# Distribution and Correlates of Incident Heart Failure Risk in South Asian Americans: The MASALA Study

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# ABSTRACT

**Background:** South Asian Americans experience disproportionately high burden of cardiovascular diseases. Estimating predicted heart failure (HF) risk distribution may facilitate targeted prevention. We estimated the distribution of 10-year predicted risk of incident HF in South Asian Americans and evaluated the associations with social determinants of health and clinical risk factors.

**Methods and Results:** In the Mediators of Atherosclerosis in South Asians Living in America (MASALA) Study, we calculated 10-year predicted HF risk using the Pooled Cohort Equations to Prevent Heart Failure multivariable model. Distributions of low (<1%), intermediate (1%–5%), and high ( $\geq$ 5%) HF risk, identified overall and by demographic and clinical characteristics, were compared. We evaluated age- and sex-adjusted associations of demographic characteristics and coronary artery calcium with predicted HF risk category using ordinal logistic regression. In 1159 participants (48% women), with a mean age of 57 ± 9 years, 40% had a low, 37% had an intermediate, and 24% had a high HF risk. Significant differences in HF risk distribution existed across demographic (income, education, birthplace) and clinical (diabetes, hypertension, body mass index, coronary artery calcium) groups (*P* < .01). Significant associations with high predicted HF risk were observed for a family of income 75,000/year or more (adjusted odds ratio 0.5 [95% confidence interval (CI) 0.4–0.7]), college education (0.6 [95% CI 0.4–0.9]), birthplace in another South Asian country (1.9 [95% CI 1.2–3.2], vs. born in India), and prevalent coronary artery calcium (2.6 [95% CI 1.9–3.6]).

**Conclusions:** Almost two-thirds of South Asian Americans in the MASALA cohort are at intermediate or high predicted 10-year HF risk, with varying risk across demographic and clinical characteristics. (*J Car-diac Fail 2021;00:1–8*)

Key Words: Heart failure, epidemiology, race and ethnicity, primary prevention.

# Patient applications/Lay Summary

 Most middle-aged South Asian American adults are estimated to be at intermediate or high predicted risk for heart failure, warranting tailored prevention and treatment of risk factors in this group.

- Diabetes is an important heart failure risk factor in South Asian Americans.
- Factors such as education, income, and birthplace may be related to the risk of heart failure in South Asian Americans.

Lay summary: Most middle-aged South Asian American adults are estimated to be at least at intermediate predicted risk for developing heart failure over the next 10 years, with diabetes having a large role in their heart failure risk.

The current estimated prevalence of heart failure (HF) in the United States is 6.5 million,<sup>1</sup> and is projected to increase to more than 8 million by 2030 if current trends continue.<sup>2</sup> Lifetime risk for HF at age 45 was estimated to be 24%-46% in Black women, 32%-39% in White women, 20%-29% in Black men, and 30%-42% in White men in the cardiovascular lifetime risk pooling project.<sup>3</sup> Cardiovascular mortality owing to HF is increasing and represents the subtype of cardiovascular disease with the fastest increases

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in mortality rates in the United States over the last decade.<sup>4</sup> HF also has an increasing global prevalence with emerging data identifying a growing burden of HF in South Asia, where the prevalence of cardiometabolic risk factors for HF is high, age of HF onset is younger than among US populations, and HF outcomes are worse.<sup>5,6</sup> Prior studies in international settings indicate that patients with HF of South Asian ancestry were younger than patients in European or US registries or patients in other Asian regions, that South Asian individuals had a 3-5 times higher HF admission rates than White individuals in the United Kingdom, and that age-adjusted HF mortality rates in South Asian American women were the highest compared with mortality rates in other Asian American subgroups.<sup>5</sup> A large gap in knowledge exists, however, regarding HF risk to guide primary prevention in South Asian Americans, a rapidly growing segment of the US population with a disproportionately high burden of cardiometabolic disease and risk factors for HF compared with US adults of other race/ethnicity.<sup>7</sup>

Contemporary HF guidelines across national and international societies promote HF prevention as a key goal.<sup>8</sup> Our group developed a risk estimation tool to aid clinicians in estimating an individual's predicted short-term (10-year) risk of HF (the Pooled Cohort Equations to Prevent Heart Failure [PCP-HF]). These models use similar methods and derivation sample as the 2013 Pooled Cohort Equations for estimating 10-year risk of atherosclerotic cardiovascular disease. To estimate the 10-year incident HF risk, the PCP-HF tool uses readily available clinical parameters, including age, sex, smoking, body mass index (BMI), systolic blood pressure (SBP), fasting blood glucose, total cholesterol, and high-density lipoprotein (HDL) cholesterol.<sup>9</sup> Although the PCP-HF tool was derived from population-based cohort data composed of predominantly White and Black individuals, it has subsequently been validated in the general patient population of a diverse, integrated health system in a major metropolitan city in the United States.<sup>10</sup> Further validation in nationally representative population data from the National Health and Nutrition Examination Survey (NHANES) demonstrates an elevated and increasing prevalence of high predicted risk of HF among Black and White US adults between 1999 and 2016.<sup>11</sup>

To inform prevention strategies for HF in South Asians in the United States, we applied the PCP-HF risk model in the Mediators of Atherosclerosis in South Asians Living in America (MASALA) cohort study, to estimate the distribution of 10-year predicted risk of incident HF in South Asian Americans. We further aimed to evaluate the association of key social determinants of health in this group, including education, income, and country of origin as measure of sociocultural factors, with predicted HF risk.

#### Methods

# Participants

Between 2010 and 2018, participants were enrolled in the MASALA Study, a community-based cohort of 1164 South

Asian Americans aged 40-84 years and free of cardiovascular disease upon enrollment, who resided in the Chicago or San Francisco metropolitan areas.<sup>12</sup> Participants were excluded from study enrollment if they self-reported a diagnosis of HF, heart attack, stroke, transient ischemic attack, angina, atrial fibrillation, or impaired cognition; had a history of cardiovascular procedures; were receiving active treatment for cancer; reported use of nitroglycerin; had a life expectancy of less than 5 years owing to a serious medical condition; had plans to move out of the study region in the 5 years subsequent to enrollment; or resided in or were on a waiting list for a nursing home. For the present analysis, participants aged more than 79 years (n=5) were excluded because the PCP-HF equations have not been validated in older individuals. A total of 1159 participants were included in the present analytic sample. The MASALA Study protocols were approved by the institutional review boards at Northwestern University and University of California San Francisco. Participants provided written informed consent.

# **Demographic and Clinical Measures**

Collection methods for demographic and clinical measures have previously been described.<sup>12</sup> We evaluated SBP, hypertension treatment (taking antihypertensive medications as assessed by medication inventory), fasting plasma glucose, diabetes treatment (taking diabetes medications as assessed by medication inventory), BMI, total and HDL cholesterol, and smoking status (current vs former/never), which are the measures included in the PCP-HF risk estimation equations. Distributions of PCP-HF estimated risk of HF were evaluated by sex, annual family income (>\$75,000 per year vs <\$75,000 per year), education (college graduate vs not a college graduate), immigrant generation (first-generation immigrant vs second-generation USborn), place of birth (India; or other South Asian country [Pakistan, Nepal, Bangladesh, or Sri Lanka]; or the United States or other diaspora country [including sub-Saharan African countries, Fiji, and Burma]), BMI (≥27.5 kg/m<sup>2</sup>vs <27.5 kg/m<sup>2</sup>, in accordance with guidance for Asian-specific BMI definition of obesity<sup>13</sup>), diagnosis of diabetes or hypertension, and prevalent coronary artery calcium (CAC; score >0 vs score =0).

### Calculation of Predicted 10-Year Risk of Incident HF

Derivation of the PCP-HF risk estimation equations has previously been described<sup>14</sup> and high predicted HF risk (>5% over 10 years) is associated with subclinical cardiac remodeling and dysfunction<sup>15</sup> and mortality,<sup>16</sup> in addition to incident HF. HF risk was estimated using the multivariable PCP-HF model, incorporating SBP, hypertension treatment, fasting plasma glucose, diabetes treatment, BMI, total and HDL cholesterol, and smoking status. The PCP-HF model estimates risk for incident HF events (hospitalizations or death) inclusive of both HF with reduced and preserved ejection fraction, and incorporates readily available clinical variables (eg, cholesterol, glucose measures, BMI, and/or treatment) in a broad eligible age range (30-79 years) compared with other scores (eg, Framingham HF, Health ABC, MESA).<sup>14</sup> The PCP-HF risk prediction model may be applied with or without inclusion of QRS duration on an electrocardiogram. Because electrocardiogram measurements were not available in MASALA, we applied the PCP-HF model using derived equation coefficients in which QRS duration was excluded.<sup>17</sup> The PCP-HF risk prediction model is sex and race specific; however, this model was not derived specifically from or validated in South Asian Americans. Therefore, we applied the model equations specific to White women and men in our analytic sample, which is based on guideline recommendations<sup>8</sup> and prior application of the PCP-HF risk prediction model to estimate incident HF risk in other non-White and non-Black populations (Hispanic Americans).<sup>11</sup> We also build on a prior application applying coefficients derived in White populations in South Asian Americans for the pooled cohort equation-based risk estimation for atherosclerotic cardiovascular disease in MASALA.<sup>18</sup> After calculation of the predicted HF risk, participants were categorized as low (<1%), intermediate (1%-5%), or high risk  $(\geq 5\%)$ , consistent with previously reported risk thresholds.<sup>11</sup> The PCP-HF model calculation is summarized in Supplemental Table 1.

#### **Statistical Analysis**

Descriptive statistics of the measures included in the PCP-HF model were calculated stratified by demographic and clinical characteristics of interest. The Cochran-Armitage trend test was used to compare unadjusted distribution of HF risk category across binary demographic and clinical characteristics, and a  $\chi^2$  test was used to compare unadjusted distribution of HF risk category by place of birth categories. We evaluated the association of demographic characteristics and CAC with an estimated HF risk category using ordinal logistic regression models, with adjustment for age and sex. These models estimated the odds of higher order category of HF risk (ie, intermediate or high) for the independent variable of interest. All participants had data available for all relevant measures, thus no participants were excluded owing to missing data. Two-sided P values of less than .05 indicated statistical significance. Analyses were conducted using SAS version 9.4.

#### Secondary Analysis

In a secondary analysis to provide a comparison to the MASALA sample, we evaluated predicted risk of incident HF in a sample of non-Hispanic White participants from NHANES cycles 2009–2018, to approximate the period of time in which MASALA participants were enrolled. Ageand sex-matched NHANES participants were randomly selected in an approximately 2:1 ratio (2 NHANES participants for each MASALA participant), with 2312 participants included in the secondary analysis. NHANES participants were excluded from the secondary analysis if they self-reported a history of congestive HF, coronary heart disease, angina, heart attack, or stroke. The same clinical measures and risk estimation equations were used to calculate the PCP-HF risk score in this sample of NHANES participants, overall and stratified by sex. Analyses with NHANES data accounted for the complex, multistage design and survey weights using survey procedures in SAS version 9.4.

# Results

Among the 1159 South Asian American participants in MASALA, there were 556 women (48%) with a mean age of 55.9  $\pm$  8.7 years and 603 men (52%) with a mean age of  $57.3 \pm 9.7$  years (Table 1). The annual family income was \$75,000 or more for 69% of participants, and 86% had a college degree. Place of birth included India (83%), another South Asian country (8%), or the United States or another diaspora country (9%). BMI was 27.5 kg/m<sup>2</sup> or greater in 32% of participants, 27% had diabetes, 44% had hypertension, and 46% had a CAC score of greater than 0. Clinical measures included in the PCP-HF model are summarized in Table 1, overall and stratified by the demographic and clinical characteristics of interest. Overall, the mean SBP was  $126 \pm 16$  mm Hg, fasting glucose was  $103 \pm 27$  mg/dL, BMI was  $26.2 \pm 4.0 \text{ kg/m}^2$ , total cholesterol was  $187 \pm 38$ mg/dL, and HDL cholesterol was 50  $\pm$  14 mg/dL. Hypertension treatment was reported in 33% of participants, 18% were receiving diabetes treatment, and 3% were current smokers.

The distribution of the PCP-HF model estimates of the 10-year risk of incident HF is displayed in Fig. 1. Overall, 462 participants (40%) had a low risk, 425 (37%) had an intermediate risk, and 272 (24%) had a high risk of incident HF. Participants had a median 1.6% (interquartile range [IQR] 0.5%-4.4%) estimated 10-year risk of HF. Median estimated 10-year risk of incident HF is shown in Supplemental Table 2 and was highest among participants who had diabetes (4.4%, IQR 1.7%-11.1%) and hypertension (4.1%, IQR 1.9%, 9.3%). Among participants with diabetes or hypertension, 85% had an intermediate or high estimated 10-year risk of incident HF.

Significantly lower age- and sex-adjusted odds of elevated HF risk category were observed in participants with a family income of \$75,000 or greater (0.5, 95% CI 0.4–0.7) and among those who graduated college (0.6, 95% CI 0.4–0.9) (Fig. 2). Compared with participants born in India, participants born in other South Asian countries had a 1.9times higher adjusted odds (95% CI 1.2–3.2) of an elevated HF risk. Significantly higher age- and sex- adjusted odds of elevated HF risk category were also found among participants with prevalent CAC (2.6, 95% CI 1.9–3.6).

A secondary analysis of the predicted incident HF risk in age- and sex-matched NHANES participants is shown in Supplemental Table 2. Overall, 721 of NHANES participants (31%) were categorized as low risk, 1059 (46%) were

| Characteristics   | Age, Years     | SBP, mm Hg   | HTN treatment | Fasting glucose,<br>mg/dL | Diabetes treatment | BMI, kg/m <sup>2</sup> | Total cholesterol, mg/dL | HDL cholesterol,<br>mg/dL | Current<br>smoking |
|---|----------------|--------------|---------------|---------------------------|--------------------|------------------------|--------------------------|---------------------------|--------------------|
| Overall (N = 1159)<br>Sex   | $56.6\pm9.3$   | $126\pm16$   | 384 (33.1)    | $103 \pm 27$              | 208 (18.0)         | $26.2\pm4.0$           | $187\pm38$               | $50 \pm 14$               | 37 (3.2)           |
| Men $(n = 603)$   | $57.3 \pm 9.7$ | $127 \pm 15$ | 229 (28.0)    | $106 \pm 27$              | 129 (21.4)         | $25.9 \pm 3.7$         | $180 \pm 38$             | $45 \pm 11$               | 31 (5.1)           |
| women, $(n = 550)$  | $33.9 \pm 8.7$ | $124 \pm 17$ | 155 (27.9)    | $100 \pm 28$              | 79 (14.2)          | $20.3 \pm 4.4$         | $194 \pm 50$             | $30 \pm 14$               | 0(1.1)             |
| Family income $>$ \$75,000 ( <i>n</i> - 795)                      | $55.2\pm9.2$   | $124\pm15$   | 232 (29.2)    | $101 \pm 24$              | 122 (15.4)         | $26.0\pm3.8$           | $187 \pm 37$             | $50 \pm 14$               | 22 (2.8)           |
| $\leq $75,000 (n = 755)$<br>Family income<br>< \$75,000 (n = 326) | $59.6\pm8.9$   | $129\pm18$   | 133 (40.8)    | $109 \pm 34$              | 78 (23.9)          | $26.7\pm4.4$           | $187 \pm 40$             | $50 \pm 13$               | 15 (4.6)           |
| Education   |                |              |               |                           |                    |                        |                          |                           |                    |
| College graduate $(n = 1001)$                                     | $56.4\pm9.4$   | $125\pm16$   | 328 (32.8)    | $103 \pm 27$              | 173 (17.3)         | $26.1\pm3.9$           | $186 \pm 38$             | $50 \pm 14$               | 30 (3.0)           |
| Not a college grad-<br>uate $(n = 158)$                           | $58.3\pm8.5$   | $128\pm15$   | 56 (35.4)     | $106\pm29$                | 35 (22.2)          | $26.9\pm4.6$           | $191 \pm 37$             | $51 \pm 14$               | 7 (4.4)            |
| Generation/Nativity   |                |              |               |                           |                    |                        |                          |                           |                    |
| Second generation<br>United States born<br>(n-21)                 | $45.5 \pm 4.5$ | $120 \pm 15$ | 1 (4.8)       | 97 ± 14                   | 1 (4.8)            | 27.7 ± 4.9             | $199 \pm 31$             | $52 \pm 15$               | 2 (9.5)            |
| First-generation<br>immigrant                                     | $56.8\pm9.2$   | $126 \pm 16$ | 383 (33.7)    | $103 \pm 28$              | 207 (18.2)         | $26.2\pm4.0$           | $187 \pm 38$             | $50 \pm 14$               | 35 (3.1)           |
| (n = 1138)  |                |              |               |                           |                    |                        |                          |                           |                    |
| Other South Asian   | $56.9\pm8.7$   | $125\pm14$   | 37 (38.5)     | $115\pm45$                | 19 (19.8)          | $27.3\pm4.8$           | $191\pm37$               | $48 \pm 12$               | 4 (4.2)            |
| United States/other<br>diaspora country<br>(n = 102)              | $55.0\pm9.5$   | $122 \pm 14$ | 25 (24.5)     | $103 \pm 31$              | 18 (17.7)          | $26.3 \pm 4.3$         | $197\pm38$               | $52 \pm 14$               | 5 (4.9)            |
| (n = 102)<br>India $(n = 961)$                                    | $56.8 \pm 9.3$ | $126 \pm 16$ | 322 (33.5)    | $102 \pm 24$              | 171 (17.8)         | $26.1 \pm 3.9$         | $185 \pm 37$             | $50 \pm 14$               | 28 (2.9)           |
| BMI   |                |              | ()            |                           | ()                 |                        |                          |                           |                    |
| $\geq 27.5 (n = 375)$   | $56.4 \pm 9.0$ | $129 \pm 17$ | 157 (41.9)    | $107 \pm 31$              | 77 (20.5)          | $30.7 \pm 3.3$         | $187 \pm 38$             | $48 \pm 12$               | 11 (2.9)           |
| <27.5 ( <i>n</i> = 784)   | $56.7 \pm 9.4$ | $124 \pm 15$ | 227 (29.0)    | $101 \pm 25$              | 131 (16.7)         | $24.1\pm2.2$           | $187 \pm 38$             | $51 \pm 14$               | 26 (3.3)           |
| Diabetes  |                |              |               |                           |                    |                        |                          |                           |                    |
| Yes $(n = 316)$   | $59.2\pm8.6$   | $129 \pm 15$ | 182 (57.6)    | $130 \pm 38$              | 208 (65.8)         | $26.9\pm4.2$           | $174 \pm 41$             | $47 \pm 12$               | 10 (3.2)           |
| No ( <i>n</i> = 841)  | $55.6\pm9.3$   | $124 \pm 16$ | 202 (24.0)    | $93 \pm 11$               | 0 (0)              | $25.9\pm4.0$           | $192 \pm 35$             | $51 \pm 14$               | 27 (3.2)           |
| Hypertension  |                |              |               |                           |                    |                        |                          |                           |                    |
| Yes $(n = 506)$   | $60.5\pm8.9$   | $135 \pm 17$ | 384 (75.9)    | $112 \pm 33$              | 159 (31.4)         | $27.1 \pm 4.4$         | $178 \pm 38$             | $49 \pm 13$               | 18 (3.6)           |
| No $(n = 653)$  | $53.6 \pm 8.5$ | $118 \pm 11$ | 0 (0)         | $97 \pm 20$               | 49 (7.5)           | $25.5 \pm 3.6$         | $194 \pm 36$             | $51 \pm 14$               | 19 (2.9)           |
| CAC   |                |              |               |                           |                    |                        |                          |                           |                    |
| Score $>0$ ( <i>n</i> = 538)                                      | $61.2 \pm 8.7$ | $130 \pm 16$ | 271 (50.4)    | $110 \pm 30$              | 150 (27.9)         | $26.4 \pm 3.9$         | $181 \pm 40$             | $48 \pm 13$               | 23 (4.3)           |
| Score = $0 (n = 612)$   | $52.7 \pm 7.9$ | $122 \pm 15$ | 112 (18.3)    | $98 \pm 24$               | 58 (9.5)           | $25.9 \pm 4.0$         | $192 \pm 35$             | $52 \pm 14$               | 13 (2.1)           |

Table 1. Components of PCP-HF Risk Estimation Stratified by Clinical and Demographic Characteristics of MASALA Participants

Values are mean  $\pm$  standard deviation or number (%).

BMI, body mass index; CAC, coronary artery calcium; HDL, high-density lipoprotein; HTN, hypertension; SBP, systolic blood pressure.

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**Fig. 1.** Distribution of predicted heart failure risk in South Asian American participants of the MASALA Study. The 10-year predicted HF risk is estimated using the pooled cohort equations to prevent heart failure multivariable model, which accounts for systolic blood pressure, hypertension treatment, fasting plasma glucose, diabetes treatment, BMI, total and high-density lipoprotein cholesterol, and smoking status. Distributions shown are unadjusted. BMI, body mass index, kg/m<sup>2</sup>; CAC, coronary artery calcium; HF, heart failure; SA, South Asian; US, United States. 1st generation indicates immigrant (born outside the US), 2nd generation indicates US born.

intermediate risk, and 532 (23%) were high risk. Among non-Hispanic White women, 472 (43%) were categorized as low risk, 474 (43%) at intermediate risk, and 161 (15%) at high risk; among non-Hispanic White men, 249 (21%) were categorized as low risk, 585 (49%) as intermediate risk, and 371 (31%) as high risk. The mean values and frequencies of PCP-HF risk score components in NHANES participants are also displayed in Supplemental Table 2. Notably, 22% of non-Hispanic White women and 21% of non-Hispanic White men reported current smoking, compared with 1% of women and 5% of men in the MASALA sample.

#### Discussion

In this community-based sample of South Asian Americans, we found that almost two-thirds are at intermediate or high predicted risk for incident HF within 10 years. The distribution of the estimated HF risk varied by sex and across demographic and clinical characteristics, with the greatest proportion of high-risk participants observed among those who had diabetes and hypertension (recognizing that these clinical factors are accounted for in the PCP-HF risk estimation model) and CAC. Significant age- and sex-adjusted associations were noted between presence of CAC, family





**Fig. 2.** Adjusted odds of heart failure risk associated with demographic or clinical characteristics in South Asian American participants of the MASALA Study. The odds ratio (95% confidence interval [CI]) for increasing heart failure risk category, across levels of sociodemographic characteristics or clinical, adjusted for age and sex. Other South Asian countries include Pakistan, Nepal, Bangladesh, or Sri Lanka. Diaspora countries include sub-Saharan African countries, Fiji, and Burma. Abbreviations as in Fig. 1.

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income, education, and place of birth and estimated HF risk category.

These findings align with recent evaluation of HF risk distribution in the US population. In a nationally representative evaluation of NHANES participants between 2013 and 2016, approximately 23% of non-Hispanic Black men, 14% of non-Hispanic Black women, 19% of non-Hispanic White men, and 18% of non-Hispanic White women had a high predicted HF risk.<sup>11</sup> Overall, we found that 24% of South Asian Americans in this sample were at high predicted HF risk. Although this is a greater proportion at high risk than observed in Black and White Americans overall in NHANES, the nationally representative NHANES population was approximately 4 years younger on average than the MASALA sample. Our secondary analysis of age- and sex-matched NHANES participants showed that South Asian Americans had a similar proportion of individuals at high predicted HF risk (24%) compared with non-Hispanic White individuals (23%). However, there were important differences observed in burden of risk factors that contribute to incident HF risk. These differences may further explain the greater proportion of non-Hispanic White individuals at intermediate risk compared with South Asian Americans. For instance, non-Hispanic Whites had a considerably greater frequency of smoking compared with South Asian Americans, which in the PCP-HF risk equations plays a large role in determining risk of incident HF, particularly in women.<sup>17</sup>

Conversely, South Asian Americans may have a different phenotype of clinical risk factors that contribute to incident HF risk. South Asians are known to have high burden of diabetes and hypertension,<sup>19,20</sup> which are important HF risk factors,<sup>21,22</sup> and the frequency of being on diabetes treatment was higher in South Asian Americans in MASALA compared with non-Hispanic White in NHANES. There are also associations between body composition, as measured by BMI, and cardiovascular diseases in multi-ethnic US populations, with the strongest associations between BMI and incident HF compared with other cardiovascular diseases.<sup>23</sup> Although South Asian Americans in MASALA had a lower BMI on average compared with non-Hispanic Whites in NHANES, Asian Americans (including South Asians) are known to have higher risks for cardiometabolic diseases at a lower BMI.<sup>13</sup> Thus, the high BMI relative to Asian-specific definitions of "normal weight" in our sample of South Asian Americans likely also contributes to their increased predicted risk of HF. The differences in contribution of cardiovascular disease risk factors to HF risk distribution using the same risk model further emphasizes the importance of future derivation and validation of HF risk prediction specific to the South Asian American population. Such efforts will allow a more robust comparison of differences in HF risk distribution across race/ethnic groups.

Additionally, the association between CAC and HF risk may be reflective of HF risk related to the disproportionate burden of atherosclerotic cardiovascular disease in South Asians,<sup>7,24</sup> which increases the risk for HF with both

reduced and preserved ejection fraction. Finally, we also found that low family income, less than a college education, and place of birth in a South Asian country other than India were associated with a higher HF risk categorization, concordant with prior work supporting the influence of nonclinical contributors, including social determinants of health on HF risk.<sup>25</sup> Differences in HF risk and cardiovascular disease risk factors between South Asian immigrant generation and between South Asian American individuals based on country of origin are likely multifactorial in etiology and may include differences in age distributions, health-related behaviors related to acculturation such as dietary patterns and physical activity, as well as a range of social determinants of health, including environmental exposures, socioeconomic status, educational attainment, health literacy, and language fluency, among others.

These data highlight the importance of addressing and decreasing HF risk factors starting at younger ages in the South Asian American population, particularly as overall rates of premature mortality from HF increase in the United States.<sup>4</sup> For instance, the mean age of onset of diabetes is up to 10 years younger in South Asian Americans at age 45 as compared with other race/ethnic groups.<sup>26</sup> Aggressive clinical risk factor modification and lifestyle and behavioral measures to support primordial and primary prevention of HF, with a particular focus on body weight, blood glucose levels, and blood pressure, are necessary to stem the increasing burden of HF in South Asian Americans that these risk estimates portend. Comprehensive culturally adapted cardiovascular health promotion prioritizing health equity, community models, and policy interventions are also necessary for HF prevention in this population. Identifying implementation strategies for the PCP-HF model in clinical risk estimation may help to identify patients at risk.<sup>27</sup>

The main strength of this analysis is the application of a clinical HF risk assessment model in a high-risk and growing subset of the US population that remains understudied. However, there are a number of limitations. Most important, the PCP-HF risk estimation models were derived and validated in White and Black Americans. Therefore, whether HF risk is overestimated or underestimated in South Asian Americans using these model coefficients based on White Americans remains to be determined. Nevertheless, we applied the coefficients derived in White adults in the PCP-HF risk model to South Asian Americans similar to guideline recommendations to apply the Pooled Cohort Equations for 10-year risk estimation of atherosclerotic cardiovascular disease in populations outside of those in which the models were derived and validated.<sup>28</sup> A prospective collection of 10-year cardiovascular events data from the MASALA study is in progress and, once available, will allow for calibration of the PCP-HF model in this highrisk population.

Notably, owing to the study MASALA exclusion criteria, the MASALA sample reflects a subset of South Asian Americans who may be healthier than the overall South Asian American population. Therefore, the predicted risk of incident HF may not necessarily generalize to HF epidemiology in the South Asian American population overall. Additionally, the PCP-HF model does not differentiate between distinct subtypes of HF with reduced vs preserved ejection fraction. However, because both of these conditions have largely overlapping risk factors, primary prevention measures guided by risk estimation are likely to be similar. At this time, a comparison with HF among South Asians living in South Asia among community samples is limited because contemporary HF epidemiology in South Asia is not well-defined at this time. Similarly, these findings may not necessarily apply to South Asian populations in other US regions, South Asia, or in diaspora countries, where the data remain sparse. Additional data on HF prevalence and incidence in South Asia and more broadly in the United States and other countries are urgently needed, and efforts are ongoing to implement HF registries are underway in India.<sup>29</sup> Such evidence would facilitate a comparison of our findings with HF epidemiology in South Asians more broadly, and could improve our understanding of how environmental, sociodemographic, and behavioral factors that vary at the regional level may influence HF risk among South Asian individuals. Future work should support broad data collection in South Asian individuals (and other groups underrepresented in contemporary surveillance and population-based research) such as via race/ethnic subgroup disaggregation in clinical trials, observational studies, and electronic health records, as well as a broader assessment of the differences in and contributors to HF risk and epidemiology by immigrant generation and country of origin.<sup>30</sup> Such efforts will facilitate a more comprehensive understanding of the epidemiology of HF in South Asian American individuals.

In conclusion, we found that a large proportion of South Asian Americans in the MASALA cohort have a high estimated 10-year predicted risk for HF that is associated with important socioeconomic, demographic, and clinical variables. A focus on early prevention is warranted to interrupt the clinical progression of risk to overt HF in this high-risk population.

#### Disclosures

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#### Supplementary materials

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