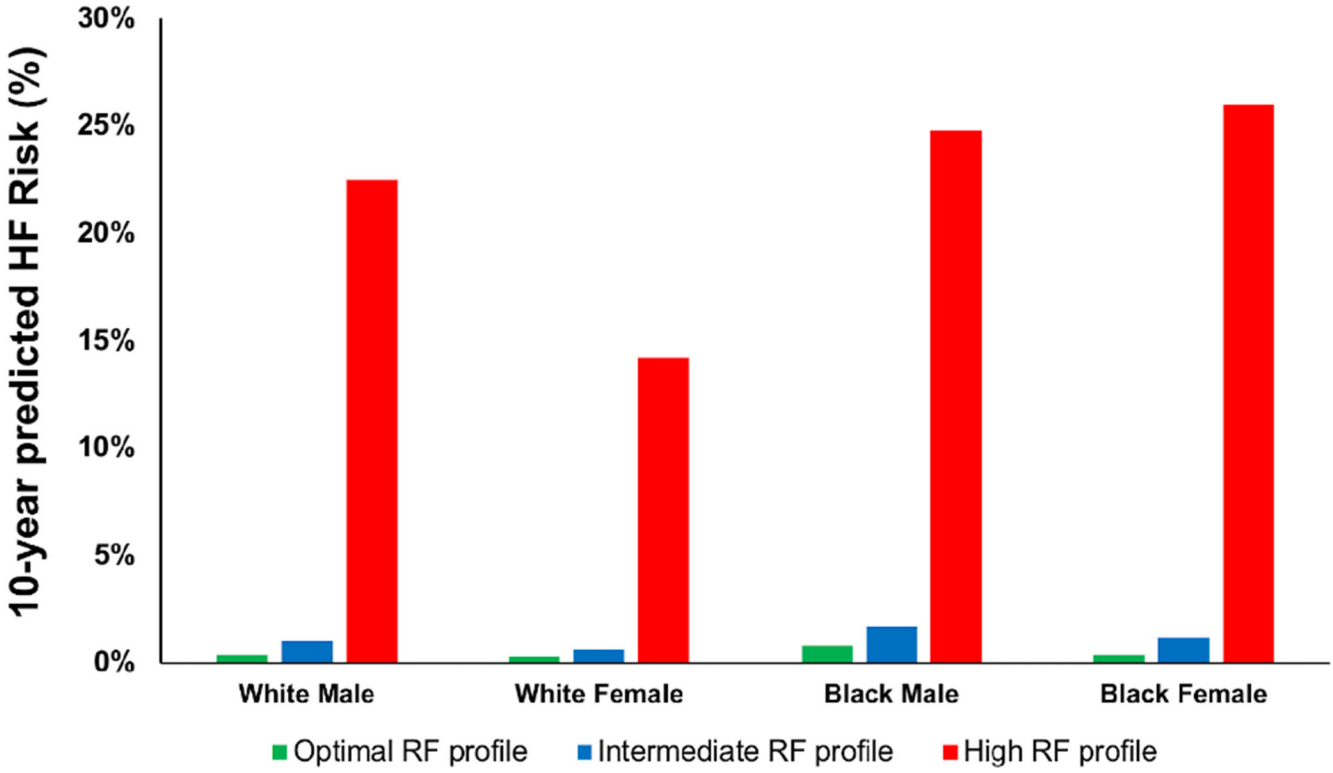


Figure 3. Sex- and Race-Specific 10-year Heart Failure Risk Estimates for a 50-year-old White and Black Man and Woman based on Optimal, Intermediate, and High Risk Profiles.

Heart failure risk estimated by the Pooled Cohort equations to Prevent Heart Failure varies significantly based on risk factor profile among race-sex groups. For an optimal RF profile (never smoker, systolic blood pressure of 120mm Hg, fasting glucose of 90mg/dL, no treatment for hypertension or diabetes, BMI of 22kg/m^2, total cholesterol of 180 mg/dL, HDL cholesterol of 55 mg/dL, and QRS duration of 90ms), 10-year risk is greatest among black men (0.8%) and lowest among white women (0.3%). Among participants with a high risk profile (current smoker, systolic blood pressure of 150mm Hg, fasting glucose of 126 mg/dL, treatment for hypertension and diabetes, BMI of 35 kg/m^2, total cholesterol of 250 mg/dL, HDL cholesterol of 30 mg/dL, and QRS duration of 120ms), 10-year predicted risk varies greatly ranging from lowest risk among white women (14%) to highest risk among black men (24%) and women (26%).

Table 1.

Baseline Characteristics among Black and White Men and Women in the Pooled Cohort Derivation and the External Validation Samples from 7 Population-Based Cohorts

	Black		White	
	PC Derivation N=2561	JHS Validation N=2770	PC Derivation N=9210	PREVEND Validation N=6699
Mean age, years (SD)	49.3 (12.8)	49.9 (11.6)	53.6 (11.6)	49.3 (12.2)
Female, n (%)	1628 (64)	1704 (62)	5213 (57)	3493 (52)
Diabetes, n (%)	290 (11)	302 (11)	522 (6)	232 (4)
Mean fasting glucose, mg/dL (SD)	102 (35)	97 (31)	99 (25)	88 (21)
Diabetes treatment, n (%)	176 (7)	225 (9)	193 (2)	99 (2)
Current smoking, n (%)	656 (26)	349 (13)	1873 (20)	2552 (38)
Mean systolic blood pressure, mm Hg (SD)	124 (20)	125 (16)	120 (18)	129 (20)
Hypertension treatment, n (%)	935 (37)	1057 (41)	2200 (24)	933 (14)
Mean total cholesterol, mg/dL (SD)	197 (44)	197 (39)	208 (41)	220 (44)
Mean HDL cholesterol, mg/dL (SD)	54 (15)	51 (14)	52 (16)	52 (16)
Mean BMI, kg/m^2	29.8 (6.3)	31.9 (7.4)	26.7 (4.7)	26.1 (4.2)
Mean QRS duration, msec (SD)	89 (13)	93 (13)	88 (13)	98 (13)

PC indicates pooled cohort, which includes ARIC, CARDIA, CHS, FOF, and MESA; JHS indicates Jackson Heart Study; PREVEND indicates Prevention of REnal and Vascular ENd-stage Disease cohort

Table 2.

Race- and Sex-Specific Equation Parameters for Estimation of 10-year Risk of HF erived from the Pooled Cohort

	White Male	White Female	Black Male	Black Female
Ln Age (y)	41.94	20.55	2.88	51.75
Ln Age, Squared	−0.88	N/A	N/A	N/A
Ln Treated Systolic BP (mm Hg)	1.03	12.95	2.31	29.0
Ln Age×Ln Treated Systolic BP	N/A	−2.96	N/A	−6.59
Ln Untreated Systolic BP (mm Hg)	0.91	11.86	2.17	28.18
Ln Age×Ln Untreated Systolic BP	N/A	−2.73	N/A	−6.42
Current Smoker (1=Yes, 0=No)	0.74	11.02	1.66	0.76
Ln Age×Current Smoker	N/A	−2.50	−0.25	N/A
Ln Treated glucose (mg/dL)	0.90	1.04	0.64	0.97
Ln Untreated glucose (mg/dL)	0.78	0.91	0.58	0.80
Ln Total Cholesterol (mg/dL)	0.49	N/A	N/A	0.32
Ln HDL–C (mg/dL)	−0.44	−0.07	−0.81	N/A
Ln BMI (Kg/m^2)	37.2	1.33	1.16	21.24
Ln Age× Ln BMI	−8.83	N/A	N/A	−5.0
Ln QRS duration (msec)	0.63	1.06	0.73	1.27
Mean Coefficient× Value *(MeanCV)*	171.5	99.73	28.73	233.9
Baseline Survival (S_0)	0.98752	0.99348	0.98295	0.99260

Calculation of the 10-year risk estimate for HF can best be described as a series of steps: 1) the natural log of age, systolic blood pressure (treated or untreated), glucose (treated or untreated), total cholesterol, HDL-C, body mass index, and QRS duration; 2) calculation of the interaction terms using the natural log of each variable; 3) multiplication of these values by the coefficients from the equation shown above for the appropriate race and sex group; 4) The sum of the coefficientxvalue is calculated for the individual *(IndX)*; **The estimated 10-year risk of a HF event is then formally calculated as:**

$$1 - S_0^{e^{(IndX - MeanCV)}}$$

N/A indicates not applicable; HF indicates heart failure; BP indicates blood pressure; HDL-C, high-density lipoprotein cholesterol; BMI, body mass index; and Ln, natural logarithm.

Table 3.

Numbers of Events, Discrimination and Calibration Statistics of the 10-year Pooled Cohort Equations to Prevent Heart Failure for Each Race and Sex Group in the Derivation and Validation Samples

	Men			Women		
	Derivation	**Validation**		**Derivation**	**Validation**	
White		**PC**	**PREVEND**		**PC**	**PREVEND**
Total N	3997	4011	3206	5213	5053	3493
Events	525	515	92	560	540	66
C statistics (95% CI)	0.83 (0.80, 0.86)	0.79 (0.76, 0.81)	0.80 (0.76, 0.84)	0.84 (0.81, 0.88)	0.85 (0.82, 0.88)	0.88 (0.84, 0.91)
GND Chi-sq× (P value)	9.45 (0.15)	13.4 (0.06)	8.7 (0.03)	7.64 (0.17)	9.76 (0.14)	3.7 (0.30)
	Derivation	**Validation**		**Derivation**	**Validation**	
Black		**PC**	**JHS**		**PC**	**JHS**
Total N	933	1075	1066	1628	1631	1704
Events	106	104	29	148	162	66
C statistics (95% CI)	0.83 (0.78, 0.87)	0.71 (0.63, 0.80)	0.74 (0.61, 0.86)	0.80 (0.73, 0.86)	0.78 (0.71, 0.85)	0.76 (0.66, 0.85)
GND Chi-sq (P value)	3.12 (0.68)	3.18 (0.78)	2.67 (0.75)	3.45 (0.75)	5.80 (0.33)	10.9 (0.06)

PC indicates pooled cohort, which includes ARIC, CARDIA, CHS, FOF, and MESA; JHS indicates Jackson Heart Study; PREVEND indicates_Prevention of Renal and Vascular End-stage Disease; CI represents confidence interval; GND represents Greenwood-Nam-D'Agostino