Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Genetically Informed Ancestry (GIA) and HARE Classification in the Million Veteran Program (MVP)

		Genetically Informed Ancestry (GIA)					HARE total (not NA)
		AFR	EAS	EUR	AMR	NA	
Harmonized Ancestry and Race/Ethnicity (HARE)	Non-Hispanic Black	**122,114**	0	0	181	*825*	**122,295**
	Asian	2	**6,684**	32	25	*1,586*	**6,743**
	Non-Hispanic White	3	1	**456,030**	5,650	*3,277*	**461,684**
	Hispanic	190	28	485	**51,195**	*285*	**51,898**
	NA	*1,019*	*363*	*1,173*	*4,060*	*3,374*	
GIA Total (not NA)		**122,309**	**6,713**	**456,547**	**57,051**		

* GIA super populations: AFR = African, EAS = East Asian, EUR = European, AMR = Ad Mixed American

eTable 1 caption: Agreement between HARE and GIA classifications were very high (>99%) for all ancestries except the AMR (Ad Mixed American) super population. 5,650 participants from the AMR-ancestry were classified as non-Hispanic White by the HARE algorithm, and a further 4,060 were excluded due to disagreement between self-identified race/ethnicity and GIA.

eTable 2. Electronic Health Record Codes (*ICD-9*, *ICD-10*, CPT/HCPCS) for ASCVD Outcomes

Outcome	ICD-9 Codes	ICD-10 Codes	CPT/HCPCS Codes
Composite ASCVD	Myocardial Infarction, Ischemic Stroke, or ASCVD Death Codes		
Composite ASCVD and Revascularization	Composite ASCVD, Percutaneous Coronary Intervention, and Coronary Artery Bypass Graft		
Myocardial Infarction	410, 411.0, I21, I22	410, 411.0, I21, I22	
Ischemic Stroke	433.x1, 434 (excluding 434.x0), 436, 437.0, 437.6	I63.xx9, I63.20, I63.22, I63.30, I63.40, I63.50, I63.59, I67.2, I67.6, I67.89	
ASCVD Death		I10, I11, I13, I16, I20-I25, I46, I63, I67, I70, I74, I75, G45	
Percutaneous Coronary Intervention			C9602-C9608, 92920-92921, 92924-92925, 92933-92934, 92937, 92995, 92966, 93540, 93564, 93570, 92928, 92929
Coronary Artery Bypass Graft			C9600-C9608, G8574, 33510-33523, 33533-33536, 33572, excluding 3351F, 3352F, 3353F, 33515

eTable 3. Baseline Characteristics and ASCVD Events Stratified by Sex

	Number (%)		
Baseline Characteristic	**Total cohort (N = 79,151)**	**Male (n = 68,503)**	**Female (n = 10,648)**
Follow-up, years, median (5th-95th percentile)	4.3 (0.7-6.9)	4.3 (0.7-6.9)	4.0 (0.5-6.8)
Age, mean (SD), y	57.8 (13.7)	59.3 (13.3)	48.6 (12.6)
Cardiovascular Risk Factors			
Total cholesterol, mean (SD), mg/dL	157.8 (40.6)	157.3 (40.3)	161.4 (42.3)
HDL-C, mean (SD), mg/dL	49.8 (17)	48.6 (16.6)	57.4 (17.4)
LDL-C, mean (SD), mg/dL	109.4 (33.3)	108.6 (33.2)	114.4 (34.1)
Systolic blood pressure, mean (SD), mm Hg	131.3 (13.4)	132.1 (13.2)	125.7 (13.1)
Current smoker	8,435 (10.7)	7,530 (11)	905 (8.5)
Former smoker	47,670 (60.2)	42,705 (62.3)	4,965 (46.6)
Never smoker	23,046 (29.1)	18,268 (26.7)	4,778 (44.9)
Diabetes	17,177 (21.7)	15,643 (22.8)	1,534 (14.4)
Medications			
Blood pressure treatment	36,673 (46.3)	33,365 (48.7)	3,308 (31.1)
No. of events (2011 - 2018)			
Composite ASCVD (%)	5,485 (6.9)	5,175 (7.6)	310 (2.9)
Composite ASCVD and revascularization (%)	6,628 (8.4)	6,265 (9.1)	363 (3.4)
ASCVD Death (%)	867 (1.1)	836 (1.2)	31 (0.3)
Acute ischemic stroke (%)	1,933 (2.4)	1,781 (2.6)	152 (1.4)
Myocardial Infarction (%)	3,186 (4)	3,036 (4.4)	150 (1.4)
Crude Incidence rate / 10k Person Years (2011 - 2018)			
Composite ASCVD (95% CI)	177.7 (173.0-182.5)	193.0 (187.8-198.3)	76.4 (68.2-85.4)
Composite ASCVD and revascularization (95% CI)	216.6 (211.4-221.9)	235.9 (230.1-241.8)	89.7 (80.7-99.5)
ASCVD Death (95% CI)	27.0 (25.2-28.8)	29.9 (27.9-32.0)	7.5 (5.1-10.6)
Acute ischemic stroke (95% CI)	61.0 (58.3-63.8)	64.5 (61.5-67.6)	37.2 (31.5-43.6)
Myocardial Infarction (95% CI)	100.9 (97.4-104.4)	110.5 (106.6-114.5)	36.5 (30.9-42.9)

eTable 4. Hazard Ratios for MVP Incident ASCVD Events for Low Traditional and Polygenic Risk Scores

High PRS definition	Hazard Ratio (95% CI)					
	Non-Hispanic White		Non-Hispanic Black		Hispanic	
Composite ASCVD Events	Polygenic Risk Score	Traditional Risk Score	Polygenic Risk Score	Traditional Risk Score	Polygenic Risk Score	Traditional Risk Score
Continuous per SD reduction	0.80 (0.77, 0.82)	0.48 (0.46, 0.50)	0.86 (0.81, 0.91)	0.45 (0.42, 0.48)	0.79 (0.72, 0.88)	0.35 (0.32, 0.40)
Bottom 20%*	0.75 (0.67, 0.84)	0.16 (0.13, 0.20)	0.95 (0.76, 1.19)	0.17 (0.12, 0.25)	0.74 (0.50, 1.10)	N/A
Bottom 10%	0.66 (0.58, 0.76)	0.10 (0.07, 0.14)	0.90 (0.68, 1.18)	N/A	0.76 (0.47, 1.24)	N/A
Bottom 5%	0.64 (0.54, 0.76)	N/A	0.79 (0.55, 1.15)	N/A	N/A	N/A
Bottom 1%	0.61 (0.42, 0.86)	N/A	N/A	N/A	N/A	N/A
Bottom 0.5%	N/A**	N/A	N/A	N/A	N/A	N/A
Myocardial Infarction						
Continuous per SD reduction	0.75 (0.73, 0.78)	0.52 (0.50, 0.54)	0.88 (0.82, 0.94)	0.47 (0.44, 0.51)	0.77 (0.68, 0.87)	0.36 (0.31, 0.41)
Bottom 20%	0.70 (0.61, 0.81)	0.19 (0.15, 0.24)	0.89 (0.67, 1.17)	0.23 (0.15, 0.35)	0.40 (0.25, 0.66)	N/A
Bottom 10%	0.63 (0.53, 0.75)	N/A	0.88 (0.63, 1.23)	N/A	0.52 (0.30, 0.91)	N/A
Bottom 5%	0.60 (0.48, 0.75)	N/A	0.62 (0.39, 0.99)	N/A	N/A	N/A
Bottom 1%	N/A	N/A	N/A	N/A	N/A	N/A
Bottom 0.5%	N/A	N/A	N/A	N/A	N/A	N/A
Ischemic Stroke						
Continuous per SD reduction	0.89 (0.84, 0.94)	0.48 (0.45, 0.52)	0.87 (0.78, 0.96)	0.43 (0.39, 0.48)	0.85 (0.69, 1.04)	0.36 (0.29, 0.44)
Bottom 20%	0.91 (0.72, 1.14)	0.23 (0.16, 0.33)	0.92 (0.63, 1.35)	N/A	0.76 (0.35, 1.63)	N/A
Bottom 10%	0.95 (0.73, 1.24)	N/A	0.75 (0.45, 1.24)	N/A	N/A	N/A
Bottom 5%	0.83 (0.59, 1.16)	N/A	0.97 (0.51, 1.83)	N/A	N/A	N/A
Bottom 1%	N/A	N/A	N/A	N/A	N/A	N/A
Bottom 0.5%	N/A	N/A	N/A	N/A	N/A	N/A
ASCVD Death						
Continuous per SD reduction	0.82 (0.77, 0.88)	0.29 (0.26, 0.32)	0.89 (0.77, 1.03)	0.31 (0.26, 0.37)	0.85 (0.68, 1.07)	0.25 (0.19, 0.34)
Bottom 20%	0.82 (0.62, 1.08)	N/A	0.58 (0.34, 0.99)	N/A	N/A	N/A
Bottom 10%	0.67 (0.48, 0.94)	N/A	0.78 (0.42, 1.44)	N/A	N/A	N/A
Bottom 5%	0.64 (0.42, 0.97)	N/A	N/A	N/A	N/A	N/A
Bottom 1%	N/A	N/A	N/A	N/A	N/A	N/A
Bottom 0.5%	N/A	N/A	N/A	N/A	N/A	N/A

* Reference group = middle 10% (45th to 55th percentiles) of risk score
** N/A = <10 events in the selected risk group.

eTable 5. Reclassification of 5-Year Predicted Myocardial Infarction Including Both Statin-Naïve and Statin Users

Correctly Reclassified | Incorrectly Reclassified

A. All participants

		Traditional x Polygenic Risk Score (GxE) Model		
	Traditional Model	**≤ 3.75%**	**> 3.75%**	**Total N (%)**
Events	**≤ 3.75%**	786	186	972 (27.9)
	> 3.75%	146	2360	2506 (72.1)
	Total N (%)	932 (26.8)	2546 (73.2)	3478 (100)
Nonevents	**Traditional Model**	**≤ 3.75%**	**> 3.75%**	**Total N (%)**
	≤ 3.75%	18657	1714	20371 (50.6)
	> 3.75%	2451	17432	19883 (49.4)
	Total N (%)	21108 (52.4)	19146 (47.6)	40254 (100)

B. Non-Hispanic White

		Traditional x Polygenic Risk Score (GxE) Model		
	Traditional Model	**≤ 3.75%**	**> 3.75%**	**Total N (%)**
Events	**≤ 3.75%**	459	149	608 (23.9)
	> 3.75%	125	1811	1936 (76.1)
	Total N (%)	584 (23.0)	1960 (77.0)	2544 (100)
Nonevents	**Traditional Model**	**≤ 3.75%**	**> 3.75%**	**Total N (%)**
	≤ 3.75%	10645	1392	12037 (43.9)
	> 3.75%	2111	13248	15359 (56.1)
	Total N (%)	12756 (46.6)	14640 (53.4)	27396 (100)

C. Non-Hispanic Black

		Traditional x Polygenic Risk Score (GxE) Model		
	Traditional Model	**≤ 3.75%**	**> 3.75%**	**Total N (%)**
Events	**≤ 3.75%**	241	23	264 (38.8)
	> 3.75%	14	403	417 (61.2)
	Total N (%)	255 (37.4)	426 (62.6)	681 (100)
Nonevents	**Traditional Model**	**≤ 3.75%**	**> 3.75%**	**Total N (%)**
	≤ 3.75%	5668	224	5892 (64.0)
	> 3.75%	200	3120	3320 (36.0)
	Total N (%)	5868 (63.7)	3344 (36.3)	9212 (100)

D. Hispanic

		Traditional x Polygenic Risk Score (GxE) Model		
	Traditional Model	**≤ 3.75%**	**> 3.75%**	**Total N (%)**
Events	**≤ 3.75%**	86	14	100 (39.5)
	> 3.75%	7	146	153 (60.5)
	Total N (%)	93 (36.8)	160 (63.2)	253 (100)
Nonevents	**Traditional Model**	**≤ 3.75%**	**> 3.75%**	**Total N (%)**
	≤ 3.75%	2344	98	2442 (67.0)
	> 3.75%	140	1064	1204 (33.0)
	Total N (%)	2484 (68.1)	1162 (31.9)	3646 (100)

eTable 6. Reclassification of 5-Year Predicted Acute Ischemic Stroke Including Both Statin-Naïve and Statin Users

Correctly Reclassified | Incorrectly Reclassified

A. All participants

		Traditional x Polygenic Risk Score (GxE) Model		
	Traditional Model	**≤ 3.75%**	**> 3.75%**	**Total N (%)**
Events	**≤ 3.75%**	1276	49	1325 (83.0)
	> 3.75%	32	239	271 (17.0)
	Total N (%)	1308 (82.0)	288 (18.0)	1596 (100)
Nonevents	**Traditional Model**	**≤ 3.75%**	**> 3.75%**	**Total N (%)**
	≤ 3.75%	37290	534	37824 (93.3)
	> 3.75%	465	2249	2714 (6.7)
	Total N (%)	37755 (93.1)	2783 (6.9)	40538 (100)

B. Non-Hispanic White

		Traditional x Polygenic Risk Score (GxE) Model		
	Traditional Model	**≤ 3.75%**	**> 3.75%**	**Total N (%)**
Events	**≤ 3.75%**	871	32	903 (86.2)
	> 3.75%	21	124	145 (13.8)
	Total N (%)	892 (85.1)	156 (14.9)	1048 (100)
Nonevents	**Traditional Model**	**≤ 3.75%**	**> 3.75%**	**Total N (%)**
	≤ 3.75%	25853	354	26207 (94.7)
	> 3.75%	291	1186	1477 (5.3)
	Total N (%)	26144 (94.4)	1540 (5.6)	27684 (100)

C. Non-Hispanic Black

		Traditional x Polygenic Risk Score (GxE) Model		
	Traditional Model	**≤ 3.75%**	**> 3.75%**	**Total N (%)**
Events	**≤ 3.75%**	303	15	318 (73.1)
	> 3.75%	11	106	117 (26.9)
	Total N (%)	314 (72.2)	121 (27.8)	435 (100)
Nonevents	**Traditional Model**	**≤ 3.75%**	**> 3.75%**	**Total N (%)**
	≤ 3.75%	7922	164	8086 (87.9)
	> 3.75%	157	956	1113 (12.1)
	Total N (%)	8079 (87.8)	1120 (12.2)	9199 (100)

D. Hispanic

		Traditional x Polygenic Risk Score (GxE) Model		
	Traditional Model	**≤ 3.75%**	**> 3.75%**	**Total N (%)**
Events	**≤ 3.75%**	102	2	104 (92.0)
	> 3.75%	0	9	9 (8.0)
	Total N (%)	102 (90.3)	11 (9.7)	113 (100)
Nonevents	**Traditional Model**	**≤ 3.75%**	**> 3.75%**	**Total N (%)**
	≤ 3.75%	3515	16	3531 (96.6)
	> 3.75%	17	107	124 (3.4)
	Total N (%)	3532 (96.6)	123 (3.4)	3655 (100)

eTable 7. Reclassification of 5-Year Predicted ASCVD Death Including Both Statin-Naïve and Statin Users

	Correctly Reclassified	Incorrectly Reclassified

A. All participants

		Traditional x Polygenic Risk Score (GxE) Model		
	Traditional Model	**≤ 3.75%**	**> 3.75%**	**Total N (%)**
Events	**≤ 3.75%**	716	21	737 (79.8)
	> 3.75%	15	172	187 (20.2)
	Total N (%)	731 (79.1)	193 (20.9)	924 (100)
Nonevents	**Traditional Model**	**≤ 3.75%**	**> 3.75%**	**Total N (%)**
	≤ 3.75%	38832	256	39088 (95.5)
	> 3.75%	249	1602	1851 (4.5)
	Total N (%)	39081 (95.5)	1858 (4.5)	40939 (100)

B. Non-Hispanic White

		Traditional x Polygenic Risk Score (GxE) Model		
	Traditional Model	**≤ 3.75%**	**> 3.75%**	**Total N (%)**
Events	**≤ 3.75%**	508	19	527 (76.5)
	> 3.75%	13	149	162 (23.5)
	Total N (%)	521 (75.6)	168 (24.4)	689 (100)
Nonevents	**Traditional Model**	**≤ 3.75%**	**> 3.75%**	**Total N (%)**
	≤ 3.75%	26142	231	26373 (94.4)
	> 3.75%	219	1332	1551 (5.6)
	Total N (%)	26361 (94.4)	1563 (5.6)	27924 (100)

C. Non-Hispanic Black

		Traditional x Polygenic Risk Score (GxE) Model		
	Traditional Model	**≤ 3.75%**	**> 3.75%**	**Total N (%)**
Events	**≤ 3.75%**	155	2	157 (90.2)
	> 3.75%	2	15	17 (9.8)
	Total N (%)	157 (90.2)	17 (9.8)	174 (100)
Nonevents	**Traditional Model**	**≤ 3.75%**	**> 3.75%**	**Total N (%)**
	≤ 3.75%	9099	18	9117 (97.7)
	> 3.75%	23	194	217 (2.3)
	Total N (%)	9122 (97.7)	212 (2.3)	9334 (100)

D. Hispanic

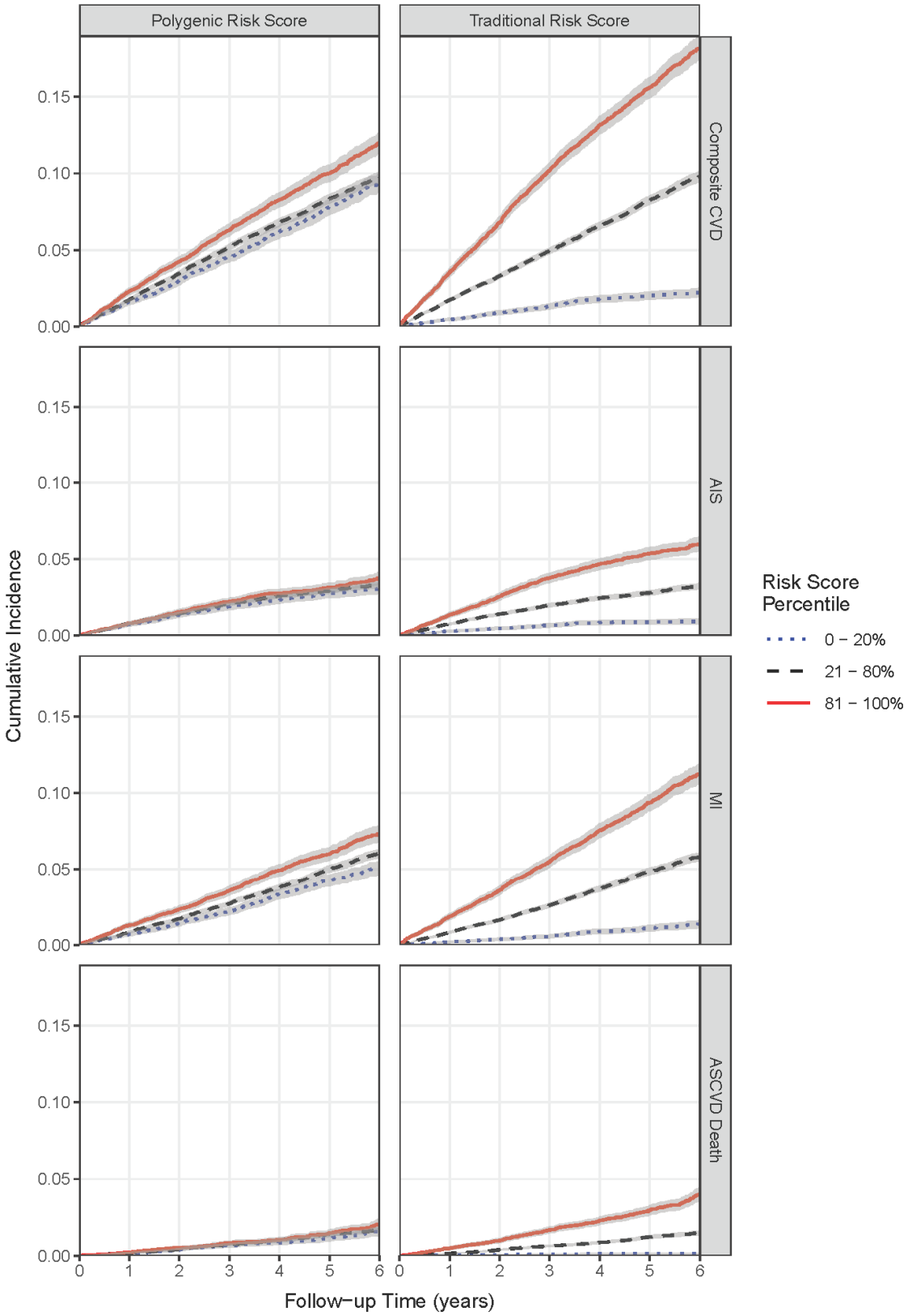
		Traditional x Polygenic Risk Score (GxE) Model		
	Traditional Model	**≤ 3.75%**	**> 3.75%**	**Total N (%)**
Events	**≤ 3.75%**	53	0	53 (86.9)
	> 3.75%	0	8	8 (13.1)
	Total N (%)	53 (86.9)	8 (13.1)	61 (100)
Nonevents	**Traditional Model**	**≤ 3.75%**	**> 3.75%**	**Total N (%)**
	≤ 3.75%	3591	7	3598 (97.7)
	> 3.75%	7	76	83 (2.3)
	Total N (%)	3598 (97.7)	83 (2.3)	3681 (100)

eTable 8. Net Reclassification Improvement From Inclusion of Polygenic Scores Stratified by Age and Sex

5-year Risk Group	Subgroup	Net Reclassified		Total N		NRI+	NRI-	NRI [95% CI]
		Event	Non-Event	Event	Non-event			
Intermediate (3.75% - 10%)	Male	-4	110	4731	23856	-0.08%	0.46%	0.38% [0.07%, 0.68%]
	Female	20	-6	287	3450	6.97%	-0.17%	6.79% [3.01%, 10.58%]
	>55 yrs	-6	72	4151	18267	-0.14%	0.39%	0.25% [0.03%, 0.47%]
	40 to 55 yrs	-2	122	777	6526	-0.26%	1.87%	1.61% [-0.07%, 3.30%]
High (≥10%)	Male	62	140	4731	23856	1.31%	0.59%	1.90% [0.97%, 2.82%]
	Female	5	15	287	3450	1.74%	0.43%	2.18% [0.11%, 4.24%]
	>55 yrs	31	194	4151	18267	0.75%	1.06%	1.81% [0.81%, 2.81%]
	40 to 55 yrs	33	-69	777	6526	4.25%	-1.06%	3.19% [1.41%, 4.97%]

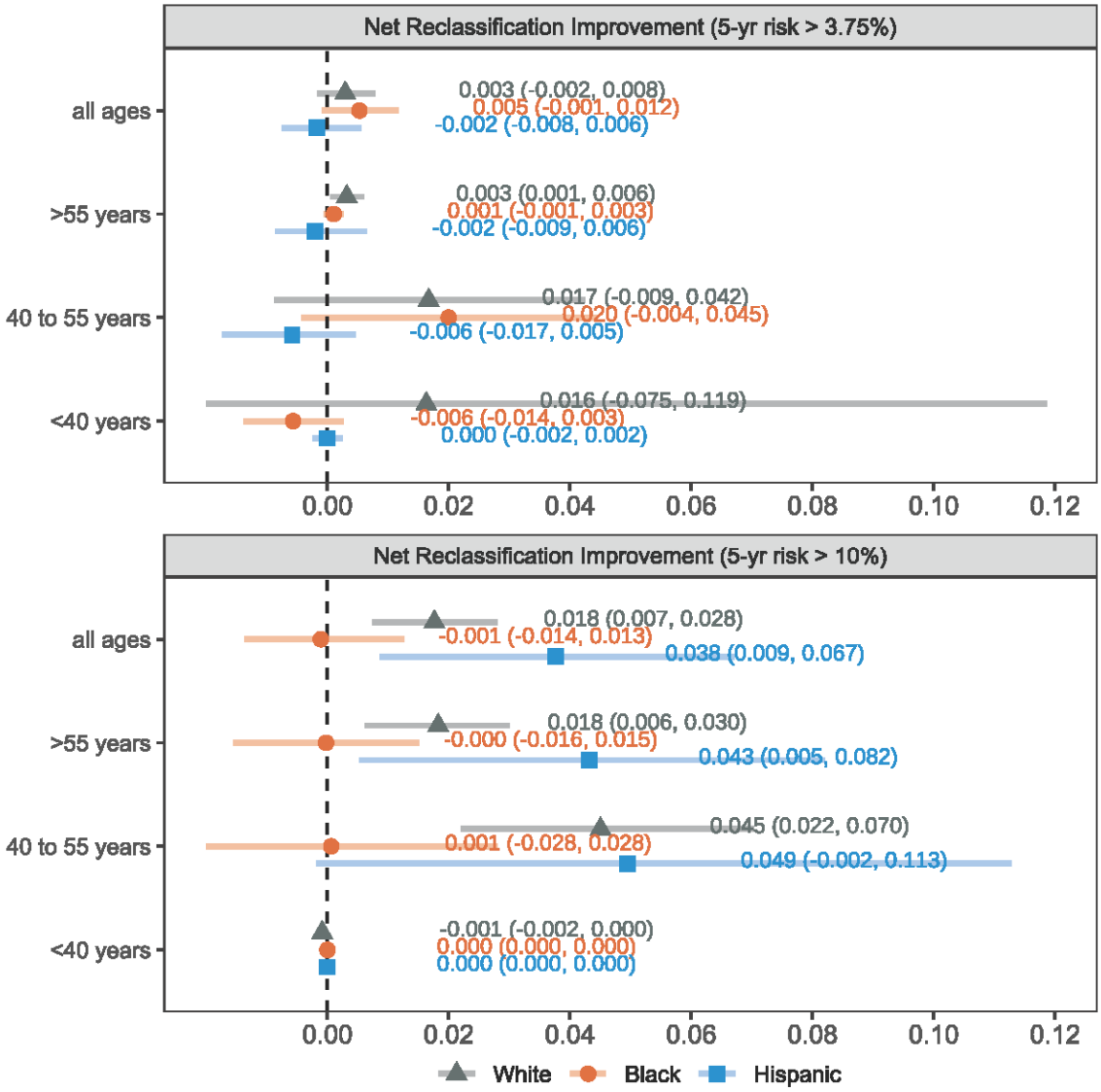
eTable 8 contains an abbreviated reclassification table for all ancestries combined. Net reclassified events are the number of events reclassified upwards (into the Intermediate or High risk groups) minus the number of events reclassified downwards. Net reclassified non-events are the number of non-events reclassified downwards minus the number of events reclassified upwards. The traditional model includes age, sex, and 5 principal components of genetic ancestry (to be comparable to the genetic model), and the 5-year risk cutoffs are half the clinically relevant 10-year risk thresholds from the ACC2019 guidelines. Among ASCVD events in the middle-aged subgroup (ages 40 to 55 years), the net proportion of correct reclassifications was NRI+ = 33/777= 4.25%, and among non-events was NRI- = -69/6526 = -1.06%. The overall net reclassification index is defined as the sum of the net reclassification proportions for events and nonevents (NRI = 4.25% + -1.06% = 3.19%).

eFigure 1. Cumulative Incidence of ASCVD Events



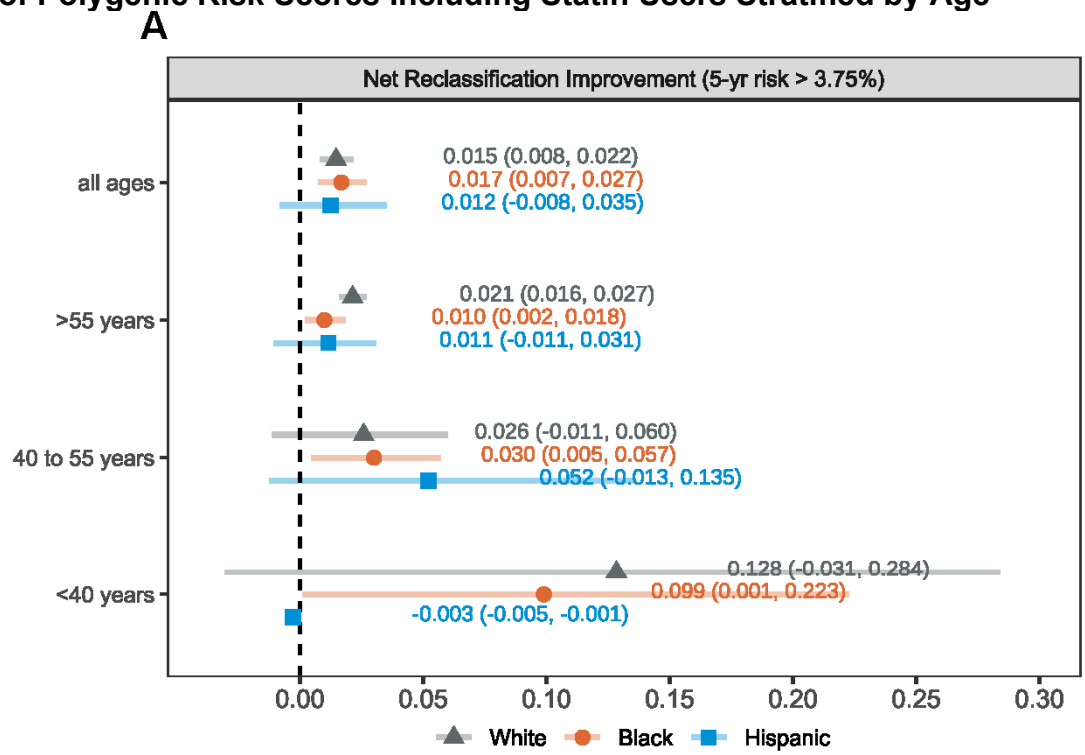
eFigure 1 caption: Cumulative incidence of Composite ASCVD, Acute Ischemic Stroke, Myocardial Infarction (MI), and ASCVD Death are plotted over 6 years of follow up according to percentile groups for Polygenic Risk Scores and Traditional Risk Scores.
Key: Risk score percentile 0-20% (dotted, blue), 21-80% (dashed, black), 81-100% (solid, red).

eFigure 2. Categorical Net Reclassification Index for Incident Composite ASCVD Among Statin-Naïve Participants Outcomes Stratified by Age Group



eFigure 2 caption:
Top Panel: Categorical Net Reclassification Improvement for intermediate risk (5-year risk >3.75%) among statin-naïve patients is shown for Composite ASCVD, Myocardial Infarction, Ischemic Stroke, and ASCVD Death.
Bottom Panel: Categorical Net Reclassification Improvement for high risk (5-year risk >10%) among statin-naïve patients is shown for Composite ASCVD, Myocardial Infarction, Ischemic Stroke, and ASCVD Death.
Key: Estimates and 95% confidence intervals are shown for White (black, triangle), Black (red, circle), and Hispanic (blue, square) population groups.

eFigure 3. Net Reclassification Index for Intermediate Risk (5-year risk > 3.75%) From Inclusion of Polygenic Risk Scores Including Statin Users Stratified by Age



		Correctly Reclassified	Incorrectly Reclassified

B All ages — NRI (95% CI) = 1.65% (1.11, 2.18%); NRI+ = 0.27%; NRI- = 1.38%

	Traditional	Traditional x PRS ≤ 3.75%	Traditional x PRS > 3.75%
Events	≤ 3.75%	404	103
	> 3.75%	88	5024
Non-events	≤ 3.75%	10663	803
	> 3.75%	1342	26276

C >55 yrs — NRI (95% CI) = 1.96% (1.48, 2.44%); NRI+ = -0.50%; NRI- = 2.46%

	Traditional	Traditional x PRS ≤ 3.75%	Traditional x PRS > 3.75%
Events	≤ 3.75%	91	33
	> 3.75%	56	4400
Non-events	≤ 3.75%	1163	246
	> 3.75%	854	22407

D 40-55 yrs — NRI (95% CI) = 2.94% (0.88, 5.00%); NRI+ = 3.10%; NRI- = -0.15%

	Traditional	Traditional x PRS ≤ 3.75%	Traditional x PRS > 3.75%
Events	≤ 3.75%	238	59
	> 3.75%	30	610
Non-events	≤ 3.75%	5066	473
	> 3.75%	458	3721

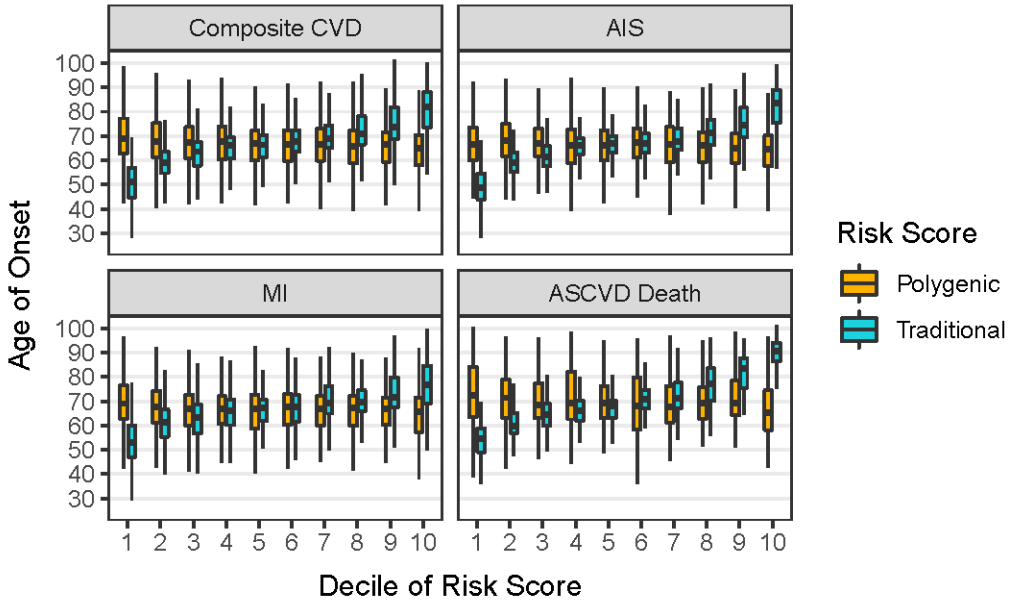
E <40 yrs — NRI (95% CI) = 7.67% (0.95, 14.40%); NRI+ = 8.82%; NRI- = -1.15%

	Traditional	Traditional x PRS ≤ 3.75%	Traditional x PRS > 3.75%
Events	≤ 3.75%	75	11
	> 3.75%	2	14
Non-events	≤ 3.75%	4434	84
	> 3.75%	30	148

eFigure 3 caption: Panel A presents net reclassification improvement (NRI) from the addition of polygenic scores to the traditional risk model for each ASCVD outcome, stratified by ancestry and age group. Panels B to E contain

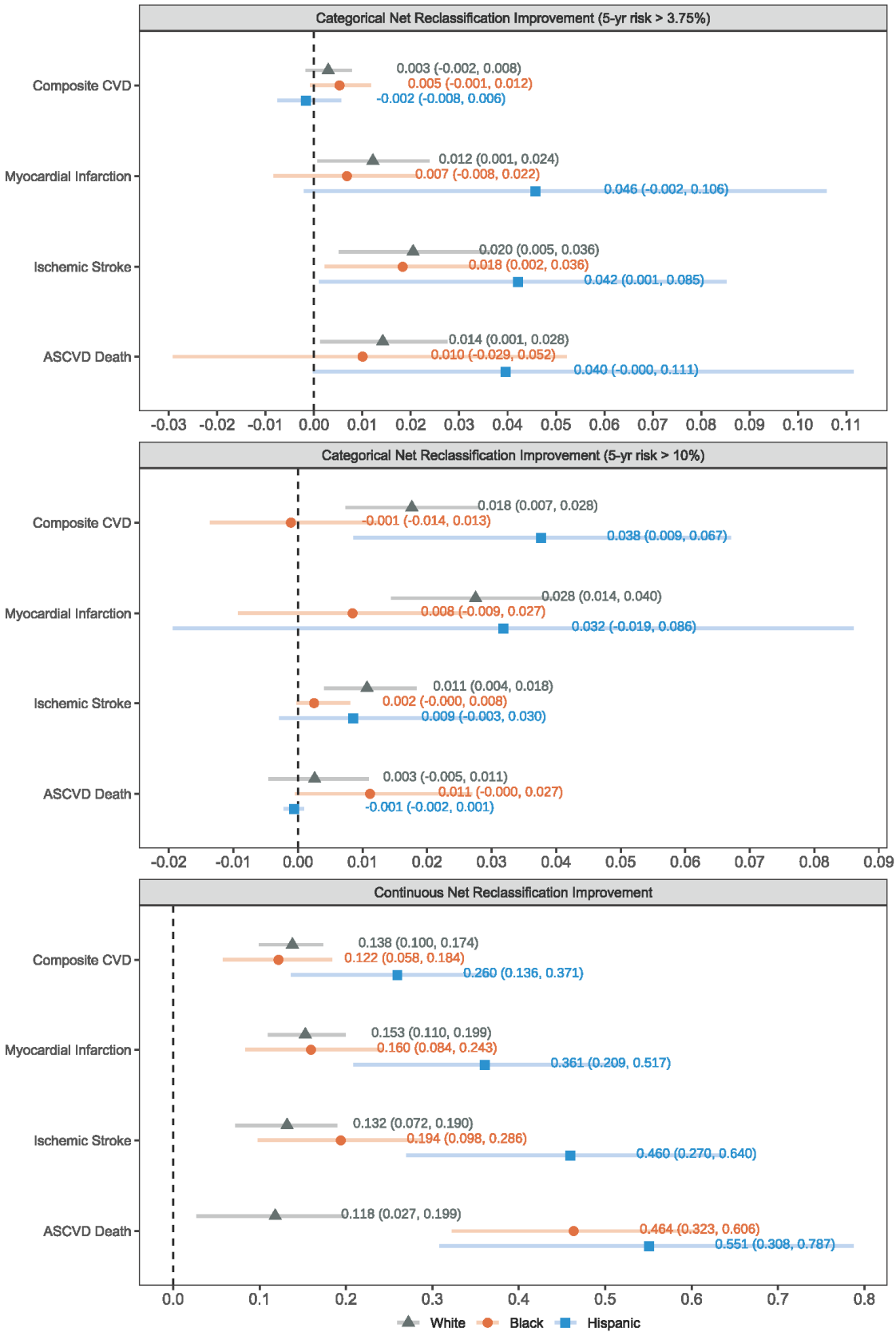
reclassification tables for all ancestries combined, stratified by age group. Rows refer to predicted 5-year risk categories from the traditional risk model, and columns refer to predicted risk from the combined traditional and polygenic risk score model. Blue cells indicate correct reclassifications: i.e. the GxE model predicted a higher risk group, compared to the traditional model, for a patient who experienced an event, or a lower risk group for a non-event. Orange shaded cells highlight incorrect reclassifications. The traditional model includes age, sex, and 5 principal components of genetic ancestry (to be comparable to the genetic model), and the risk cutoff (>3.75%) represents a clinically relevant 5-year risk. Among ASCVD events in the youngest subgroup (ages < 40, panel E), the net proportion of correct reclassifications was NRI+ = (11-2)/102 = 8.82%, and among non-events was NRI- = (30-84)/4696 = -1.15%. The overall net reclassification index is defined as the sum of the net reclassification proportions for events and nonevents (NRI = 8.82% + -1.15% = 7.67%).
Key: Estimates and 95% confidence intervals are shown for White (black, triangle), Black (red, circle), and Hispanic (blue, square) population groups.

eFigure 4. Age of Onset for Incident Composite ASCVD Events



eFigure 4 Caption: Boxplots are shown for the age of onset of incident ASCVD events by decile of traditional and polygenic risk scores. The lower and upper hinges correspond to the first and third quartiles (25^{th} and 75^{th} percentiles) of age of onset within each risk score decile, while the whiskers extend from the lower (or upper) hinge to the smallest (or largest) observed age that is at most 1.5 times the interquartile range (IQR = 25^{th} – 75^{th} percentile) away from the box. Median age at incident event increased monotonically across deciles of traditional risk score by approximately 2.8 years per decile for composite ASCVD events, 3.1 years for ischemic stroke, 1.7 years for MI, and 3.9 years for ASCVD death. For composite ASCVD, this translated to a difference of 25 years between median age of onset in the lowest decile (50 years) compared to the top decile (75 years). On the other hand, age of onset decreased slightly across deciles of PRS by approximately 0.3 years per decile for composite ASCVD and 0.4 years per decile for ASCVD death; age of onset was effectively constant at approximately 65 years of age across deciles of PRS for ischemic stroke and MI.

eFigure 5. Continuous and Categorical Net Reclassification Index for Incident ASCVD Outcomes



eFigure 5 caption:

Top Panel: Categorical Net Reclassification Improvement for intermediate risk (5-year risk >3.75%) is shown for Composite ASCVD, Myocardial Infarction, Ischemic Stroke, and ASCVD Death.
Middle Panel: Categorical Net Reclassification Improvement for high risk (5-year risk >10%) is shown for Composite ASCVD, Myocardial Infarction, Ischemic Stroke, and ASCVD Death.
Bottom Panel: Continuous Net Reclassification Improvement for 5-year risk is shown for Composite ASCVD, Myocardial Infarction, Ischemic Stroke, and ASCVD Death.
Key: Estimates and 95% confidence intervals are shown for White (black, triangle), Black (red, circle), and Hispanic (blue, square) population groups.