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Supplementary Material

Performance of Contemporary Cardiovascular Risk Stratification Scores in Brazil: An Evaluation in the ELSA-Brasil Study

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SUMMARY

1. Method used to lower individual 10-year risk to correspond to lower length of follow-up:

For each subject with <10 years of follow-up, including those who died, we lowered their 10-year risk estimate to correspond to their length of follow-up using an exponential survival function to scale the risk score. If A10 denotes the 10-year estimation according to the risk score, then the 1-year risk estimation is A1 = −ln(1−A10)/10. So, for a person with 4.2 years of follow-up, A4.2 = 1 − exp(−A1 × 4.2).

$$1\ YEAR\ RISK = -\frac{\ln(1 - 10\ YEAR\ RISK)}{10}$$

$$4\ YEAR\ RISK = 1 - \exp(-1\ YEAR\ RISK \times 4)$$

2. ELSA- Brasil definition of diabetes mellitus, systolic blood pressure, total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and body mass index:

Diabetes Mellitus was defined as the report of a medical diagnosis, report of using hypoglycemic agents or insulin, fasting serum glucose ≥126 mg/dL, glycated hemoglobin (HbA1c) level ≥ 6.5%, or a 2-hour oral glucose tolerance test ≥ 200 mg/dL measured twice. Systolic blood pressure was measured at the right arm after 5 minutes of rest, with the participant sitting in a quiet, temperature-controlled room (20-24°C) using a validated device (Omron HEM 705). Three measurements were taken at intervals of 1 minute each. The mean of the second and third measures was used as casual SBP. Total cholesterol and high-density lipoprotein cholesterol were determined by the enzymatic colorimetric method. Low-density lipoprotein cholesterol was calculated by the Friedewald equation or directly with triglyceride > 400 mg/dL. Body mass index (BMI) was calculated by anthropometric measurements and classified as normal weight (≤ 24.9 kg/m2), overweight (between 25 and 29.9 kg/m2), or obesity (≥30 kg/m2).

Supplementary Table 1: Age, laboratory parameters for risk score calculation, risk factors included in the model, outcomes measured, and risk classification for each CVD risk score included in the study.

CVD Risk Score	Age group	Lab. Parameters	Risk factors	10-year outcomes	Risk Classification
FGR	40-80	SBP: 90-200mmHg TC: 130-320mg/dL HDL-C: 20-100mg/dL	Age, smoking, SBP, history of DM, hypertension treatment and TC.	Coronary, cerebrovascular, and peripheral arterial disease and HF	≥ 20.0% (high)
PCE	40-79	SBP: 90-200mmHg TC: 130-320mg/dL HDL-C: 20-100mg/dL	Age, sex, smoking status, SBP, history of DM and TC.	Fatal CHD; fatal or nonfatal MI or stroke	≤5% (low) 5-7.5% (borderline) 7.5-20% (intermediate) ≥ 20.0% (high)
WHO	40-80	SBP: 90-200mmHg TC: 140-300mg/dL HDL-C: 20-100mg/dL	Age, sex, smoking status, SBP, history of DM and TC.	Fatal and non-fatal MI or stroke	≤5% (low) 5-10% (moderate) 10-20% (high) ≥ 20.0% (very high)
Globorisk-LAC	40-75	SBP: 70−270mmHg TC: 1.75−20mmol/l BMI: 10−80kg/m2	Age, sex, smoking status, SBP, DM, BMI	Fatal/non-fatal CHD and stroke	≤5% (low) 5-10% (moderate) 10-20% (high) ≥ 20.0% (very high)
SCORE2	40-69	SBP: 90-200mmHg TC: 130-320mg/dL HDL-C: 20-100mg/dL	Age, sex, smoking status, history of DM, SBP, TC and HDL-c	Fatal and non-fatal MI or stroke	≤5% (low) 5-10% (moderate) ≥ 10.0% (high)

SBP: systolic blood pressure; DM: diabetes mellitus; TC: total cholesterol; HDL-C: high-density lipoprotein cholesterol; MI: myocardial infarction; CHD: coronary heart disease; BMI: body mass index.

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Supplementary Table 2: Baseline characteristics stratified by race and sex. ELSA-Brasil (2008), N=12,155.

	White		"Pardo"		Black		Other	
	Men	Women	Men	Women	Men	Women	Men	Women
N	2868	3460	1615	1803	764	1213	186	246
Age, mean (SD)	53.7 (8.7)	53.4 (8.2)	51.8 (7.7)	52.6 (7.7)	52.5 (7.9)	52.4 (7.8)	54.9 (8.8)	54.8 (8.1)
Education ≤Middle School, N (%)	286 (10.0)	173 (5.0)	357 (22.1)	221 (12.3)	238 (31.2)	198 (16.3)	49 (26.3)	24 (9.8)
Smoking, N (%)	377 (13.1)	444 (12.8)	265 (16.4)	213 (11.8)	133 (17.4)	169 (13.9)	32 (17.2)	21 (8.5)
Diabetes, N (%)	478 (16.7)	356 (10.3)	325 (20.1)	247 (13.7)	199 (26.0)	253 (20.9)	46 (24.7)	41 (16.7)
Statin Use, N (%)	378 (13.2)	472 (13.6)	106 (6.6)	178 (9.9)	51 (6.7)	131 (10.8)	21 (11.3)	49 (19.9)
Antihypertensive, N (%)	777 (27.1)	773 (22.3)	412 (25.5)	508 (28.2)	255 (33.4)	474 (39.1)	49 (26.3)	72 (29.3)
SBP mmHg, mean (SD)	123.2 (15.4)	115.5 (15.5)	127.3 (17.0)	119.2 (16.8)	132.4 (18.9)	123.4 (18.3)	126.2 (17.7)	117.3 (16.8)
BMI Kg/m^2, mean (SD)	26.9 (4.2)	26.5 (4.9)	26.7 (4.2)	27.3 (4.8)	27.3 (4.4)	28.4 (5.5)	26.4 (3.9)	25.7 (4.3)
Total Cholesterol mg/dL, mean (SD)	199.2 (41.1)	204.6 (38.2)	201.0 (42.4)	206.3 (40.2)	204.0 (44.8)	200.7 (41.4)	203.5 (43.8)	204.7 (37.7)
HDL-Cholesterol mg/dL, mean (SD)	48.0 (10.5)	58.7 (13.3)	48.2 (11.5)	57.2 (13.0)	51.3 (13.0)	58.4 (13.4)	50.4 (12.8)	58.8 (13.5)
Predicted Risk Across Scores								
FGR 10-year risk, median [IQR]	5.74 [2.72, 11.71]	1.70 [0.76, 3.98]	7.20 [4.46, 12.30]	2.48 [0.89, 6.44]	8.79 [5.01, 15.36]	2.89 [0.94, 8.23]	8.30 [3.54, 14.78]	2.02 [0.89, 4.49]
PCE-race specific 10-year risk, median [IQR]	5.75 [2.72, 11.64]	1.70 [0.76, 3.94]	7.20 [4.46, 12.26]	2.46 [0.89, 6.44]	8.81 [4.99, 15.19]	2.90 [0.94, 8.23]	8.30 [3.54, 14.09]	2.02 [0.89, 4.49]
PCE-White American 10-year risk, median [IQR]	5.75 [2.72, 11.64]	1.70 [0.76, 3.94]	5.37 [2.55, 10.53]	1.76 [0.80, 4.06]	6.37 [2.82, 12.60]	1.95 [0.82, 4.88]	8.30 [3.54, 14.09]	2.02 [0.89, 4.49]
WHO 10-year risk, median [IQR]	3.98 [2.48, 6.35]	2.58 [1.59, 4.09]	3.76 [2.48, 5.82]	2.54 [1.65, 4.02]	4.36 [2.68, 6.76]	2.72 [1.73, 4.40]	4.72 [3.17, 6.84]	2.83 [1.84, 4.38]
Globorisk-LAC 10-year risk, median [IQR]	5.80 [3.80, 9.09]	3.17 [2.00, 5.23]	6.03 [3.84, 9.99]	3.39 [2.13, 5.79]	7.45 [4.45, 12.38]	3.76 [2.22, 6.94]	7.27 [4.39, 10.90]	3.68 [2.23, 6.19]

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SCORE2 low-risk 10-year risk, median [IQR]	3.85 [2.39, 6.29]	1.93 [1.08, 3.41]	3.80 [2.33, 6.10]	1.98 [1.14, 3.52]	4.30 [2.54, 7.01]	2.10 [1.15, 4.02]	4.86 [2.83, 7.08]	2.26 [1.23, 3.75]
CVD Events, N (%)	47 (1.6)	16 (0.5)	29 (1.8)	13 (0.7)	22 (2.9)	18 (1.5)	1 (0.5)	3 (1.2)

SD. Standard Deviation; SBP. Systolic Blood Pressure; BMI. Body Mass Index; HDL. High-density Lipoprotein Cholesterol; IQR. interquartile range. FGR. Framingham General Risk. PCE. Pooled Cohort Equations. PCE-w. WHO. World Health Organization recalibrated score.

Supplementary Table 3: Frequency of cardiovascular events, cumulative incidences, and incidence rates in the total study population and stratified by race. ELSA-Brasil (2008-2013). N= 12,155.

	Total	White	"Pardo"	Black	Other
Population, N	12155	6328	3418	1977	432
Events, n	149	63	42	40	4
Non-fatal MI, N (%)	47 (31.5)	28(44.4)	15(35.7)	7(17.5)	2(50.0)
Non-fatal stroke, N (%)	49 (32.9)	19(30.2)	17(40.5)	18(45.0)	2(50.0)
Heart Failure, N (%)	24 (16.1)	10(15.9)	7(16.7)	10(25.0)	0
Peripheral Arterial Disease, N (%)	11 (7.4)	3(4.8)	6(14.3)	4(10.0)	0
Fatal CVD events, N (%)	33 (22.1)	9(14.3)	12(28.6)	12(30.0)	0
Cumulative Incidence CVD Events* (%)	149 (1.23)	63 (1.0)	42 (1.2)	40 (2.2)	4 (0.9)
Incidence rate/1000 person-years (95%CI)	2.56 (2.16-3.03)	2.17 (1.68-2.80)	2.57 (1.87-3.53)	3.88 (2.76-5.46)	2.11 (0.79-5.62)

*Number of events (coronary heart disease death, nonfatal myocardial infarction, or fatal or nonfatal ischemic stroke) divided by number of individuals. Differences in sums are due to individuals presenting multiple events.

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Supplementary Table 4: Sensitivity analysis limited to the population not taking statins, without Diabetes Mellitus and LDL-C between 70-190mg/dL. ELSA-Brasil (2008-2013).

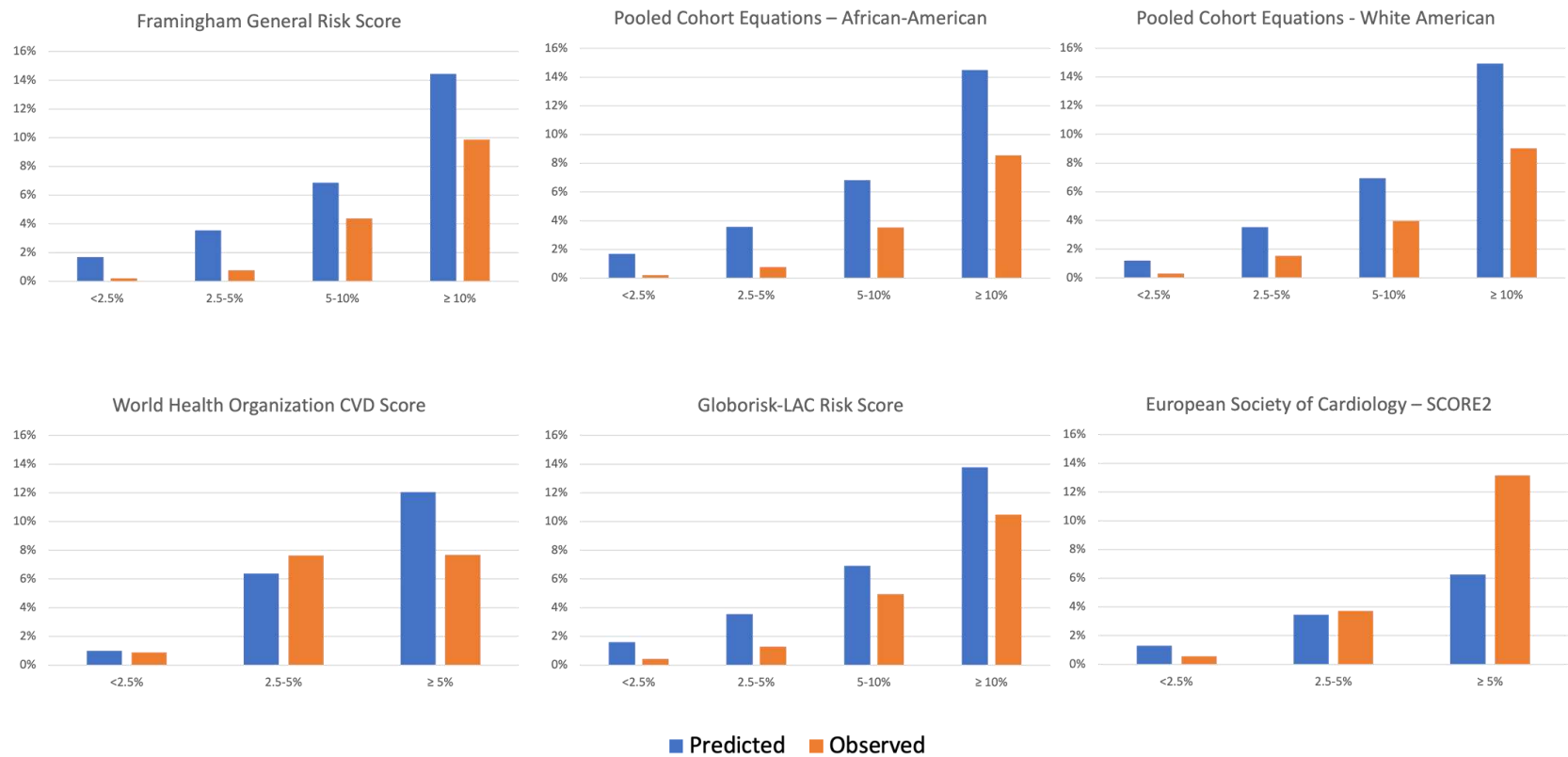|		Total Population (N = 8,537)	MEN (N = 3,686)		WOMEN (N = 4,851)	
			White	Black/"Pardo"	White	Black/"Pardo"
AUC (95% CI)	**FGR**	0.76 (0.70-0.82)	0.79 (0.71-0.86)	0.85 (0.77-0.93)	0.59 (0.43-0.74)	0.76 (0.66-0.86)
	PCE	0.74 (0.68-0.81)	0.79 (0.70-0.87)	0.85 (0.76-0.93)	0.59 (0.43-0.74)	0.73 (0.62-0.84)
	PCE-w	0.74 (0.68-0.80)	0.79 (0.71-0.86)	0.83 (0.73-0.93)	0.59 (0.42-0.75)	0.72 (0.60-0.84)
	WHO	0.74 (0.67-0.80)	0.77 (0.69-0.86)	0.81 (0.70-0.93)	0.55 (0.37-0.73)	0.74 (0.63-0.86)
	Globorisk-LAC	0.73 (0.67-0.79)	0.73 (0.63-0.82)	0.79 (0.67-0.91)	0.59 (0.71-0.77)	0.76 (0.64-0.88)
	SCORE2	0.74 (0.67-0.80)	0.80 (0.72-0.87)	0.83 (0.72-0.93)	0.55 (0.36-0.73)	0.73 (0.62-0.85)
P/O Ratio (95% CI)	**FGR**	2.13 (1.78-2.48)	3.66 (2.96-4.36)	3.26 (2.76-3.76)	2.58 (2.19-2.97)	1.54 (1.29-1.79)
	PCE	2.31 (1.92-2.70)	3.47 (2.97-3.97)	5.73 (5.03-6.43)	2.31 (1.92-2.70)	2.33 (1.94-2.72)
	PCE-w	2.00 (1.64-2.36)	3.47 (2.97-3.97)	3.28 (2.79-3.77)	2.31 (1.92-2.70)	1.27 (1.05-1.49)
	WHO	1.96 (1.63-2.29)	1.85 (1.53-2.17)	1.32 (0.96-1.68)*	1.90 (1.33-2.47)	1.25 (0.87-1.63)*
	Globorisk-LAC	2.71 (2.22-3.20)	1.57 (1.19-1.95)	1.54 (1.29-1.79)	3.29 (2.79-3.79)	1.57 (1.31-1.83)
	SCORE2	1.78 (1.48-2.08)	1.41 (1.17-1.65)	1.15 (0.95-1.35)*	1.59 (1.32-1.86)	0.68 (0.56-0.80)

FGR. Framingham General Risk. PCE. Pooled Cohort Equations. PCE-w. Pooled Cohort White-American Equation. WHO. World Health Organization recalibrated score. SCORE2. score from the European Society of Cardiology (2021). P/O. Predicted to Observed. AUC. Area under the Receiver Operating Characteristic Curve. 95% CI. Confidence intervals at 95%. *Groenersby-Borgman χ2<20 and p>0.05.

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Supplementary Table 5: Discrimination and Calibration of Framingham General Risk, Pooled Cohort Equations, World Health Organization, Globorisk-LAC and SCORE2 for the total study population stratified by education. ELSA-Brasil (2008-2013).

		College	High School	Middle School
AUC	**FGR**	0.75 (0.67-0.83)	0.77 (0.71-0.82)	0.74 (0.66-0.82)
	PCE	0.73 (0.64-0.81)	0.77 (0.70-0.83)	0.72 (0.64-0.81)
	PCE-w	0.72 (0.63-0.80)	0.78 (0.72-0.84)	0.73 (0.64-0.82)
	WHO	0.71 (0.62-0.80)	0.77 (0.70-0.83)	0.74 (0.65-0.83)
	Globorisk-LAC	0.71 (0.62-0.80)	0.76 (0.69-0.82)	0.73 (0.64-0.82)
	SCORE2	0.72 (0.63-0.81)	0.77 (0.71-0.83)	0.75 (0.66-0.84)
P/O Ratio	**FGR**	3.21 (2.73-3.69)	2.09 (1.72-2.46)	2.08 (1.71-2.45)
	PCE	3.72 (3.19-4.25)	2.61 (2.17-3.05)	2.20 (1.82-2.58)
	PCE-w	3.43 (2.95-3.91)	2.20 (1.82-2.58)	1.75 (1.44-2.06)
	WHO	1.69 (1.39-1.99)	1.07 (0.88-1.26)*	0.84 (0.69-0.99)
	Globorisk-LAC	3.10 (2.65-3.55)	2.37 (1.96-2.78)	1.88 (1.55-2.21)
	SCORE2	1.34 (1.11-1.57)	0.88 (0.73-1.03)*	0.72 (0.59-0.85)

FGR. Framingham General Risk. PCE. Pooled Cohort Equations. PCE-w. Pooled Cohort White-American Equation. WHO. World Health Organization recalibrated score. SCORE2. score from the European Society of Cardiology (2021). P/O. Predicted to Observed. AUC. Area under the Receiver Operating Characteristic Curve. 95% CI. Confidence intervals at 95%. *Groenersby-Borgman $\chi 2 < 20$ and $p > 0.05$.
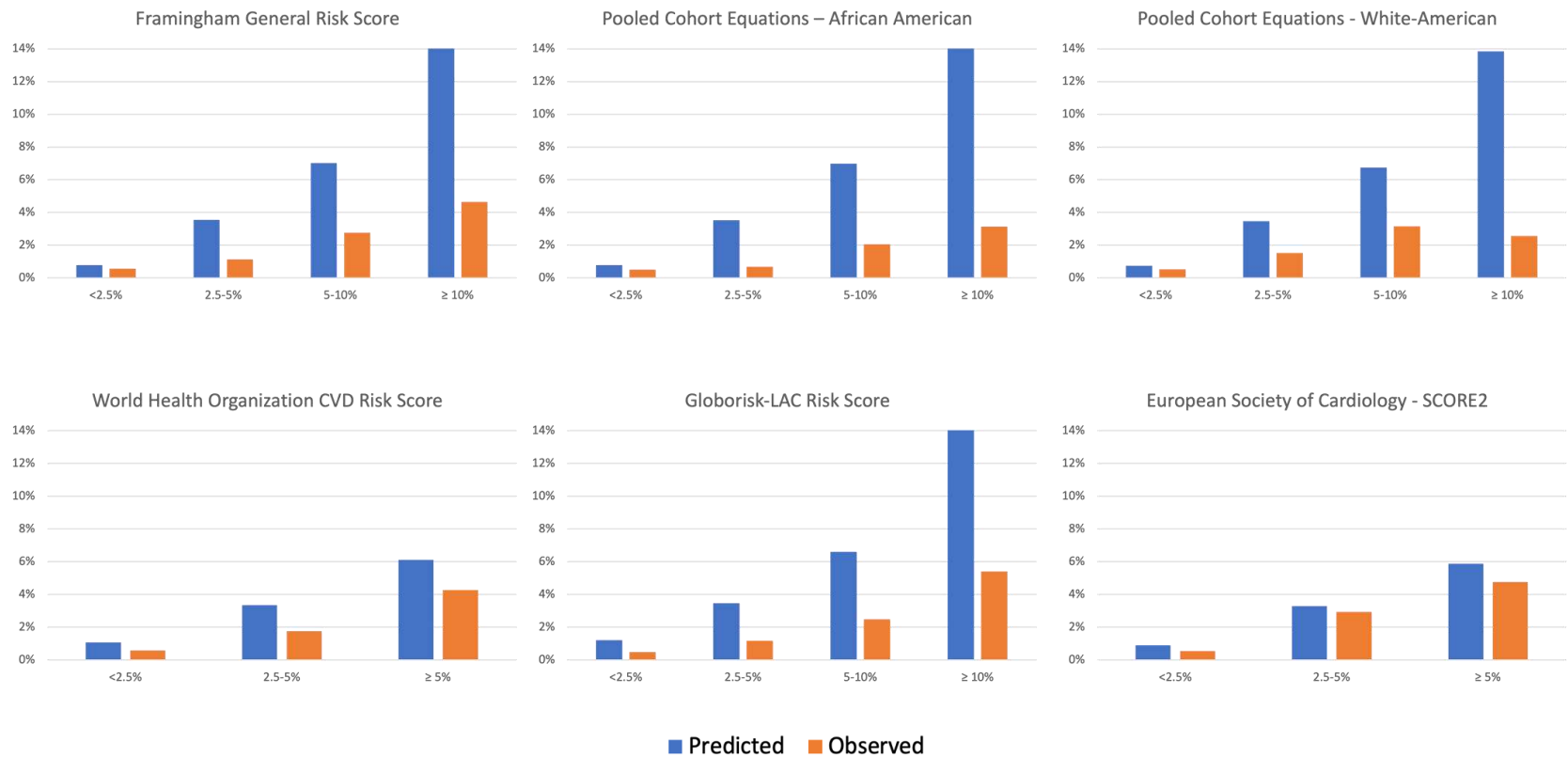
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Supplementary Figure 1: Calibration for the Framingham General Risk, Pooled Cohort Equations, World Health Organization CVD score, Globorisk-LAC and SCORE2 for Black and "Pardo" men by risk categories. ELSA-Brasil (2008-2013). N=2,379.

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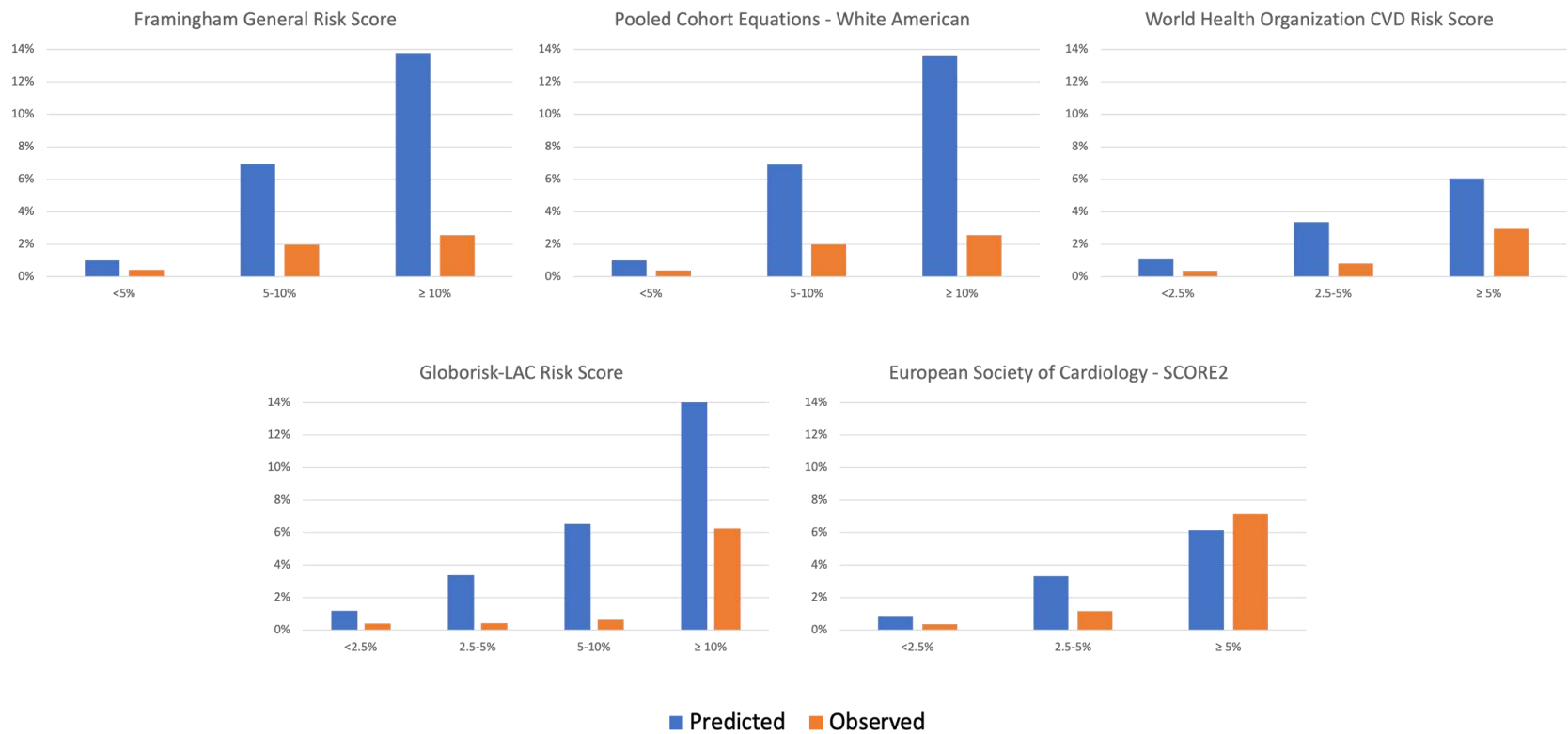
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Supplementary Figure 2: Calibration for the Framingham General Risk, Pooled Cohort Equations, World Health Organization CVD score, Globorisk-LAC and SCORE2 for White men by risk categories. ELSA-Brasil (2008-2013). N=2,868.

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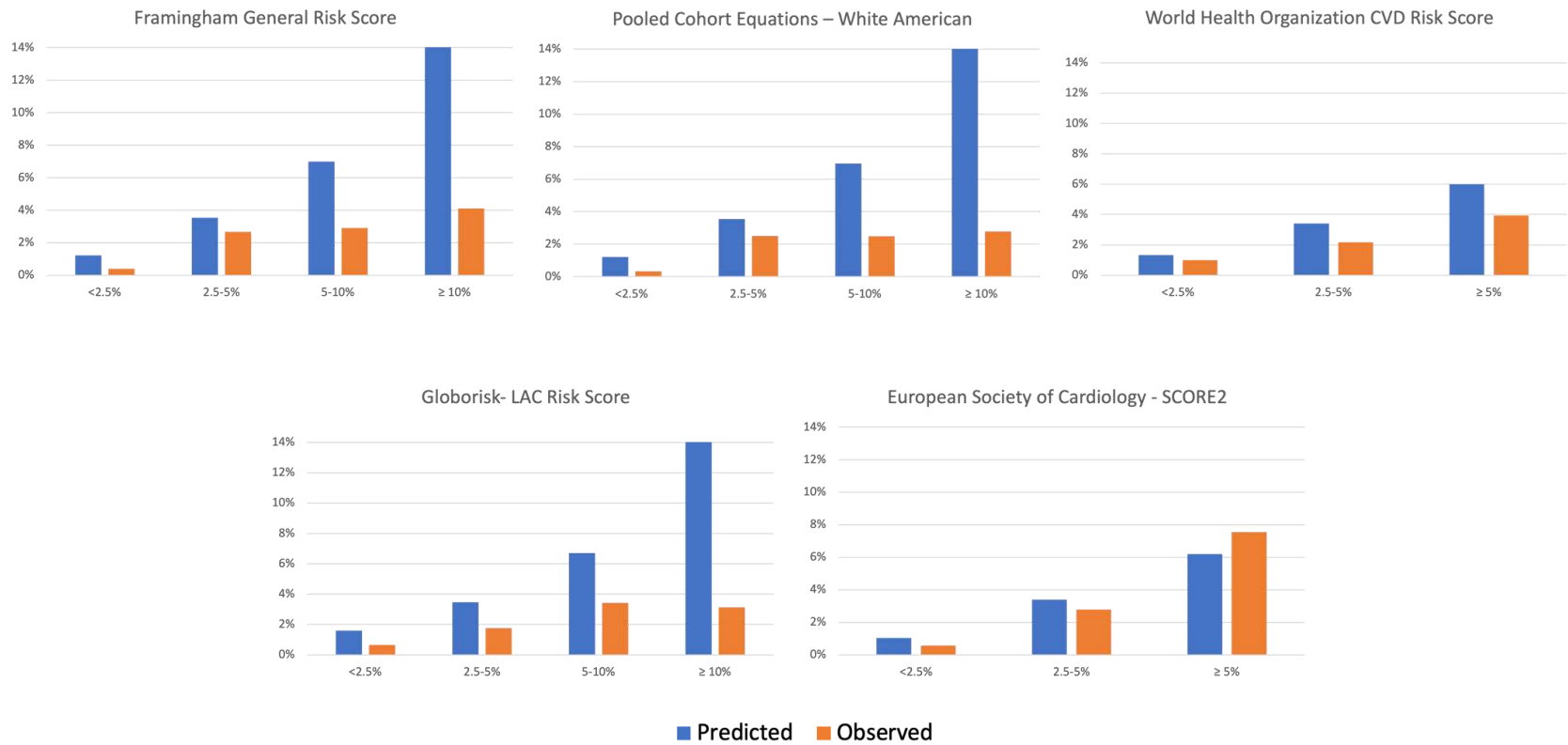
Supplementary Figure 3: Calibration for the Framingham General Risk, Pooled Cohort Equations, World Health Organization CVD score, Globorisk-LAC and SCORE2 for Black and Pardo women by risk categories. ELSA-Brasil (2008-2013). N=3,016.

Supplementary Figure 4: Calibration for the Framingham General Risk, Pooled Cohort Equations, World Health Organization CVD score, Globorisk-LAC and SCORE2 for White women by risk categories. ELSA-Brasil (2008-2013). N= 3,460.

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Supplementary Figure 5: Calibration of PCE-African American vs. PCE White-American equations for Black/"Pardo" men and women. ELSA-Brasil (2008-2013)
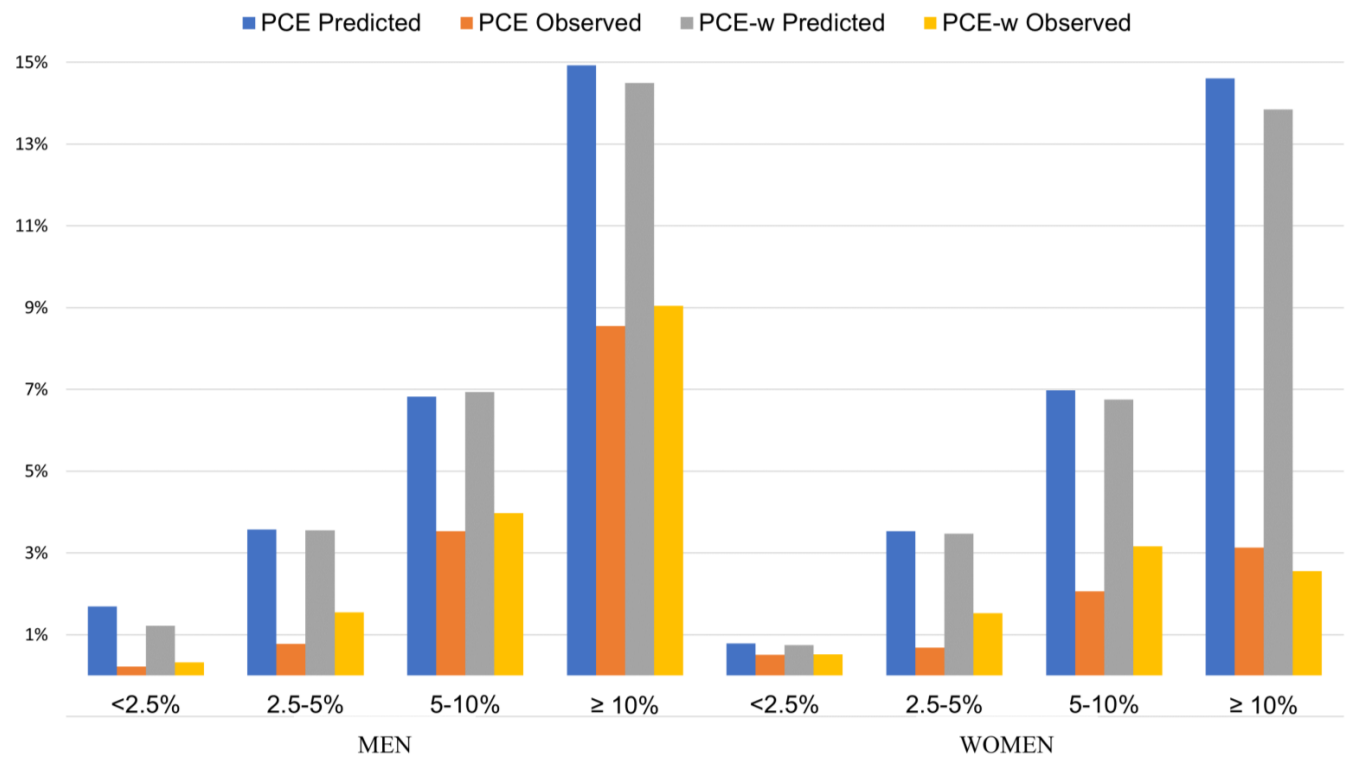
PCE: Pooled Cohort Equations. PCE-w: Pooled Cohort Equations White-American.

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