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# Performance of contemporary cardiovascular risk stratification scores in Brazil: an evaluation in the ELSA-Brasil study

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## ABSTRACT

**Aims** Despite notable population differences in high-income and low- and middle-income countries (LMICs), national guidelines in LMICs often recommend using US-based cardiovascular disease (CVD) risk scores for treatment decisions. We examined the performance of widely used international CVD risk scores within the largest Brazilian community-based cohort study (Brazilian Longitudinal Study of Adult Health, ELSA-Brasil).

**Methods** All adults 40–75 years from ELSA-Brasil (2008–2013) without prior CVD who were followed for incident, adjudicated CVD events (fatal and non-fatal MI, stroke, or coronary heart disease death). We evaluated 5 scores—Framingham General Risk (FGR), Pooled Cohort Equations (PCEs), WHO CVD score, Globorisk-LAC and the Systematic Coronary Risk Evaluation 2 score (SCORE-2). We assessed their discrimination using the area under the receiver operating characteristic curve (AUC) and calibration with predicted-to-observed risk (P/O) ratios—overall and by sex/race groups.

**Results** There were 12 155 individuals (53.0±8.2 years, 55.3% female) who suffered 149 incident CVD events. All scores had a model AUC>0.7 overall and for most age/sex groups, except for white women, where AUC was <0.6 for all scores, with higher overestimation in this subgroup. All risk scores overestimated CVD risk with 32%–170% overestimation across scores. PCE and FGR had the highest overestimation (P/O ratio: 2.74 (95% CI 2.42 to 3.06)) and 2.61 (95% CI 1.79 to 3.43)) and the recalibrated WHO score had the best calibration (P/O ratio: 1.32 (95% CI 1.12 to 1.48)).

**Conclusion** In a large prospective cohort from Brazil, we found that widely accepted CVD risk scores overestimate risk by over twofold, and have poor risk discrimination particularly among Brazilian women. Our work highlights the value of risk stratification strategies tailored to the unique populations and risks of LMICs.

### WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Cardiovascular disease (CVD) risk scores developed in high-income Western countries are being adopted in national guidelines in low-income and middle-income countries (LMICs) without a systematic assessment of their performance in these populations.

### WHAT THIS STUDY ADDS

⇒ In a large, well-characterised cohort study from Brazil, we identify a high overestimation of risk by commonly used CVD risk scores, exceeding those seen in validation studies performed in other Western nations.

⇒ Current CVD risk scores, including those recalibrated for LMICs, fail to accurately capture risk in a Brazilian population and perform poorly among Brazilian women.

### HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The study highlights the critical need for new calibration strategies and risk assessment tools to inform policy decisions regarding CVD prevention and resource allocation in Brazil and similar LMIC settings.

## INTRODUCTION

Despite the increasing focus on personalised cardiovascular prevention based on risk assessment, accurately defining the risk of cardiovascular disease (CVD) remains a challenge.[1 2] This challenge is magnified in low- and middle-income countries (LMICs), which account for over 75% of global CVD deaths but lack sufficient high-quality data to inform effective risk assessment strategies.[3 4] This is particularly important as population demographics and lifestyle choices may result in differing levels of risk among LMIC populations compared with those in the USA and Europe. However, risk stratification strategies used in LMICs, such as Brazil, are predominantly derived and validated in the USA and Europe.[5 6]

In recent years, novel cardiovascular risk scores targeted for LMICs have emerged,

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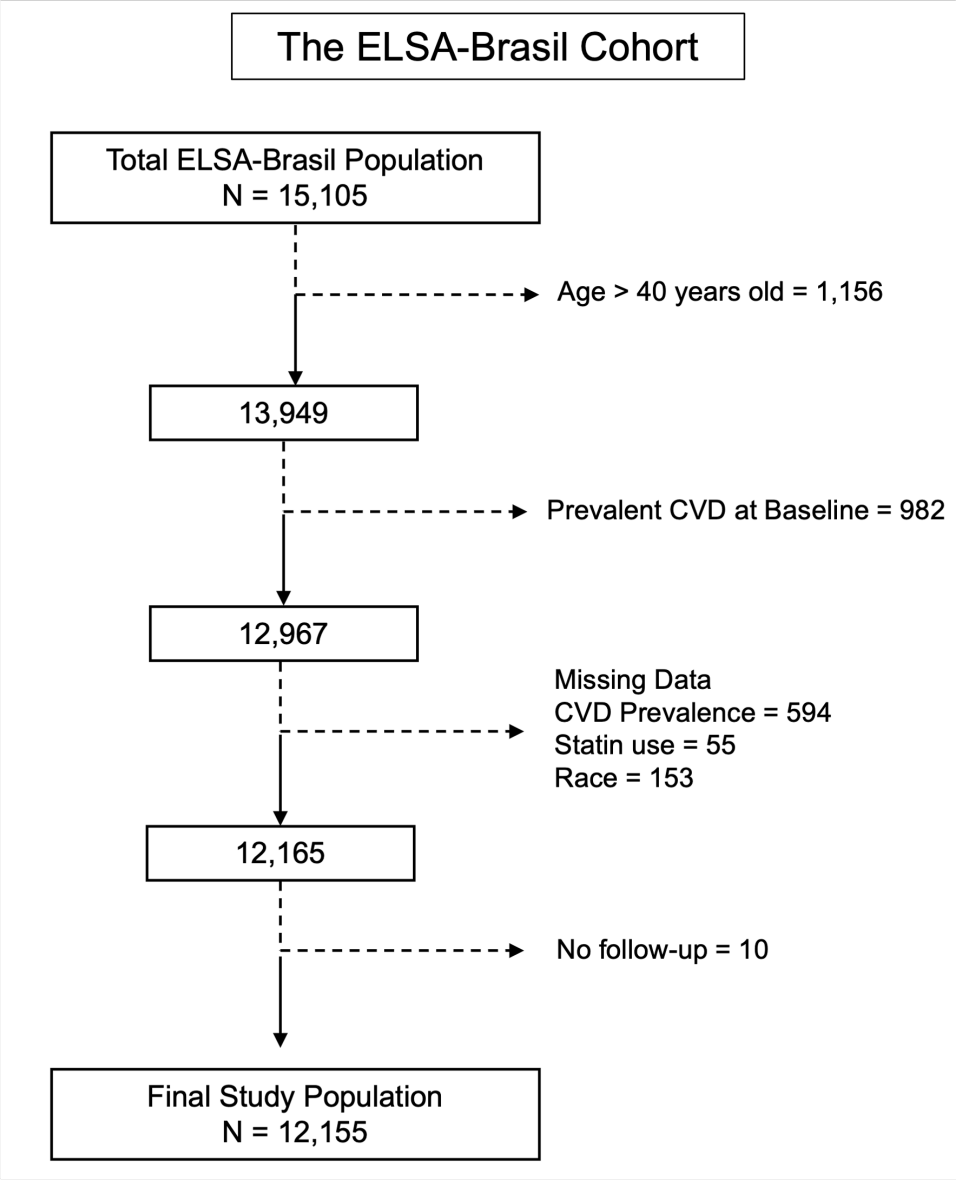


**Figure 1** Flow chart of the study population. Brazilian Longitudinal Study of Adult Health (ELSA-Brasil, 2008). CVD, cardiovascular disease.

aiming to enhance risk prediction in diverse populations.[7 8] Brazil has considerable racial and demographic diversity, characterised by a unique interplay of dietary and lifestyle patterns as well as environmental exposures, shaping the prevalence of risk factors and contributing to a distinct susceptibility to cardiovascular-related outcomes.[9 10] These differences emphasise the critical need for targeted risk stratification algorithms in tailoring preventive strategies, ensuring efficient resource allocation and addressing the specific needs of a population facing cardiovascular risk factors in a developing country.[11]

In this study, we leverage the largest and the most racially diverse cohort in Brazil—the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil) to examine the performance of contemporary cardiovascular risk scores, including Framingham General Risk (FGR),[12] Pooled Cohort Equation (PCE),[13] WHO CVD risk score,[7] Globorisk-LAC[8] and European Society of Cardiology's Systematic Coronary Risk Evaluation 2 (SCORE-2)[14] in predicting incident CVD events.

## METHODS

### Data source

The ELSA-Brasil is a large-scale multicentre and multiracial cohort study aimed at investigating risk factors and determinants of chronic diseases, especially CVD, in the Brazilian population. The study began in 2008 and included 15 105 public servants from higher education and research institutes, 35–75 years old, from 6 state capitals in Brazil. Follow-up visits were conducted every 3–4 years to ascertain exposure status and identify changes in baseline subclinical and clinical parameters. In addition,



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**Table 1** Descriptive analysis of the study's population

| | Overall | White | 'Pardo' | Black | Other |
|---|---|---|---|---|---|
| N | 12155 | 6328 | 3418 | 1977 | 432 |
| Age, mean (SD) | 53.0 (8.2) | 53.5 (8.4) | 52.2 (7.7) | 52.4 (7.8) | 54.8 (8.4) |
| Female, N (%) | 6722 (55.3) | 3460 (54.7) | 1803 (52.8) | 1213 (61.4) | 246 (56.9) |
| Education<middle school, N (%) | 1546 (12.7) | 459 (7.3) | 578 (16.9) | 436 (22.1) | 73 (16.9) |
| Smoking, N (%) | 1654 (13.6) | 821 (13.0) | 478 (14.0) | 302 (15.3) | 53 (12.3) |
| Diabetes, N (%) | 1945 (16.0) | 834 (13.2) | 572 (16.7) | 452 (22.9) | 87 (20.1) |
| Statin use, N (%) | 1386 (11.4) | 850 (13.4) | 284 (8.3) | 182 (9.2) | 70 (16.2) |
| Antihypertensive use, N (%) | 3320 (27.3) | 1550 (24.5) | 920 (26.9) | 729 (36.9) | 121 (28.0) |
| SBP mm Hg, mean (SD) | 121.5 (17.2) | 119.0 (15.9) | 123.1 (17.4) | 126.9 (19.1) | 121.1 (17.7) |
| BMI kg/m$^2$, mean (SD) | 27.0 (4.7) | 26.7 (4.6) | 27.0 (4.6) | 28.0 (5.1) | 26.0 (4.2) |
| Total cholesterol mg/dL, mean (SD) | 202.7 (40.7) | 202.1 (39.7) | 203.8 (41.4) | 202.0 (42.8) | 204.2 (40.4) |
| HDL-cholesterol mg/dL, mean (SD) | 53.9 (13.3) | 53.8 (13.2) | 52.9 (13.1) | 55.6 (13.7) | 55.2 (13.8) |
| Predicted Risk Across Scores | | | | | |
| FGR 10-year risk, median (IQR) | 3.94 (1.48 to 8.89) | 3.08 (1.25 to 7.31) | 4.91 (2.21 to 9.63) | 5.27 (1.98 to 11.71) | 3.56 (1.52 to 9.42) |
| PCE-race specific 10-year risk, median (IQR) | 3.92 (1.47 to 8.87) | 3.07 (1.25 to 7.29) | 4.89 (2.19 to 9.62) | 5.26 (1.97 to 11.73) | 3.56 (1.53 to 9.35) |
| PCE-White American 10-year risk, median (IQR) | 3.08 (1.27 to 7.45) | 3.07 (1.25 to 7.29) | 3.01 (1.31 to 7.21) | 3.11 (1.22 to 7.92) | 3.56 (1.53 to 9.35) |
| WHO 10-year risk, median (IQR) | 3.15 (1.98 to 5.10) | 3.12 (1.94 to 5.09) | 3.07 (1.97 to 4.86) | 3.26 (2.06 to 5.40) | 3.46 (2.15 to 5.75) |
| Globorisk-LAC 10-year risk, median (IQR) | 4.46 (2.66 to 7.61) | 4.22 (2.59 to 7.05) | 4.52 (2.72 to 7.73) | 4.95 (2.81 to 9.31) | 4.84 (3.00 to 8.40) |
| SCORE-2 low-risk 10-year risk, median (IQR) | 2.77 (1.57 to 4.89) | 2.73 (1.56 to 4.76) | 2.77 (1.58 to 4.82) | 2.88 (1.57 to 5.20) | 3.18 (1.72 to 5.56) |
| CVD events, N (%) | 149 (1.2) | 63 (1.0) | 42 (1.2) | 40 (2.0) | 4 (0.9) |

Baseline ELSA-Brasil (2008). N=12 155.
BMI, body mass index; CVD, cardiovascular disease; ELSA-Brasil, Brazilian Longitudinal Study of Adult Health; FGR, Framingham General Risk; HDL, high-density lipoprotein cholesterol; LAC, Latin-American countries; PCE, Pooled Cohort Equations; SBP, systolic blood pressure; SCORE-2, Systematic Coronary Risk Evaluation 2.

all participants (or their proxy) were interviewed yearly via telephone to obtain information on new diagnoses, hospitalisation and death. Details about the design and cohort profile have been previously published,[15 16] and details on key elements are provided in the following sections. All six investigation centres approved the ELSA-Brasil protocol, and all participants signed an informed consent.

### Study population

To construct a primary prevention cohort suitable for applying current cardiovascular risk scores, we included all ELSA-Brasil participants aged 40–75 years who did not report any previous CVD at baseline, including myocardial infarction (MI), stroke, coronary revascularisation or heart failure. Participants with missing data about race (n=153, 1.24%), CVD prevalence (n=594, 4.26%) or statin use (n=55, 0.44%), and those who did not participate in follow-up visits (n=10, 0.08%) were excluded (figure 1).

### Cardiovascular risk scores

We calculated five risk prediction scores, using six different equations: FGR[12]—currently recommended by Ministry of Health's Brazilian guidelines[17] and by the Brazilian Society of Cardiology in an adapted version, PCE (PCEs from the American College of Cardiology/American Heart Association),[13] African-American and White-American equations, WHO (WHO CVD risk score) recalibrated for Tropical Americas,[7] Globorisk-LAC recalibrated for Brazil[8] and SCORE-2 recalibrated to low-risk populations, from the European Society of Cardiology.[14]

The PCEs, WHO, Globorisk-LAC, and SCORE-2 predict 10-year individual risk of coronary heart disease (CHD) death, non-fatal MI and fatal or non-fatal ischaemic stroke. For the FGR, the Framingham Heart Study defines CVD as a composite of CHD (coronary death, MI, coronary insufficiency, and angina), cerebrovascular events (including ischaemic stroke, haemorrhagic stroke, and transient ischaemic attack), peripheral artery disease (intermittent claudication) and heart failure.

Events were censored on 31 December 2013, with a median follow-up time of 4.2 years. Employing a method used by previous studies,[18 19] we lowered individual 10-year risk estimates to correspond to their length of follow-up using an exponential survival function to scale the predicted risk, described in further detail in online supplemental file 1.

Details about the risk scores can be found in online supplemental table 1.



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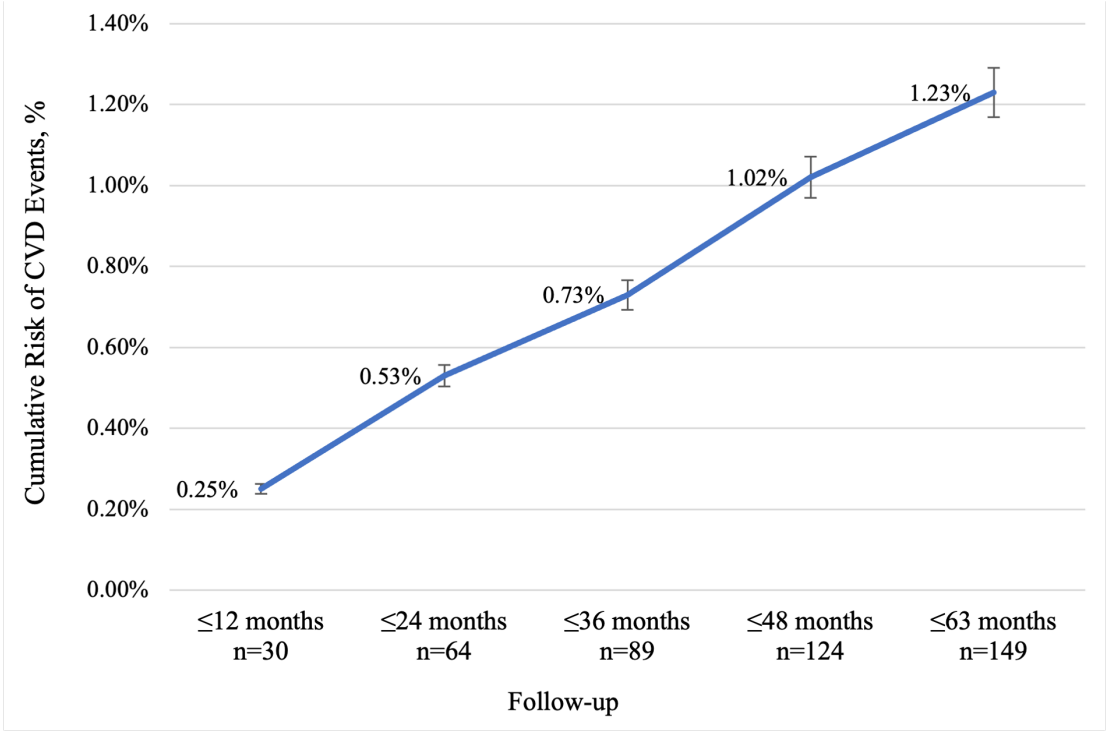


**Figure 2** Cumulative risk of CVD events during 5-year follow-up. ELSA-Brasil (2008–2013) N=12 155. (N represents the cumulative number of events observed during each follow-up period for calculating the annual cumulative risk of CVD events among all eligible adults 40–75 years of age in the ELSA-Brasil (2008–2013)). CVD, cardiovascular disease; ELSA-Brasil, Brazilian Longitudinal Study of Adult Health.

### Study outcomes and adjudication of events

The study outcomes were aligned with the outcomes predicted by each of the five scores. They spanned major adverse cardiovascular events, such as fatal or non-fatal MI, fatal or non-fatal stroke, and cardiovascular death, and included heart failure and peripheral artery disease for the FGR score. In the ELSA study, the events were identified either by in-person interview or the annual telephone call and then investigated by a designated committee that contacted health providers and requested copies of medical records for all hospitalisations, outpatient diagnoses, and death certificates. More details about the follow-up for events in the ELSA-Brasil can be found in a previous publication.[20] After investigation, the cardiovascular events were then adjudicated according to predefined definitions by the independent review of two cardiologists. A third senior cardiologist defined the event in case of disagreement.

MI was defined as an increase in cardiac biomarkers (such as troponin) above the 99th percentile of the reference population, with at least one of the following: symptoms of ischaemia, ECG changes indicative of new ischaemia, development of pathological Q waves on the ECG, imaging evidence of new loss of viable myocardium or new regional wall motion abnormality or identification of an intracoronary thrombus by angiography or autopsy. Stroke was defined as a sudden onset of a focal neurological deficit persisting for at least 24 hours, or leading to death, and attributable to a vascular cause. Heart failure was defined by medical diagnosis and specific treatment and/or pulmonary oedema in X-rays, and/or ventricular function on echocardiogram/radionuclide scintigraphy or contrast ventriculography; and peripheral arterial disease was defined based on symptoms, diagnostic procedure or therapeutic intervention. Death due to cardiovascular causes includes deaths caused by CHD, MI, stroke, heart failure and arrhythmias.

The classification of underlying causes of death in the ELSA study is based on the guidelines of the Brazilian Ministry of Health, which follows the 10th revision of the International Classification of Diseases. The cause of death is ascertained by death certificates, hospital records and autopsy reports. In cases where the cause of death was unclear or disputed, an expert panel reviewed the available data to confirm the underlying cause of death.

### Study covariates

The risk factors used to calculate risk scores were age, sex, total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), systolic blood pressure (SBP), smoking status, history of diabetes mellitus (DM), hypertension treatment (PCE and FGR) and race (PCE). For PCE, the model specifications recommend that all non-black individuals have their risk calculated according to the equation for whites. In our study, we used the African-American and the White-American equations to measure the risk for the black and 'Pardo' populations.



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**Table 2** Discrimination and calibration of the FGR, PCE, WHO, Globorisk-LAC, and SCORE-2 for the total study population and for sex and race groups.

| | | Total population | Men (N=5433) | | Women (N=6722) | |
|---|---|---|---|---|---|---|
| | | (N=12–155) | White | Black/Pardo | White | Black/Pardo |
| AUC (95% CI) | FGR | 0.77 (0.72 to 0.81) | 0.73 (0.68 to 0.79) | 0.84 (0.79 to 0.89) | 0.60 (0.45 to 0.74) | 0.73 (0.64 to 0.82) |
| | PCE | 0.76 (0.72 to 0.81) | 0.73 (0.68 to 0.79) | 0.83 (0.78 to 0.89) | 0.59 (0.43 to 0.75) | 0.71 (0.61 to 0.81) |
| | PCE-w | 0.76 (0.72 to 0.80) | 0.73 (0.68 to 0.79) | 0.81 (0.75 to 0.88) | 0.59 (0.43 to 0.75) | 0.70 (0.59 to 0.82) |
| | WHO | 0.76 (0.71 to 0.80) | 0.73 (0.66 to 0.79) | 0.81 (0.74 to 0.88) | 0.56 (0.40 to 0.73) | 0.72 (0.62 to 0.81) |
| | Globorisk-LAC | 0.75 (0.71 to 0.80) | 0.71 (0.63 to 0.78) | 0.80 (0.73 to 0.87) | 0.58 (0.43 to 0.73) | 0.73 (0.64 to 0.83) |
| | SCORE-2 | 0.76 (0.71 to 0.80) | 0.74 (0.67 to 0.80) | 0.81 (0.75 to 0.88) | 0.56 (0.40 to 0.73) | 0.71 (0.61 to 0.81) |
| | FGR | 2.61 (1.79 to 3.43) | 3.82 (2.94 to 4.70) | 2.60 (1.56 to 3.64) | 2.84 (2.15 to 3.53) | 2.57 (1.55 to 3.59) |
| P/O ratio (95% CI) | PCE | 2.74 (2.42 to 3.06) | 3.30 (2.44 to 4.16) | 3.97 (2.94 to 5.00) | 3.82 (2.75 to 4.89) | 3.70 (2.74 to 4.66) |
| | PCE-w | 2.41 (2.00 to 2.83) | 3.30 (2.44 to 4.16) | 2.38 (1.37 to 3.39) | 3.82 (2.75 to 4.89) | 2.81 (1.68 to 3.94) |
| | WHO | 1.32 (1.12 to 1.48) | 1.30 (1.08 to 1.52) | 1.18 (0.83 to 1.53)* | 2.07 (1.70 to 2.44) | 1.47 (0.98 to 1.96)* |
| | Globorisk-LAC | 2.38 (2.08 to 2.69) | 2.71 (1.98 to 3.44) | 2.27 (1.88 to 2.66) | 5.94 (5.08 to 6.83) | 2.68 (1.64 to 3.72) |
| | SCORE-2 | 1.59 (1.41 to 1.77) | 1.47 (1.14 to 1.80) | 1.23 (0.87 to 1.59)* | 2.91 (1.93 to 3.89) | 1.32 (0.86 to 1.78)* |

ELSA-Brasil (2008–2013).
*Groenersby-Borgman $\chi^2$<20 and p>0.05.
AUC, area under the curve; ELSA-Brasil, Brazilian Longitudinal Study of Adult Health; FGR, Framingham General Risk; LAC, Latin-American countries; PCE, pooled cohort equation; P/O, predicted to observed; SCORE-2, Systematic Coronary Risk Evaluation 2.

Race and smoking status were self-reported. Race was categorised as black, 'Pardo' (mixed), white, or other (Asian and Indigenous were combined due to the low number of events in each separate population). The ELSA-Brasil routines, organisation of clinical tests and definition of DM, SBP, TC, HDL-c and body mass index can be found in previous publications[21] and in online supplemental material (p. 03). All participants were requested to bring to the investigation centre all continuous medication they were taking during the 2 weeks preceding the interview. To be considered under antihypertensive or statin medication, the participant should declare taking at least one medication from these classes.

### Statistical analysis

Categorical variables were defined as counts and percentages, and differences between racial groups were assessed by the $\chi^2$ test. Continuous variables were defined by median and IQR, and differences between racial groups were tested by the analysis of variance.

We evaluate the performance of risk scores across both model discrimination and calibration, as these models serve as out-of-box tools used directly in each candidate population. We used the c-statistic reflecting the area under the receiver operating characteristic curve (AUC) to assess discrimination. We compared mean 4-year predicted CVD risk to observed 4-year cumulative CVD events incidence across baseline deciles of risk estimates and by risk categories. To account for lower risk estimates due to shorter follow-up time, we categorised risk as <2.5%, 2.5%–5%, 5%–10% and ≥10%, similar to previous studies.[22 23] We assessed calibration by predicted-to-observed risk (P/O) ratios and calculated the Grønnesby-Borgan goodness-of-fit test. A P/O ratio >1 indicated an overestimation of risk, a P/O ratio <1 underestimation and a P/O ratio=1 perfect calibration. All analyses were performed for the total population and then stratified by sex/race groups (black/'Padro' men; white men; black/'Pardo' women; white women).

As a sensitivity analysis, we limited the population to participants with clinical criteria consistent with guideline recommendations for using CVD risk scores to guide statin therapy (not taking statins at baseline, not having DM, and with an LDL-c between 70 and 189 mg/dL). We also performed an analysis stratified by education (college/high school/middle school), a proxy for socioeconomic status.

We used Stata V.14.0 software (Stata) and R-Studio V.4.2.2 to perform all analyses.

### Patient and public involvement

The participants were not involved in the planning of the study or in the dissemination of the study results.

## RESULTS

We included 12 155 individuals with a mean (SD) age of 53.0 (8.2) years, including 6722 (55.3%) females, and 6328 (52.1%) individuals self-reported as white. Antihypertensive medications and statins were being used by 27.3% and 11.4%, of the individuals at baseline, respectively. Baseline characteristics and risk factors varied according to race categories except for TC values (table 1).

Over a median (IQR) follow-up of 4.2 (3.7–4.5) years, 149 (1.2%) fatal and non-fatal cardiovascular events were



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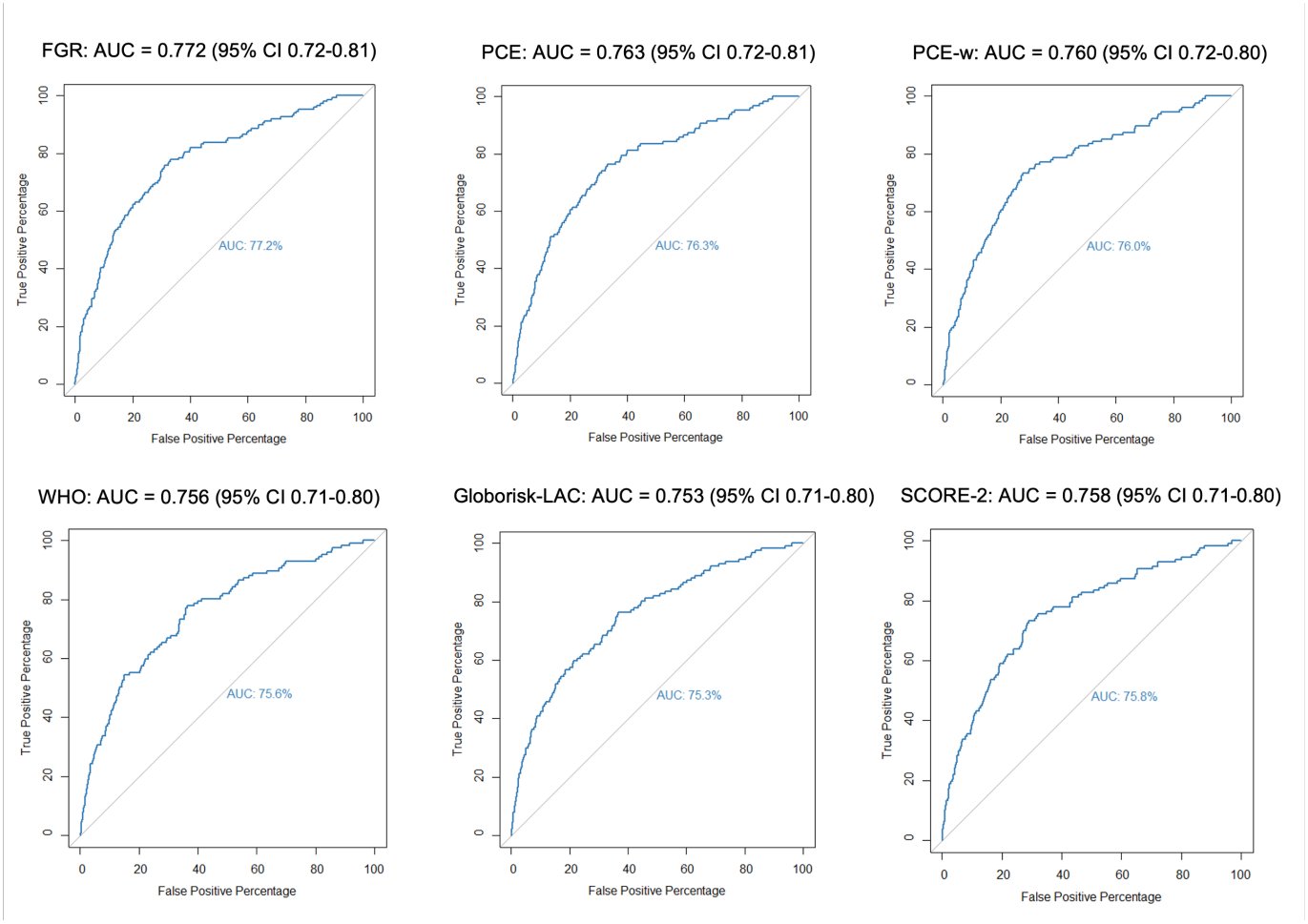


**Figure 3** Receiver operating characteristic curves for the Framingham General Risk (FGR), Pooled Cohort Equations (PCE), WHO CVD score, Globorisk-LAC and SCORE-2 for the overall study population. ELSA-Brasil (2008–2013). N=12 155. AUC, area under curve; CVD, cardiovascular disease; ELSA-Brasil, Brazilian Longitudinal Study of Adult Health; LAC: Latin-American countries; SCORE-2, Systematic Coronary Risk Evaluation 2.

observed, representing an overall incidence rate of 2.56 (95% CI 2.16 to 3.03) per 1000 person-years. There were 47 (31.5%) non-fatal MI, 49 (32.9%) non-fatal stroke, 24 (16.1%) heart failure, 11 (7.4%) peripheral arterial disease and 33 (22.1%) fatal CVD events. The cumulative risk of CVD events increased linearly during the 5-year follow-up period (figure 2).

### Risk scores accuracy

The discrimination of the 5 scores within the overall ELSA-Brasil population was comparable to their performance in the cohorts where they were originally developed, with an AUC varying between 0.75 (95% CI 0.71 to 0.80) and 0.77 (95% CI 0.72 to 0.81) (table 2 and figure 3). However, in the analysis stratified by sex and race, all tested scores had poor discrimination for women self-reported as white (AUC FGR: 0.60, 95% CI 0.45 to 0.74; AUC PCE: 0.59, 95% CI 0.43 to 0.75; AUC Globorisk-LAC: 0.58; 95% CI 0.43 to 0.73; AUC WHO and SCORE-2: 0.56, 95% CI 0.40 to 0.73) and highest discrimination values among men self-declared as black or 'Pardo' (AUC FGR: 0.84, 95% CI 0.79 to 0.89; AUC PCE: 0.83, 95% CI 0.78 to 0.89; AUC PCE-w: 0.81 (0.75 to 0.88); AUC Globorisk-LAC: 0.80, 95% CI 0.73 to 0.87; AUC WHO: 0.81, 95% CI 0.74 to 0.88; SCORE-2: 0.81, 95% CI 0.75 to 0.88) (table 2).

In the calibration assessment for the entire population, it was observed that all scores overestimated CVD risk by percentages ranging from 32% to more than 170% (P/O ratio: FGR: 2.61, 95% CI 1.79 to 3.43; PCE race-specific: 2.74, 95% CI 2.42 to 3.06; PCE White-American: 2.41, 95% CI 2.00 to 2.83; WHO recalibrated: 1.32 95% CI 1.12 to 1.48; Globorisk-LAC: 2.38, 95% CI 2.08 to 2.69 and SCORE-2: 1.59, 95% CI 1.41 to 1.77) (table 2), with a GrønnesbyBorgan $\chi^2$>20 and p<0.05.

Discordance between observed and predicted risk was found for both men and women throughout the risk continuum, with the highest gap among those with a predicted risk ≥10% (figure 4). We observed higher overestimation in whites compared with blacks/'Pardos' and all 5 scores showed the worst calibration results among white women (online supplemental figure 4).

The use of PCE African American equation for risk estimation in Brazilian Blacks and 'Pardos' showed worse calibration compared with the use of the white-American



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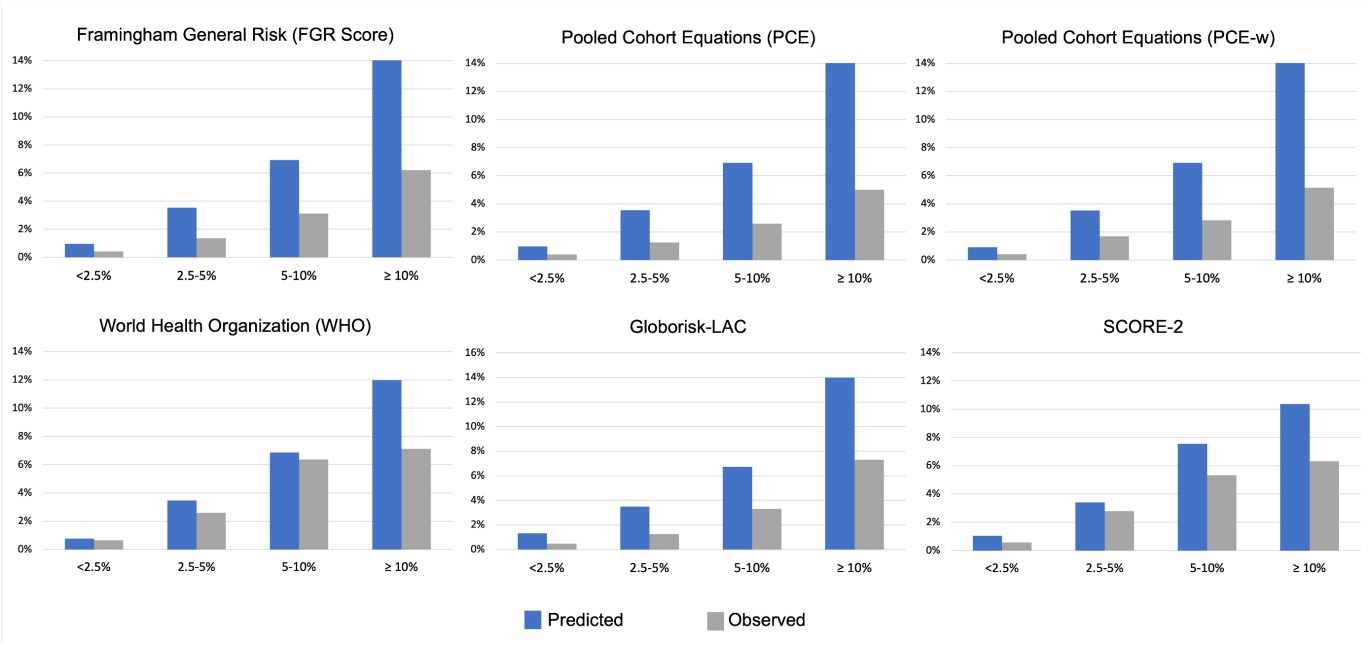


**Figure 4** Calibration for the FGR, PCE, WHO CVD score, Globorisk-LAC and SCORE-2 for the overall study population by risk categories. ELSA-Brasil (2008–2013). N=12 155. CVD, cardiovascular disease.

equation in this population (men: P/O ratio 3.97 95% CI 2.94 to 5.00 vs 2.38 95% CI 1.37 to 3.39 and women: P/O ratio 3.70 95% CI 2.74 to 4.66 vs 2.81 95% CI 1.68 to 3.94, respectively) (online supplemental figure 5).

The sensitivity analysis, limited to ELSA participants that met the criteria for the use of CVD risk score to guide statin therapy (not taking statins at baseline with an LDL-c between 70 and 189 mg/dL and without DM), demonstrated similar discrimination results (AUC between 0.73, 95% CI 0.63 to 0.78 and 0.78, 95% CI 0.70 to 0.82). There was continued overestimation in this population, apart from SCORE-2, which underestimated the risk for those with risk ≥5% and for black/'Pardo' women. All results for the sensitivity analysis are summarised in online supplemental table 4.

The stratified analysis by education showed similar discrimination results but better calibration among individuals with lower education (middle school) compared with those with higher education backgrounds (college) for the FGR, PCE and Globorisk-LAC. In the population with lower educational attainment, WHO and SCORE-2 underestimated the CVD risk (online supplemental table 5).

## DISCUSSION

To our knowledge, this is the first large cohort study to assess the performance of CVD risk scores in Brazil and the first to test calibration and discrimination of widely used CVD predictive scores in a South American country. In the large prospective ELSA-Brasil, while current scores had cardiovascular risk discrimination consistent with the development cohorts, the models performed poorly for many key demographic groups. Specifically, models performed poorly for white women, representing nearly half of all women in ELSA Brasil. Moreover, despite their purported use as out-of-box calculators, all risk scores overestimated the CVD risk nearly twofold throughout the risk continuum, with WHO score recalibrated for Tropical Americas closest aligning between predicted risk and observed events. These differences persisted in the subpopulation where CVD risk scores are used to guide statin therapy.

Estimating the absolute cardiovascular risk is the foundation of national guidelines for CVD prevention, defining blood pressure targets and optimal utilisation of cholesterol-lowering medication.[17 24] While many studies assessing the performance of different CVD risk scores have suggested risk overestimation,[25–27] the degree of overprediction in ELSA-Brasil is substantially higher. Brazil boasts significant racial and demographic diversity, setting its population apart from the typically less diverse, high-income cohorts used to derive cardiovascular risk scores.[9 28] Genetic variations, dietary and lifestyle habits, and differences in environmental exposures contribute to variations in susceptibility to cardiovascular events.[29 30] The downstream cardiovascular outcomes might also be affected by the ubiquitous public health access granted by Brazil's universal health system.[31] Despite challenges in quality metrics and coordination between levels of care, the system has achieved significant gains over the past 30 years enhancing coverage and access to healthcare services and consequently yielding improved health outcomes overall.[31 32] The disparity in the relevance of risk factors between the cohorts used to formulate these scores and contemporary populations in developing countries may underlie the inadequate estimation of the



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impact of individual risk factors incorporated into the models.[33 34] Moreover, even recently developed scores are rooted in older cohorts that exhibit fundamental differences from the Brazilian population,[8 35] differences that can limit adequate risk calibration and hinder the effectiveness of recalibration.[18 36]

We observed a higher overestimation of risk when applying the PCE African American equation to black and 'Pardo' Brazilians compared with the use of the white-American equation in the same population. A recent study comparing estimates for 10-year CVD risk in Black and White individuals with identical risk profiles showed that the PCE might yield significantly different CVD risk estimates for these two racial groups. They examined these aspects through computer simulations and in two distinct community-based samples.[37] Similar Yadlowski *et al* showed that PCE had risk estimates varying from 80% lower to more than 500% higher for black adults compared with white adults, with otherwise identical risk factors.[38] These findings hold significant clinical importance, particularly in a country like Brazil where there is a large mixed-race population. Discrepancies in risk assessment based on race could potentially lead to inaccurate clinical recommendations for CVD prevention.[39] Efforts to address systemic racism in medicine have led to a reevaluation of race modifiers in medical algorithms, such as those for estimating glomerular filtration rate (eGFR),[40] with studies indicating that racial disparities in eGFR prevalence may be predominantly attributed to health inequalities, discouraging the application of race corrections.[41]

Our study has several key strengths that enhance the reliability and significance of our results. First, the data from this investigation present new findings from the Brazilian population, highlighting the relevance of our research in an understudied population subset. Second, the study benefits from a large sample size, enabling robust statistical analyses and reliable assessments of risk scores' performance. The events collection and adjudication process in the ELSA study is rigorous and includes successfully obtaining medical records and classifying 87% of hospital and outpatient reports of CVD events, and achieving more than 90% of follow-up telephone interviews of living participants. Finally, the results were robust in sensitivity analyses that explicitly focused on populations without any risk modification with lipid-lowering therapy at baseline, suggesting that the patterns observed are not driven by differences in baseline risk management.

It is important to acknowledge some limitations. One notable limitation is the shorter follow-up duration, with a median follow-up of 4 years. The shorter follow-up may have influenced our ability to capture long-term changes in risk profiles, considering the disproportionate risk increase during middle age (50–70 years), which is the mean age of our population. A more extended follow-up would have provided a more comprehensive understanding of risk trends. However, we observed a linear cumulative risk of CVD during the 5-year follow-up, which supports the extrapolation of our results to 10-year risk. Another key consideration is that the ELSA-Brasil cohort comprises individuals enrolled from the community and does not represent a high-risk group. However, the observed event rates in ELSA-Brasil over the follow-up period are consistent with those in similar studies.[25] Despite focusing exclusively on individuals in the primary prevention of CVD, the cohort includes a significant proportion of higher-risk individuals, with 14% of the population having a CVD risk greater than 10% according to PCE. The ELSA-Brasil study comprises adults from six diverse regions of Brazil, representing a spectrum of socioeconomic and educational backgrounds.

Notably, 12.5% of Brazilian adults are government employees, representing a substantial proportion of the population. These employees span a broad socioeconomic spectrum and are not limited to professional staff at these institutions. This diversity is reflected in the educational and socioeconomic distribution captured in ELSA-Brasil, where 19% were manual workers, 46% were in a middle socio-occupational category, and 38% were in a higher socio-occupational category, representing managerial or professional occupations.[42] Similarly, 12% were in the low-income category, and nearly 40% were in the middle-income category. Moreover, less than half had a university degree, with 34% with a high school education and 10% with an elementary school education or less. National assessments indicate that the lower and middle classes represent 20% and 65% of the population, respectively.[42] Therefore, while like other cohort studies, ELSA-Brasil does not include a fully representative sample of Brazilian adults, it includes a wide range of socioeconomic, educational and occupational classes. To further address the potential limitations in generalisability, we identified persistent overprediction of risk across educational categories, arguing against differences between individuals in our study cohort and the general population.

In conclusion, in this large prospective cohort study from Brazil, we found that widely accepted CVD risk scores overestimate risk by over twofold and particularly do not adequately define risk for Brazilian women and other demographic groups. The recalibrated WHO score for Tropical Americas was best calibrated but still had performance issues. Our study highlights the value of risk stratification strategies tailored to the unique populations and risks of LMICs.

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**Competing interests** RK is an Associate Editor at JAMA. In addition to the funding listed above, he also receives research support, through Yale, from Bristol-Myers Squibb, Novo Nordisk and BridgeBio. He is a coinventor of Pending Patent Applications WO2023230345A1, US20220336048A1, 63/346 610, 63/484 426, 63/508 315, 63/580 137, 63/606 203, 63/619 241 and 63/562 335, unrelated to current work. He is also a co-founder of Evidence2Health and Ensight-AI, both representing precision health platforms to improve evidence-based cardiovascular care. The other authors declare no conflicts of interest.

**Patient consent for publication** Not applicable.

**Ethics approval** This study involves human participants and the ELSA-Brasil was approved by the Research Ethics Committee of all participating institutions and by the National Research Ethics Commission (CONEP 976/2006) from the Brazilian Ministry of Health. Participants gave informed consent to participate in the study before taking part.

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**Data availability statement** Data are available on reasonable request. Access to the database is currently restricted from public use. However, the data underlying this article will be shared on reasonable request to the corresponding author and to the ELSA-Brasil administration using the provided link http://www.elsa.org.br/contatos.html.

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