

ESM Methods

Development of trans-ancestry PRS

To increase statistical power and expand the ancestral diversity of our study, we incorporated recently published type 1 diabetes GWAS datasets from individuals of African ancestry (AFR) and the Hispanic (AMR) population. We conducted separate meta-analyses of GWAS summary statistics using the sample-size weighted fixed-effects model implemented in Metal, which allows for the combination of studies with different measurement scales. The first meta-analysis included summary statistics from individuals of African ancestry ($N_{\text{AFR_Michalek}} = 891$, $N_{\text{AFR_Verma}} = 115861$)[1], while the second focused on those from the Hispanic population ($N_{\text{AMR_Michalek}} = 308$, $N_{\text{AMR_Verma}} = 57429$)[1,2].

The PRS-CSx method was applied using the python package available on Github (getian107/PRS-CSx) which allows to estimate posterior SNP effect sizes inferred according to continuous coupled shrinkage (CS) priors between populations. PRS-CSx offers LD reference panels from UKB or 1K Genomes Project, but to avoid overfitting with our controls, we chose to use the UKB reference panel. PRS-CSx requires a shrinkage parameter. We tried a set of different shrinkage parameters ($\phi = 10^{-2}; 10^{-4}; 10^{-6}; 10^{-8}; 10^{-10}; 10^{-12}$) and selected the one yielding the scores with the best prediction performance. PRS-CSx generated a set of ancestry specific PRS (AS, at a range of $\phi = 10^{-2}; 10^{-4}; 10^{-6}; 10^{-8}; 10^{-10}; 10^{-12}$) for AFR, AMR, EAS and EUR, as well as a set of Trans Ancestry PRS (TA, at a range of $\phi = 10^{-2}; 10^{-4}; 10^{-6}; 10^{-8}; 10^{-10}; 10^{-12}$).

The JointPRS method is similar to PRS-CSx but uses a slightly different algorithm which also allows the estimation of posterior effect sizes of SNPs from multi-ancestry GWAS and LD reference panels. The python package is available on Github (LeqiXu/JointPRS). In the absence

25 of tuning data, we ran JointPRS in its "JointPRS-auto" version. Similarly, to PRS-CSx, we used
26 the LD reference panels from UKB. JointPRS generated only ancestry- specific PRS for AFR,
27 AMR, EAS and EUR populations.

28 Finally, we constructed an enhanced European PRS using LDpred2 to optimize the non-HLA
29 part of the GRS2x. To do this, we used as reference the GWAS by Chiou et al, which is the
30 largest European GWAS to date. We conducted LDpred2 using SNPs present in HapMap3+ and
31 in total, 1,422,515 SNPs matched between the reference GWAS and HapMap3+.

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33 **Type 1 diabetes GWAS**

34 We sought to exclude bias due to residual population stratification (ie extreme variability
35 between cases and controls) due to batch effects when matching type 1 diabetes cases with
36 controls in our Montreal-based cohort . To test this, we performed a pseudo-GWAS using
37 REGENIE[3] in European samples and with PLINK[4] (in other ancestries), since REGENIE is
38 not suitable for GWAS with less than 300 case-control samples. We did not adjust for batch
39 effects (to account for differences in genotyping array or genotyping versus sequencing
40 platform) since we sought to estimate the impact of this effect. The European GWAS
41 included 2113 type 1 diabetes cases of European ancestry from the Montreal-based cohort
42 and 1877 controls from the CaCo cohort (both cases and controls with TOPMed-imputed
43 genotypes). Additionally, we performed pseudo-GWAS in each of the non-European
44 case/control subcohorts included in the MTL-based cohort, which included the following
45 number of cases (all genotyped and TopMed-imputed) and controls: AMR (N=226;
46 N_cases=103; N_controls=123, among which N=23 from CaCo (genotyped and TopMed-
47 imputed); and 100 from 1000 Genomes (with WGS); AFR(N=136; N_cases=48 ;

48 N_controls=88, among which 43 from CaCo and 45 de 1000 Genomes); SAS (N=119;
49 N_cases=47; N_controls=72, among which 48 from CaCo and 24 from 1000Genomes);
50 Unfortunately, we could not perform a GWAS for EAS, due to extremely low number of cases
51 and controls (N=51; N_cases=21; N_controls=30, among which 3 from CaCo; and 27 from
52 1000 Genomes). Following quality control (missingness <1%, imputation INFO-SCORE >0.4,
53 MAF >0.01, HWE p-value <10⁻⁶), and exclusion of indels and the MHC region, we ran the
54 GWAS. including the 5 first PC following a PCA analysis using FastPCA[5] as covariates. The
55 Manhattan plot and QQ plot of the ancestry-specific GWAS are shown in **ESM Fig. 1**.
56 Genomic inflation factor (lambda) was 1.014 in the EUR and SAS GWAS, 1.054 in the AFR
57 GWAS and 1.177 in the AMR GWAS. Based on these results, we conclude that there was no
58 significant bias due to population stratification among cases and controls we used for
59 validation of the various PRS.

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62 **Validation of the PRS in independent datasets**

63 We tested the performance of the various PRS in independent case/control or population-
64 based cohorts of various ancestries (**ESM Table 4**). Specifically, in the multi-ancestry All of Us
65 Biobank (AoU, N = 89,699), in a case-control multi-ancestry cohort from the Children's
66 Hospital of Philadelphia (CHOP-CAG, N = 6498), in the UK Biobank (UKB, N = 427,847) and in a
67 Chinese case/control cohort set up in pediatric centers named Genetic Risk Assessment for
68 Chinese Eaglet-T1D (GRACE, N = 597).

69 Within AoU (N_{cases} = 1084; N_{CTL} = 88,635), type 1 diabetes diagnosis (T1D-EHR) was defined
70 according to previously published criteria [6] and cases of undefined diabetes were excluded
71 from the controls. More precisely, the cases were defined as follows: At least 1 ICD-9, ICD-10,

72 or SNOMED code of type 1 diabetes in EHR data, must have been prescribed insulin, must not
73 have been prescribed any other diabetes medication besides insulin and no diagnosis of
74 cancer, cystic fibrosis, drug-induced diabetes, maturity-onset diabetes of the young (MODY),
75 gestational diabetes mellitus (GDM), or post-transplant diabetes. While the controls were
76 defined as follows: must have EHR data, no EHR record of any type of diabetes, must have at
77 least 1 measurement of fasting glucose, random glucose, or HbA1c, no record of fasting
78 glucose $\geq 100\text{mg/dl}$, random glucose $\geq 200\text{mg/dl}$, or HbA1c $\geq 5.7\%$, no self-reported medical
79 history of any type of diabetes, must not have been prescribed any other diabetes medication,
80 no diagnosis of cancer or cystic fibrosis.

81 In UKB ($N_{\text{cases}} = 778$; $N_{\text{CTL}} = 427,069$), the type 1 diabetes definition was made according to
82 following criteria: insulin-dependent diabetes (ICD-10), and reported age < 25 years at
83 diagnosis. For controls we excluded type 2 diabetes and undefined diabetes. For the subgroup
84 analyses, age at diagnosis was defined based on the data-field 2976 and sex was defined based
85 on the Genetic sex field (data-field 22001). To define European versus non-European ancestry,
86 we used Genetic ethnic grouping (data-field 22006) .

87 In the CHOP-CAG ($N_{\text{cases}} = 1094$; $N_{\text{CTL}} = 5404$) and GRACE cohorts ($N_{\text{cases}} = 294$; $N_{\text{CTL}} = 303$), the
88 diagnosis of type 1 diabetes was made by clinicians and retrieved from patient hospital
89 records.

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91 **Selection of the best-performing trans-ancestry PRS**

92 Regarding PRS-CSx we tried a set of shrinkage parameters (ϕ), the results obtained are
93 presented in **ESM Table 6** and **ESM Fig. 2**. In the main manuscript, TA-PS refers to the trans-
94 ancestry score developed with PRS-CSx with $\phi = 10^{-6}$. This ϕ value, among all generated

95 TA scores, is the one that performs the best across all ancestries ($AUROC_{\text{mean}} = 0.86$, $AUC_{\text{sd}} =$
96 0.03 , $AUROC_{\text{min}} = 0.82$ (EAS) and $AUROC_{\text{max}} = 0.90$ (SAS)).

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98 **Comparison of MAFs of the TA-PS SNPs across ancestries**

99 We compared the minor allele frequencies (MAFs) of the SNPs included in TA-PS (S) across
100 ancestries using data from the 1000 Genomes project. The results of the Pearson correlation
101 of the MAFs are shown in **ESM Fig. 4 (panels a and b)**. As expected, the MAFs were more
102 discordant between European (EUR) and African (AFR) populations, and showed the highest
103 correlation between European (EUR) and Hispanic (AMR) populations. The MAFs of the rare
104 SNPs (MAF <5% in EUR) within TA-PS were less correlated across ancestries compared to the
105 common SNPs (MAF >5% in EUR). Also, the percentage of rare SNPs in TA-PS varied between
106 14% and 26% across ancestries (**ESM Fig 4 panel c**).

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ESM Tables

Tables' content:

Table #	Title
1	List of GWAS used to develop the trans-ancestry PRS.
2	Summary of the multi-ancestry testing cohort. The ancestry was determined by PCA using the 1000 Genomes Project.
3	Coefficients used to combine the HLA portion of GRS2x with the non-HLA trans-ancestral PRS developed with PRS-CSx ($\phi = 10^{-6}$).
4	Validation cohorts used in our study.
5	AUROC of the different PRS tested by ancestry. AUROC and confidence intervals (95%). AS-PS (csx) corresponds to the ancestry-specific PRS (one per ancestry) developed with PRS-CSx + the HLA part of GRS2x. AS-PS (jt) corresponds to the ancestry-specific PRS (one per ancestry) developed with JointPRS + the HLA part of GRS2x. TA-PS corresponds to the trans-ancestral PRS developed with PRS-CSx + HLA part of GRS2x. LDPRED-PS corresponds to the PRS developed with LDpred2 and the HLA part of GRS2x. We only added the HLA part of GRS2x (GRS2xInt + GRS2xHLA).
6	AUROC by PRS developed with PRS-CSx with different shrinkage parameters (ϕ) in different ancestries. Additive model (Non HLA from PRS-CSx + HLA from GRS2x)
7	Comparison of AUROC with the Delong Test for each AUROC and each ancestry (Figure 2 and TS6). AS-PS (csx) corresponds to the ancestry-specific PRS (one per ancestry) developed with PRS-CSx + the HLA part of GRS2x. AS-PS (jt) corresponds to the ancestry-specific PRS (one per ancestry) developed with JointPRS + the HLA part of GRS2x. TA-PS corresponds to the trans-ancestral PRS developed with PRS-CSx + HLA part of GRS2x. LDPRED-PS corresponds to the PRS developed with LDpred2 and the HLA part of GRS2x. We only added the HLA part of GRS2x (GRS2xInt + GRS2xHLA).
8	AUROC for each PRS and each ancestry (Figure 3). TA-PS corresponds to the trans-ancestral PRS (TA) developed with PRS csx with ϕ value = 10^{-6} and the HLA part of GRS2x. (Scale) and (MinMax) versions of TA-PS with different weights are shown.
9	Comparison of AUROC with the Delong Test for each ancestry and each PRS (Figure 3).
10	Sensitivity, specificity, and other metrics for different thresholds for the various PRS. Thresholds were calculated in European controls.
11	Comparison of sensitivity, specificity and F1 score between GRS2x and trans-ancestral scores (TA-PS), based on the Z-test.
12	AUROC of the various PRS tested in the validation cohorts.
13	Delong Test in the validation cohorts.
14	Metrics (sensitivity, specificity, F1) of the PRS by cutoff in the validation cohorts.

117 **ESM Table 1:** List of GWAS used to develop the trans-ancestry PRS.

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Authors	Title	Ancestry	N	Cases	Controls	SNPs	Accession	PRS development			Meta analysis (METAL)				
								PRS-CSx	LDpred2	Joint PRS	Conducted	Ancestry	N	Cases	Controls
Chiou et al	Interpreting type 1 diabetes risk with genetics and single-cell epigenomics.	EUR	520580	18942	501638	62116689	GCST90014023	YES	YES	YES					
Sakaue et al	A cross-population atlas of genetic associations for 220 human phenotypes.	EAS	133251	1219	132032	13421694	GCST90018705	YES	NO	YES					
Verma et al	Diversity and scale: Genetic architecture of 2068 traits in the VA Million Veteran Program.	AFR	115861	6451	109410	44300000	GCST90475660	YES	NO	YES	YES	AFR	116752	6860	109892
Michalek et al	A multi-ancestry genome-wide association study in type 1 diabetes	AFR	891	409	482	13387148	GCST90432064	YES	NO	YES	YES				
Verma et al	Diversity and scale: Genetic architecture of 2068 traits in the VA Million Veteran Program.	AMR	57429	2295	55134	44300000	GCST90475659	YES	NO	YES	YES	AMR	57737	2448	55292
Michalek et al	A multi-ancestry genome-wide association study in type 1 diabetes	AMR	308	153	158	6841431	GCST90432065	YES	NO	YES	YES				

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121 **ESM Table 2:** Summary of the multi-ancestry testing cohort. The ancestry was determined by PCA using the 1000 Genomes Project.

Cohort Name	Sub- cohort	All cohorts			Ancestry specific																
					AFR			AMR			EAS			EUR			SAS				
		N	Cases	Controls	N	Cases	Controls	N	Cases	Controls	N	Cases	Controls	N	Cases	Controls	N	Cases	Controls	Phenotype	Data
Montreal- based cohort	JDRF	1086	1086	0	21	21	0	34	34	0	10	10	0	1011	1011	0	10	10	0	T1D	Genotyped
	CaCo	2541	514	2027	53	10	43	32	9	23	9	6	3	2382	474	1908	65	15	50	T1D/Ctl	Genotyped
	MTL	482	482	0	3	3	0	1	1	0	1	1	0	469	469	0	8	8	0	T1D	Genotyped
	ADDAM2	205	205	0	11	11	0	50	50	0	1	1	0	133	133	0	10	10	0	T1D	Genotyped
	ADDAM1	129	129	0	3	3	0	11	11	0	5	5	0	106	106	0	4	4	0	T1D	Genotyped
	1K	214	0	214	48	0	48	108	0	108	30	0	30	0	0	0	0	28	0	28	Ctl
TOTAL		4657	2416	2241	139	48	91	236	105	131	56	23	33	4101	2193	1908	125	47	78		

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124 **ESM Table 3:** Coefficients used to combine the HLA portion of GRS2x with the non-HLA trans-ancestral PRS developed with PRS-CSx ($\phi = 10^{-6}$).
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Coefficient	Additive	Weighted model	
		Scale	MinMax
a (TA)	1	0.78592139	5.81014241
b (GRS2x Interaction term)	1	1.68363223	6.74227604
c (GRS2x HLA term)	1	0.7671705	5.37493571

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EDM Table 4: Validation cohorts used in our study.

Cohort Name		Country of origin	Type of Cohort	All cohorts (MA)			Ancestry specific																						
	Acronym						AFR			AMR			EAS			EUR			SAS			Other/Unclassified			Non EUR				
				N	Cases	Controls	N	Cases	Controls	N	Cases	Controls	N	Cases	Controls	N	Cases	Controls	N	Cases	Controls	N	Cases	Controls	N	Cases	Controls	Phenotype	Data
All of Us	AoU	USA	Population based	89699	10664	88635	14974	201	14773	18753	261	18492	2148	8	2140	52283	584	51699	11195	7	1188	340	7	343				T1D/CTL	WGS (30x)
Children's Hospital of Philadelphia - Center for Applied Genomics	CHOP-CAG	USA	Case/control	6498	1094	5404	1687	371	1316	279	7	272	104	10	94	2828	474	2354	315	30	285	1285	202	1083				T1D/CTL	Illumina genotyping arrays with at least 550K SNPs (Illumina HumanHap550 Genotyping BeadChip or newer versions), Imputed with TOPMed R3
Genetic Risk Assessment for Chinese Eaglet - T1D	GRACE	China	Case/control	597	294	303							597	294	303													T1D/CTL	GSA genotype array(Infinium® Global Screening Array-24 v3.0)+ TOPMed R3
UK Biobank	UKB	UK	Population based	427847	778	427069										406390	733	405657							21457	45	21421	T1D/CTL	TOPMed R2

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132 **ESM Table 5:** AUROC of the different PRS tested by ancestry. AUROC and confidence intervals (95%). AS-PS (csx) corresponds to the ancestry-
133 specific PRS (one per ancestry) developed with PRS-CSx + the HLA part of GRS2x. AS-PS (jt) corresponds to the ancestry-specific PRS (one per
134 ancestry) developed with JointPRS + the HLA part of GRS2x. TA-PS corresponds to the trans-ancestral PRS developed with PRS-CSx + HLA part of
135 GRS2x. LDPRED-PS corresponds to the PRS developed with LDpred2 and the HLA part of GRS2x We only added the HLA part of GRS2x (GRS2xInt
136 + GRS2xHLA).
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Ancestry+A4:F24	PRS	AUROC	CI lower (95%)	CI upper (95%)	Phi for PRScsx
AFR	GRS2x	0.8342803	0.76050494	0.90805566	
AFR	LDPRED-PS	0.83546402	0.7619734	0.90895463	
AFR	AS-PS (csx)	0.83783144	0.77035194	0.90531093	AFR_phi1e-10
AFR	TA-PS	0.85653409	0.79095648	0.9221117	META_phi1e-06
AFR	AS-PS (jt)	0.87215909	0.80454842	0.93976976	
AMR	GRS2x	0.81182414	0.75497681	0.86867147	
AMR	LDPRED-PS	0.80937722	0.75182345	0.86693099	
AMR	AS-PS (csx)	0.85571079	0.8063127	0.90510888	AMR_phi1e-02
AMR	TA-PS	0.85997316	0.81088602	0.90906031	META_phi1e-06
AMR	AS-PS (jt)	0.76927934	0.70674966	0.83180903	
EAS	GRS2x	0.81111111	0.67345499	0.94876723	
EAS	LDPRED-PS	0.83492063	0.70417734	0.96566393	
EAS	AS-PS (csx)	0.83333333	0.70240077	0.9642659	EAS_phi1e-06
EAS	TA-PS	0.82380952	0.69046626	0.95715279	META_phi1e-06
EAS	AS-PS (jt)	0.82380952	0.69316557	0.95445348	
EUR	GRS2x	0.85644302	0.84490569	0.86798034	
EUR	LDPRED-PS	0.86778072	0.8566625	0.87889895	
EUR	AS-PS (csx)	0.88176221	0.87123968	0.89228475	EUR_phi1e-04
EUR	TA-PS	0.877046	0.86634757	0.88774442	META_phi1e-06
EUR	AS-PS (jt)	0.87998616	0.86939309	0.89057924	
SAS	GRS2x	0.86613475	0.7982312	0.93403831	
SAS	LDPRED-PS	0.84367612	0.77221571	0.91513653	
SAS	TA-PS	0.89686761	0.83886938	0.95486584	META_phi1e-06

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139 **ESM Table 6:** AUROC by PRS developed with PRS-CSx with different shrinkage parameters (ϕ) in different ancestries. Additive model (Non HLA
140 from PRS-CSx + HLA from GRS2x).
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Ancestry	PRS Name (ϕ value)	PRS type	AUROC	CI lower (95%)	CI upper (95%)	Present in Figure 2
AFR	AFR_phi1e-02_PS	Ancestry Specific	0.77320076	0.68644299	0.85995852	
AFR	AFR_phi1e-04_PS	Ancestry Specific	0.76941288	0.67961796	0.8592078	
AFR	AFR_phi1e-06_PS	Ancestry Specific	0.80492424	0.72646339	0.8833851	
AFR	AFR_phi1e-08_PS	Ancestry Specific	0.8342803	0.76599657	0.90256404	
AFR	AFR_phi1e-10_PS	Ancestry Specific	0.83783144	0.77035194	0.90531093	YES
AFR	AFR_phi1e-12_PS	Ancestry Specific	0.83380682	0.76669639	0.90091725	
AFR	META_phi1e-02_PS	Trans-Ancestry	0.81723485	0.73896861	0.89550109	
AFR	META_phi1e-04_PS	Trans-Ancestry	0.8359375	0.76211132	0.90976368	
AFR	META_phi1e-06_PS	Trans-Ancestry	0.85653409	0.79095648	0.9221117	YES
AFR	META_phi1e-08_PS	Trans-Ancestry	0.85037879	0.78327722	0.91748035	
AFR	META_phi1e-10_PS	Trans-Ancestry	0.84824811	0.78096225	0.91553396	
AFR	META_phi1e-12_PS	Trans-Ancestry	0.85203598	0.78624978	0.91782218	
AMR	AMR_phi1e-02_PS	Ancestry Specific	0.85571079	0.8063127	0.90510888	YES
AMR	AMR_phi1e-04_PS	Ancestry Specific	0.84110822	0.78995986	0.89225657	
AMR	AMR_phi1e-06_PS	Ancestry Specific	0.82524272	0.77176559	0.87871985	
AMR	AMR_phi1e-08_PS	Ancestry Specific	0.80416765	0.7474225	0.86091281	
AMR	AMR_phi1e-10_PS	Ancestry Specific	0.81513932	0.75916741	0.87111122	
AMR	AMR_phi1e-12_PS	Ancestry Specific	0.80369406	0.74592791	0.8614602	
AMR	META_phi1e-02_PS	Trans-Ancestry	0.81608651	0.76049262	0.8716804	
AMR	META_phi1e-04_PS	Trans-Ancestry	0.84316047	0.79170249	0.89461846	
AMR	META_phi1e-06_PS	Trans-Ancestry	0.85997316	0.81088602	0.90906031	YES
AMR	META_phi1e-08_PS	Trans-Ancestry	0.86360407	0.81567956	0.91152858	
AMR	META_phi1e-10_PS	Trans-Ancestry	0.85918383	0.81028172	0.90808595	
AMR	META_phi1e-12_PS	Trans-Ancestry	0.85713158	0.80802441	0.90623875	
EAS	EAS_phi1e-02_PS	Ancestry Specific	0.82063492	0.68743578	0.95383407	
EAS	EAS_phi1e-04_PS	Ancestry Specific	0.81428571	0.67801722	0.95055421	

EAS	EAS_phi1e-06_PS	Ancestry Specific	0.83333333	0.70240077	0.9642659	YES
EAS	EAS_phi1e-08_PS	Ancestry Specific	0.82857143	0.69645776	0.9606851	
EAS	EAS_phi1e-10_PS	Ancestry Specific	0.82857143	0.69546941	0.96167345	
EAS	EAS_phi1e-12_PS	Ancestry Specific	0.82380952	0.68358807	0.96403098	
EAS	META_phi1e-02_PS	Trans-Ancestry	0.81269841	0.6638119	0.96158493	
EAS	META_phi1e-04_PS	Trans-Ancestry	0.83650794	0.70172686	0.97128901	
EAS	META_phi1e-06_PS	Trans-Ancestry	0.82380952	0.69046626	0.95715279	YES
EAS	META_phi1e-08_PS	Trans-Ancestry	0.81746032	0.68554827	0.94937237	
EAS	META_phi1e-10_PS	Trans-Ancestry	0.8047619	0.66884213	0.94068168	
EAS	META_phi1e-12_PS	Trans-Ancestry	0.80634921	0.67082398	0.94187443	
EUR	EUR_phi1e-02_PS	Ancestry Specific	0.86944811	0.85836385	0.88053236	
EUR	EUR_phi1e-04_PS	Ancestry Specific	0.88176221	0.87123968	0.89228475	YES
EUR	EUR_phi1e-06_PS	Ancestry Specific	0.8804864	0.86991682	0.89105599	
EUR	EUR_phi1e-08_PS	Ancestry Specific	0.87549056	0.86468371	0.88629742	
EUR	EUR_phi1e-10_PS	Ancestry Specific	0.87566151	0.86486024	0.88646278	
EUR	EUR_phi1e-12_PS	Ancestry Specific	0.87467944	0.86385639	0.88550249	
EUR	META_phi1e-02_PS	Trans-Ancestry	0.87079905	0.85980373	0.88179438	
EUR	META_phi1e-04_PS	Trans-Ancestry	0.88017728	0.86958998	0.89076459	
EUR	META_phi1e-06_PS	Trans-Ancestry	0.877046	0.86634757	0.88774442	YES
EUR	META_phi1e-08_PS	Trans-Ancestry	0.87411188	0.86325279	0.88497097	
EUR	META_phi1e-10_PS	Trans-Ancestry	0.87475987	0.86393832	0.88558142	
EUR	META_phi1e-12_PS	Trans-Ancestry	0.87367341	0.86281116	0.88453567	
SAS	META_phi1e-02_PS	Trans-Ancestry	0.83687943	0.76320138	0.91055748	
SAS	META_phi1e-04_PS	Trans-Ancestry	0.87204492	0.80870882	0.93538101	
SAS	META_phi1e-06_PS	Trans-Ancestry	0.89686761	0.83886938	0.95486584	YES
SAS	META_phi1e-08_PS	Trans-Ancestry	0.89450355	0.83679214	0.95221496	
SAS	META_phi1e-10_PS	Trans-Ancestry	0.8998227	0.84341593	0.95622946	
SAS	META_phi1e-12_PS	Trans-Ancestry	0.90425532	0.84974102	0.95876961	

143 **ESM Table 7:** Comparison of AUROC with the Delong Test for each AUROC and each ancestry (Figure 2 and TS6). AS-PS (csx) corresponds to the
144 ancestry-specific PRS (one per ancestry) developed with PRS-CSx + the HLA part of GRS2x. AS-PS (jt) corresponds to the ancestry-specific PRS
145 (one per ancestry) developed with JointPRS + the HLA part of GRS2x. TA-PS corresponds to the trans-ancestral PRS developed with PRS-CSx +
146 HLA part of GRS2x. LDPRED-PS corresponds to the PRS developed with LDpred2 and the HLA part of GRS2x We only added the HLA part of
147 GRS2x (GRS2xInt + GRS2xHLA).
148

Ancestry	PRS1	PRS2	AUROC1	AUROC2	Delta	P-value	CI lower (95%)	CI upper (95%)
AFR	GRS2x	LDPRED-PS	0.8342803	0.83546402	-0.0011837	0.90947997	-0.0215896	0.01922214
AFR	GRS2x	AS-PS (csx)	0.8342803	0.83783144	-0.0035511	0.86428129	-0.0442709	0.03716862
AFR	GRS2x	TA-PS	0.8342803	0.85653409	-0.0222538	0.15444077	-0.052883	0.00837544
AFR	GRS2x	AS-PS (jt)	0.8342803	0.87215909	-0.0378788	0.04794127	-0.0754143	-0.0003433
AMR	GRS2x	LDPRED-PS	0.81182414	0.80937722	0.00244692	0.80140679	-0.0166201	0.02151395
AMR	GRS2x	AS-PS (csx)	0.81182414	0.85571079	-0.0438867	0.0077828	-0.0762072	-0.0115661
AMR	GRS2x	TA-PS	0.81182414	0.85997316	-0.048149	0.0006457	-0.0758102	-0.0204878
AMR	GRS2x	AS-PS (jt)	0.81182414	0.76927934	0.04254479	0.20792401	-0.0236719	0.10876145
EAS	GRS2x	LDPRED-PS	0.81111111	0.83492063	-0.0238095	0.20735527	-0.0608203	0.01320124
EAS	GRS2x	AS-PS (csx)	0.81111111	0.83333333	-0.0222222	0.35392788	-0.069207	0.02476254
EAS	GRS2x	TA-PS	0.81111111	0.82380952	-0.0126984	0.61251857	-0.0618383	0.03644144
EAS	GRS2x	AS-PS (jt)	0.81111111	0.82380952	-0.0126984	0.60949154	-0.0614229	0.03602606
EUR	GRS2x	LDPRED-PS	0.85644302	0.86778072	-0.0113377	2.36E-09	-0.0150595	-0.0076159
EUR	GRS2x	AS-PS (csx)	0.85644302	0.88176221	-0.0253192	2.72E-20	-0.0306959	-0.0199425
EUR	GRS2x	TA-PS	0.85644302	0.877046	-0.020603	1.23E-12	-0.026289	-0.0149169
EUR	GRS2x	AS-PS (jt)	0.85644302	0.87998616	-0.0235431	1.54E-20	-0.0285102	-0.0185761
SAS	GRS2x	LDPRED-PS	0.86613475	0.84367612	0.02245863	0.0874981	-0.0033019	0.04821911
SAS	GRS2x	TA-PS	0.86613475	0.89686761	-0.0307329	0.04433867	-0.0606876	-0.0007781
AMR	AS-PS (csx)	AS-PS (jt)	0.85571079	0.76927934	0.08643145	0.01024824	0.02044774	0.15241515
AMR	TA-PS	AS-PS (jt)	0.86360407	0.76927934	0.09432473	0.00207594	0.03428437	0.15436508
EAS	GRS2x	LDPRED-PS	0.81111111	0.83492063	-0.0238095	0.20735527	-0.0608203	0.01320124
EAS	GRS2x	AS-PS (csx)	0.81111111	0.83333333	-0.0222222	0.35392788	-0.069207	0.02476254
EAS	GRS2x	TA-PS	0.81111111	0.83650794	-0.0253968	0.42066456	-0.0872108	0.03641714

EAS	GRS2x	AS-PS (jt)	0.81111111	0.82380952	-0.0126984	0.60949154	-0.0614229	0.03602606
EAS	LDPRED-PS	AS-PS (csx)	0.83492063	0.83333333	0.0015873	0.95319603	-0.0514175	0.05459215
EAS	LDPRED-PS	TA-PS	0.83492063	0.83650794	-0.0015873	0.9646553	-0.0717944	0.06861982
EAS	LDPRED-PS	AS-PS (jt)	0.83492063	0.82380952	0.01111111	0.67697325	-0.0411633	0.06338556
EAS	AS-PS (csx)	TA-PS	0.83333333	0.83650794	-0.0031746	0.93084331	-0.0748712	0.06852199
EAS	AS-PS (csx)	AS-PS (jt)	0.83333333	0.82380952	0.00952381	0.60975109	-0.0270461	0.0460937
EAS	TA-PS	AS-PS (jt)	0.83650794	0.82380952	0.01269841	0.71273695	-0.0548996	0.08029645
EUR	GRS2x	LDPRED-PS	0.85644302	0.86778072	-0.0113377	2.36E-09	-0.0150595	-0.0076159
EUR	GRS2x	AS-PS (csx)	0.85644302	0.88176221	-0.0253192	2.72E-20	-0.0306959	-0.0199425
EUR	GRS2x	TA-PS	0.85644302	0.88017728	-0.0237343	1.44E-15	-0.029562	-0.0179065
EUR	GRS2x	AS-PS (jt)	0.85644302	0.87998616	-0.0235431	1.54E-20	-0.0285102	-0.0185761
EUR	LDPRED-PS	AS-PS (csx)	0.86778072	0.88176221	-0.0139815	6.10E-08	-0.0190414	-0.0089216
EUR	LDPRED-PS	TA-PS	0.86778072	0.88017728	-0.0123966	8.93E-06	-0.0178669	-0.0069262
EUR	LDPRED-PS	AS-PS (jt)	0.86778072	0.87998616	-0.0122054	5.69E-07	-0.0169885	-0.0074224
EUR	AS-PS (csx)	TA-PS	0.88176221	0.88017728	0.00158493	0.24271593	-0.0010742	0.00424402
EUR	AS-PS (csx)	AS-PS (jt)	0.88176221	0.87998616	0.00177605	0.08396835	-0.0002383	0.00379039
EUR	TA-PS	AS-PS (jt)	0.88017728	0.87998616	0.00019112	0.91508971	-0.0033221	0.00370439
SAS	GRS2x	LDPRED-PS	0.86613475	0.84367612	0.02245863	0.0874981	-0.0033019	0.04821911
SAS	GRS2x	TA-PS	0.86613475	0.90425532	-0.0381206	0.02286231	-0.0709518	-0.0052893
SAS	LDPRED-PS	TA-PS	0.84367612	0.90425532	-0.0605792	0.00182645	-0.0986702	-0.0224882

150 **ESM Table 8:** AUROC for each PRS and each ancestry (Figure 3). TA-PS corresponds to the trans-ancestral PRS (TA) developed with PRS csx
 151 with phi value = 10-06 and the HLA part of GRS2x. (Scale) and (MinMax) versions of TA-PS with different weights are shown.

Ancestry	PRS	AUROC	CI lower (95%)	CI uppr (95%)
MA	GRS2x	0.85381794	0.84290234	0.86473353
MA	TA-PS	0.87664106	0.86659973	0.88668238
MA	TA-PS (S)	0.89202793	0.88262583	0.90143003
MA	TA-PS (M)	0.89054802	0.88106964	0.9000264
NonEUR	GRS2x	0.83087517	0.79525246	0.86649787
NonEUR	TA-PS	0.86397654	0.8320362	0.89591688
NonEUR	TA-PS (S)	0.86953477	0.83803244	0.9010371
NonEUR	TA-PS (M)	0.85936657	0.82782059	0.89091254
AFR	GRS2x	0.8342803	0.76050494	0.90805566
AFR	TA-PS	0.85653409	0.79095648	0.9221117
AFR	TA-PS (S)	0.83925189	0.76718284	0.91132095
AFR	TA-PS (M)	0.8420928	0.77207712	0.91210848
AMR	GRS2x	0.81182414	0.75497681	0.86867147
AMR	TA-PS	0.85997316	0.81088602	0.90906031
AMR	TA-PS (S)	0.89201989	0.84972618	0.9343136
AMR	TA-PS (M)	0.895414	0.8540609	0.9367671
EAS	GRS2x	0.81111111	0.67345499	0.94876723
EAS	TA-PS	0.82380952	0.69046626	0.95715279
EAS	TA-PS (S)	0.7984127	0.65480008	0.94202531
EAS	TA-PS (M)	0.79047619	0.65044051	0.93051188
EUR	GRS2x	0.85644302	0.84490569	0.86798034
EUR	TA-PS	0.877046	0.86634757	0.88774442
EUR	TA-PS (S)	0.89618923	0.88636709	0.90601137
EUR	TA-PS (M)	0.89618923	0.88636709	0.90601137
SAS	GRS2x	0.86613475	0.7982312	0.93403831
SAS	TA-PS	0.89686761	0.83886938	0.95486584
SAS	TA-PS (S)	0.89539007	0.83726558	0.95351456
SAS	TA-PS (M)	0.89125296	0.83214197	0.95036394

152

153 **ESM Table 9:** Comparison of AUROC with the Delong Test for each ancestry and each PRS (Figure 3).
154

Ancestry	PRS1	PRS2	AUROC1	AUROC2	Delta	P-value	CI lower (95%)	CI upper (95%)
MA	GRS2x	TA-PS	0.85381794	0.87664106	-0.0228231	6.10E-17	-0.0281718	-0.0174745
MA	GRS2x	TA-PS (S)	0.85381794	0.89202793	-0.03821	4.67E-31	-0.044672	-0.0317479
MA	GRS2x	TA-PS (M)	0.85381794	0.89054802	-0.0367301	1.49E-26	-0.0434802	-0.0299799
MA	TA-PS	TA-PS (S)	0.87664106	0.89202793	-0.0153869	2.01E-11	-0.0198845	-0.0108892
MA	TA-PS	TA-PS (M)	0.87664106	0.89054802	-0.013907	1.95E-08	-0.0187599	-0.009054
MA	TA-PS (S)	TA-PS (M)	0.89202793	0.89054802	0.00147991	0.07668536	-0.0001586	0.00311841
NonEUR	GRS2x	TA-PS	0.83087517	0.86397654	-0.0331014	4.99E-05	-0.0490959	-0.0171068
NonEUR	GRS2x	TA-PS (S)	0.83087517	0.86953477	-0.0386596	0.00071382	-0.0610493	-0.0162699
NonEUR	GRS2x	TA-PS (M)	0.83087517	0.85936657	-0.0284914	0.03626263	-0.0551595	-0.0018233
NonEUR	TA-PS	TA-PS (S)	0.86397654	0.86953477	-0.0055582	0.4904584	-0.0213562	0.01023969
NonEUR	TA-PS	TA-PS (M)	0.86397654	0.85936657	0.00460998	0.65576743	-0.0156594	0.0248794
NonEUR	TA-PS (S)	TA-PS (M)	0.86953477	0.85936657	0.01016821	0.09715976	-0.0018462	0.02218263
AFR	GRS2x	TA-PS	0.8342803	0.85653409	-0.0222538	0.15444077	-0.052883	0.00837544
AFR	GRS2x	TA-PS (S)	0.8342803	0.83925189	-0.0049716	0.82671348	-0.0494819	0.03953874
AFR	GRS2x	TA-PS (M)	0.8342803	0.8420928	-0.0078125	0.75355887	-0.0565853	0.04096026
AFR	TA-PS	TA-PS (S)	0.85653409	0.83925189	0.0172822	0.36182943	-0.0198634	0.05442778
AFR	TA-PS	TA-PS (M)	0.85653409	0.8420928	0.01444129	0.43046748	-0.0214601	0.05034273
AFR	TA-PS (S)	TA-PS (M)	0.83925189	0.8420928	-0.0028409	0.62549889	-0.0142492	0.00856741
AMR	GRS2x	TA-PS	0.81182414	0.85997316	-0.048149	0.0006457	-0.0758102	-0.0204878
AMR	GRS2x	TA-PS (S)	0.81182414	0.89201989	-0.0801958	2.61E-05	-0.1175747	-0.0428168
AMR	GRS2x	TA-PS (M)	0.81182414	0.895414	-0.0835899	0.00010009	-0.1257023	-0.0414774
AMR	TA-PS	TA-PS (S)	0.85997316	0.89201989	-0.0320467	0.00367183	-0.0536678	-0.0104257
AMR	TA-PS	TA-PS (M)	0.85997316	0.895414	-0.0354408	0.00587768	-0.0606585	-0.0102232

AMR	TA-PS (S)	TA-PS (M)	0.89201989	0.895414	-0.0033941	0.3641831	-0.0107251	0.00393691
EAS	GRS2x	TA-PS	0.81111111	0.82380952	-0.0126984	0.61251857	-0.0618383	0.03644144
EAS	GRS2x	TA-PS (S)	0.81111111	0.7984127	0.01269841	0.64435744	-0.0412176	0.06661441
EAS	GRS2x	TA-PS (M)	0.81111111	0.79047619	0.02063492	0.55517537	-0.0479111	0.08918092
EAS	TA-PS	TA-PS (S)	0.82380952	0.7984127	0.02539683	0.45240188	-0.0408472	0.09164084
EAS	TA-PS	TA-PS (M)	0.82380952	0.79047619	0.03333333	0.38734339	-0.0422436	0.10891029
EAS	TA-PS (S)	TA-PS (M)	0.7984127	0.79047619	0.00793651	0.56398049	-0.0190252	0.03489822
EUR	GRS2x	TA-PS	0.85644302	0.877046	-0.020603	1.23E-12	-0.026289	-0.0149169
EUR	GRS2x	TA-PS (S)	0.85644302	0.89618923	-0.0397462	2.70E-31	-0.0464409	-0.0330515
EUR	GRS2x	TA-PS (M)	0.85644302	0.89618923	-0.0397462	2.70E-31	-0.0464409	-0.0330515
EUR	TA-PS	TA-PS (S)	0.877046	0.89618923	-0.0191432	8.20E-17	-0.0236484	-0.0146381
EUR	TA-PS	TA-PS (M)	0.877046	0.89618923	-0.0191432	8.20E-17	-0.0236484	-0.0146381
EUR	TA-PS (S)	TA-PS (M)	0.89618923	0.89618923	0	1	0	0
SAS	GRS2x	TA-PS	0.86613475	0.89686761	-0.0307329	0.04433867	-0.0606876	-0.0007781
SAS	GRS2x	TA-PS (S)	0.86613475	0.89539007	-0.0292553	0.11972777	-0.0661078	0.00759714
SAS	GRS2x	TA-PS (M)	0.86613475	0.89125296	-0.0251182	0.28203287	-0.0708818	0.02064535
SAS	TA-PS	TA-PS (S)	0.89686761	0.89539007	0.00147754	0.92145133	-0.0278912	0.0308463
SAS	TA-PS	TA-PS (M)	0.89686761	0.89125296	0.00561466	0.73296872	-0.0266397	0.03786905
SAS	TA-PS (S)	TA-PS (M)	0.89539007	0.89125296	0.00413712	0.52368907	-0.0085789	0.01685311

156 **ESM Table 10:** Sensitivity, specificity, and other metrics for different thresholds for the various PRS. Thresholds were calculated in European
157 controls.

				Sensitivity			Specificity			Recall			Precision			F1-score		
Ancestry	PRS	Cutoff (Score)	Cutoff (%)	Value	CI lower (95%)	CI upper (95%)	Value	CI lower (95%)	CI upper (95%)	Value	CI lower (95%)	CI upper (95%)	Value	CI lower (95%)	CI upper (95%)	Value	CI lower (95%)	CI upper (95%)
MA	GRS2x	2.367	0.05	0.420	0.399	0.439	0.951	0.942	0.960	0.420	0.399	0.439	0.902	0.884	0.919	0.573	0.552	0.591
NonEUR	GRS2x	2.367	0.05	0.410	0.347	0.477	0.962	0.939	0.981	0.410	0.347	0.477	0.884	0.818	0.941	0.560	0.495	0.623
AFR	GRS2x	2.367	0.05	0.146	0.056	0.259	0.989	0.963	1.000	0.146	0.056	0.259	0.889	0.583	1.000	0.250	0.105	0.406
AMR	GRS2x	2.367	0.05	0.464	0.374	0.562	0.952	0.907	0.984	0.464	0.374	0.562	0.893	0.793	0.961	0.610	0.518	0.696
EAS	GRS2x	2.367	0.05	0.429	0.208	0.650	1.000	1.000	1.000	0.429	0.208	0.650	1.000	1.000	1.000	0.600	0.345	0.788
EUR	GRS2x	2.367	0.05	0.421	0.400	0.443	0.950	0.940	0.960	0.421	0.400	0.443	0.905	0.887	0.924	0.575	0.554	0.596
SAS	GRS2x	2.367	0.05	0.560	0.408	0.691	0.933	0.863	0.986	0.560	0.408	0.691	0.846	0.694	0.960	0.674	0.535	0.775
MA	TA-PS	2.715	0.05	0.419	0.399	0.439	0.954	0.945	0.962	0.419	0.399	0.439	0.906	0.888	0.923	0.573	0.552	0.593
NonEUR	TA-PS	2.715	0.05	0.300	0.244	0.358	0.975	0.957	0.990	0.300	0.244	0.358	0.894	0.812	0.957	0.450	0.381	0.512
AFR	TA-PS	2.715	0.05	0.205	0.098	0.326	0.989	0.964	1.000	0.205	0.098	0.326	0.917	0.714	1.000	0.338	0.174	0.480
AMR	TA-PS	2.715	0.05	0.418	0.330	0.510	0.960	0.922	0.992	0.418	0.330	0.510	0.898	0.795	0.976	0.570	0.474	0.658
EAS	TA-PS	2.715	0.05	0.000	0.000	0.000	1.000	1.000	1.000	0.000	0.000	0.000	NA	NA	NA	NA	NA	NA
EUR	TA-PS	2.715	0.05	0.430	0.410	0.450	0.950	0.940	0.960	0.430	0.410	0.450	0.907	0.888	0.924	0.584	0.564	0.604
SAS	TA-PS	2.715	0.05	0.275	0.156	0.415	0.973	0.929	1.000	0.275	0.156	0.415	0.875	0.692	1.000	0.419	0.264	0.563
MA	TA-PS (S)	1.552	0.05	0.505	0.485	0.525	0.948	0.938	0.956	0.505	0.485	0.525	0.912	0.896	0.926	0.650	0.632	0.668
NonEUR	TA-PS (S)	1.552	0.05	0.563	0.496	0.627	0.933	0.901	0.960	0.563	0.496	0.627	0.854	0.787	0.908	0.680	0.620	0.733
AFR	TA-PS (S)	1.552	0.05	0.542	0.381	0.674	0.877	0.798	0.938	0.542	0.381	0.674	0.707	0.548	0.842	0.611	0.468	0.719
AMR	TA-PS (S)	1.552	0.05	0.545	0.446	0.638	0.968	0.933	0.992	0.545	0.446	0.638	0.935	0.864	0.985	0.689	0.597	0.760
EAS	TA-PS (S)	1.552	0.05	0.571	0.333	0.789	0.968	0.882	1.000	0.571	0.333	0.789	0.929	0.727	1.000	0.706	0.485	0.865
EUR	TA-PS (S)	1.552	0.05	0.500	0.478	0.520	0.950	0.940	0.960	0.500	0.478	0.520	0.918	0.902	0.934	0.647	0.627	0.665
SAS	TA-PS (S)	1.552	0.05	0.617	0.471	0.756	0.932	0.864	0.975	0.617	0.471	0.756	0.857	0.720	0.950	0.716	0.587	0.815
MA	TA-PS (M)	11.172	0.05	0.503	0.484	0.523	0.943	0.933	0.953	0.503	0.484	0.523	0.904	0.888	0.919	0.646	0.630	0.663
NonEUR	TA-PS (M)	11.172	0.05	0.533	0.468	0.602	0.902	0.865	0.932	0.533	0.468	0.602	0.792	0.716	0.852	0.635	0.578	0.695
AFR	TA-PS (M)	11.172	0.05	0.457	0.321	0.595	0.888	0.818	0.947	0.457	0.321	0.595	0.688	0.520	0.833	0.548	0.411	0.660
AMR	TA-PS (M)	11.172	0.05	0.555	0.457	0.653	0.961	0.919	0.992	0.555	0.457	0.653	0.923	0.841	0.984	0.694	0.609	0.767
EAS	TA-PS (M)	11.172	0.05	0.750	0.556	0.933	0.606	0.429	0.778	0.750	0.556	0.933	0.571	0.370	0.750	0.651	0.465	0.800
EUR	TA-PS (M)	11.172	0.05	0.499	0.478	0.521	0.950	0.939	0.959	0.499	0.478	0.521	0.918	0.902	0.933	0.646	0.627	0.666
SAS	TA-PS (M)	11.172	0.05	0.467	0.333	0.609	0.945	0.892	0.987	0.467	0.333	0.609	0.852	0.708	0.966	0.600	0.469	0.722
MA	GRS2x	1.603	0.10	0.556	0.534	0.575	0.899	0.887	0.911	0.556	0.534	0.575	0.855	0.836	0.872	0.673	0.655	0.691
NonEUR	GRS2x	1.603	0.10	0.529	0.460	0.595	0.894	0.861	0.926	0.529	0.460	0.595	0.777	0.713	0.843	0.629	0.567	0.683
AFR	GRS2x	1.603	0.10	0.318	0.185	0.447	0.932	0.872	0.978	0.318	0.185	0.447	0.714	0.500	0.913	0.438	0.286	0.571

AMR	GRS2x	1.603	0.10	0.572	0.475	0.661	0.861	0.795	0.919	0.572	0.475	0.661	0.775	0.676	0.863	0.659	0.568	0.731
EAS	GRS2x	1.603	0.10	0.526	0.312	0.739	0.903	0.781	1.000	0.526	0.312	0.739	0.800	0.563	1.000	0.629	0.417	0.791
EUR	GRS2x	1.603	0.10	0.558	0.538	0.579	0.900	0.887	0.914	0.558	0.538	0.579	0.864	0.845	0.882	0.678	0.661	0.695
SAS	GRS2x	1.603	0.10	0.664	0.513	0.795	0.905	0.831	0.969	0.664	0.513	0.795	0.821	0.675	0.933	0.732	0.607	0.824
MA	TA-PS	1.739	0.10	0.619	0.599	0.637	0.905	0.892	0.918	0.619	0.599	0.637	0.874	0.857	0.891	0.724	0.708	0.740
NonEUR	TA-PS	1.739	0.10	0.502	0.433	0.566	0.934	0.906	0.960	0.502	0.433	0.566	0.840	0.775	0.902	0.630	0.564	0.682
AFR	TA-PS	1.739	0.10	0.308	0.179	0.447	0.922	0.859	0.976	0.308	0.179	0.447	0.682	0.467	0.880	0.425	0.262	0.559
AMR	TA-PS	1.739	0.10	0.575	0.478	0.670	0.935	0.886	0.976	0.575	0.478	0.670	0.882	0.794	0.956	0.695	0.607	0.767
EAS	TA-PS	1.739	0.10	0.375	0.188	0.588	1.000	1.000	1.000	0.375	0.188	0.588	1.000	1.000	1.000	0.545	0.316	0.741
EUR	TA-PS	1.739	0.10	0.630	0.610	0.651	0.900	0.886	0.912	0.630	0.610	0.651	0.876	0.860	0.891	0.733	0.716	0.749
SAS	TA-PS	1.739	0.10	0.596	0.439	0.740	0.917	0.847	0.974	0.596	0.439	0.740	0.824	0.680	0.944	0.692	0.553	0.804
MA	TA-PS (S)	0.727	0.10	0.715	0.694	0.733	0.896	0.882	0.908	0.715	0.694	0.733	0.879	0.865	0.894	0.789	0.774	0.802
NonEUR	TA-PS (S)	0.727	0.10	0.748	0.685	0.807	0.870	0.830	0.904	0.748	0.685	0.807	0.803	0.748	0.851	0.774	0.727	0.815
AFR	TA-PS (S)	0.727	0.10	0.750	0.612	0.868	0.830	0.744	0.902	0.750	0.612	0.868	0.706	0.574	0.825	0.725	0.615	0.816
AMR	TA-PS (S)	0.727	0.10	0.738	0.649	0.821	0.911	0.850	0.952	0.738	0.649	0.821	0.874	0.791	0.934	0.799	0.731	0.856
EAS	TA-PS (S)	0.727	0.10	0.769	0.571	0.941	0.870	0.733	0.967	0.769	0.571	0.941	0.808	0.615	0.950	0.783	0.621	0.897
EUR	TA-PS (S)	0.727	0.10	0.710	0.690	0.729	0.900	0.886	0.913	0.710	0.690	0.729	0.889	0.873	0.904	0.790	0.775	0.804
SAS	TA-PS (S)	0.727	0.10	0.769	0.638	0.881	0.849	0.757	0.926	0.769	0.638	0.881	0.769	0.634	0.882	0.765	0.659	0.857
MA	TA-PS (M)	10.347	0.10	0.712	0.694	0.730	0.893	0.880	0.905	0.712	0.694	0.730	0.876	0.861	0.890	0.786	0.772	0.799
NonEUR	TA-PS (M)	10.347	0.10	0.726	0.665	0.785	0.850	0.813	0.892	0.726	0.665	0.785	0.772	0.714	0.829	0.748	0.700	0.792
AFR	TA-PS (M)	10.347	0.10	0.640	0.500	0.786	0.843	0.759	0.913	0.640	0.500	0.786	0.684	0.545	0.820	0.659	0.543	0.771
AMR	TA-PS (M)	10.347	0.10	0.780	0.693	0.852	0.911	0.857	0.956	0.780	0.693	0.852	0.878	0.807	0.938	0.825	0.764	0.876
EAS	TA-PS (M)	10.347	0.10	0.762	0.571	0.941	0.467	0.300	0.654	0.762	0.571	0.941	0.500	0.324	0.676	0.600	0.440	0.746
EUR	TA-PS (M)	10.347	0.10	0.710	0.691	0.729	0.900	0.887	0.913	0.710	0.691	0.729	0.888	0.875	0.903	0.789	0.775	0.803
SAS	TA-PS (M)	10.347	0.10	0.683	0.543	0.813	0.918	0.846	0.972	0.683	0.543	0.813	0.844	0.714	0.946	0.753	0.638	0.847
MA	GRS2x	1.318	0.15	0.706	0.689	0.724	0.849	0.833	0.864	0.706	0.689	0.724	0.832	0.815	0.849	0.764	0.750	0.778
NonEUR	GRS2x	1.318	0.15	0.702	0.645	0.761	0.840	0.799	0.880	0.702	0.645	0.761	0.756	0.692	0.815	0.727	0.679	0.776
AFR	GRS2x	1.318	0.15	0.605	0.467	0.745	0.923	0.862	0.976	0.605	0.467	0.745	0.811	0.667	0.932	0.690	0.567	0.800
AMR	GRS2x	1.318	0.15	0.729	0.639	0.809	0.785	0.704	0.853	0.729	0.639	0.809	0.738	0.652	0.822	0.734	0.663	0.800
EAS	GRS2x	1.318	0.15	0.720	0.500	0.909	0.833	0.700	0.940	0.720	0.500	0.909	0.750	0.550	0.917	0.727	0.552	0.864
EUR	GRS2x	1.318	0.15	0.706	0.687	0.725	0.850	0.833	0.866	0.706	0.687	0.725	0.841	0.824	0.858	0.768	0.754	0.783
SAS	GRS2x	1.318	0.15	0.745	0.615	0.863	0.849	0.754	0.924	0.745	0.615	0.863	0.765	0.628	0.879	0.753	0.644	0.851
MA	TA-PS	1.111	0.15	0.736	0.719	0.753	0.853	0.839	0.868	0.736	0.719	0.753	0.842	0.827	0.858	0.786	0.773	0.798
NonEUR	TA-PS	1.111	0.15	0.649	0.585	0.710	0.875	0.837	0.910	0.649	0.585	0.710	0.783	0.724	0.842	0.710	0.658	0.757
AFR	TA-PS	1.111	0.15	0.500	0.358	0.643	0.899	0.830	0.957	0.500	0.358	0.643	0.730	0.577	0.875	0.593	0.457	0.710
AMR	TA-PS	1.111	0.15	0.698	0.616	0.787	0.837	0.769	0.899	0.698	0.616	0.787	0.781	0.697	0.864	0.738	0.667	0.804
EAS	TA-PS	1.111	0.15	0.579	0.353	0.778	0.933	0.833	1.000	0.579	0.353	0.778	0.862	0.636	1.000	0.687	0.476	0.839
EUR	TA-PS	1.111	0.15	0.745	0.727	0.764	0.850	0.834	0.866	0.745	0.727	0.764	0.848	0.831	0.864	0.793	0.779	0.807

SAS	TA-PS	1.111	0.15	0.725	0.587	0.846	0.888	0.814	0.957	0.725	0.587	0.846	0.809	0.674	0.919	0.761	0.653	0.854
MA	TA-PS (S)	0.251	0.15	0.796	0.779	0.811	0.840	0.825	0.855	0.796	0.779	0.811	0.842	0.826	0.857	0.818	0.804	0.829
NonEUR	TA-PS (S)	0.251	0.15	0.810	0.760	0.859	0.782	0.734	0.826	0.810	0.760	0.859	0.722	0.664	0.779	0.763	0.719	0.807
AFR	TA-PS (S)	0.251	0.15	0.837	0.714	0.933	0.786	0.694	0.862	0.837	0.714	0.933	0.673	0.560	0.791	0.745	0.653	0.830
AMR	TA-PS (S)	0.251	0.15	0.787	0.706	0.859	0.782	0.710	0.857	0.787	0.706	0.859	0.752	0.667	0.827	0.769	0.701	0.826
EAS	TA-PS (S)	0.251	0.15	0.762	0.550	0.938	0.769	0.594	0.909	0.762	0.550	0.938	0.696	0.478	0.875	0.727	0.545	0.857
EUR	TA-PS (S)	0.251	0.15	0.795	0.778	0.812	0.850	0.833	0.866	0.795	0.778	0.812	0.856	0.841	0.872	0.825	0.812	0.837
SAS	TA-PS (S)	0.251	0.15	0.854	0.750	0.945	0.792	0.690	0.879	0.854	0.750	0.945	0.726	0.600	0.837	0.784	0.687	0.865
MA	TA-PS (M)	9.871	0.15	0.794	0.778	0.811	0.839	0.822	0.853	0.794	0.778	0.811	0.840	0.824	0.855	0.817	0.804	0.829
NonEUR	TA-PS (M)	9.871	0.15	0.790	0.736	0.842	0.773	0.724	0.815	0.790	0.736	0.842	0.709	0.653	0.764	0.747	0.703	0.789
AFR	TA-PS (M)	9.871	0.15	0.771	0.640	0.886	0.820	0.739	0.904	0.771	0.640	0.886	0.702	0.574	0.826	0.734	0.623	0.822
AMR	TA-PS (M)	9.871	0.15	0.826	0.750	0.898	0.788	0.715	0.856	0.826	0.750	0.898	0.766	0.679	0.841	0.793	0.730	0.849
EAS	TA-PS (M)	9.871	0.15	0.767	0.571	0.944	0.394	0.238	0.571	0.767	0.571	0.944	0.471	0.312	0.645	0.582	0.417	0.733
EUR	TA-PS (M)	9.871	0.15	0.796	0.776	0.813	0.850	0.834	0.866	0.796	0.776	0.813	0.856	0.842	0.871	0.825	0.811	0.837
SAS	TA-PS (M)	9.871	0.15	0.745	0.614	0.867	0.845	0.757	0.926	0.745	0.614	0.867	0.760	0.628	0.880	0.755	0.638	0.840
MA	GRS2x	0.965	0.20	0.760	0.743	0.776	0.800	0.783	0.817	0.760	0.743	0.776	0.802	0.785	0.818	0.781	0.768	0.792
NonEUR	GRS2x	0.965	0.20	0.735	0.676	0.794	0.802	0.760	0.843	0.735	0.676	0.794	0.723	0.662	0.781	0.729	0.681	0.773
AFR	GRS2x	0.965	0.20	0.643	0.511	0.776	0.863	0.789	0.929	0.643	0.511	0.776	0.721	0.587	0.844	0.675	0.568	0.781
AMR	GRS2x	0.965	0.20	0.769	0.685	0.843	0.739	0.659	0.809	0.769	0.685	0.843	0.711	0.620	0.795	0.739	0.664	0.797
EAS	GRS2x	0.965	0.20	0.714	0.500	0.900	0.829	0.692	0.963	0.714	0.500	0.900	0.750	0.550	0.938	0.732	0.552	0.864
EUR	GRS2x	0.965	0.20	0.762	0.744	0.779	0.800	0.781	0.818	0.762	0.744	0.779	0.811	0.793	0.829	0.786	0.772	0.799
SAS	GRS2x	0.965	0.20	0.769	0.639	0.878	0.819	0.723	0.899	0.769	0.639	0.878	0.735	0.608	0.843	0.750	0.645	0.838
MA	TA-PS	0.702	0.20	0.791	0.775	0.808	0.804	0.788	0.822	0.791	0.775	0.808	0.811	0.794	0.828	0.801	0.787	0.814
NonEUR	TA-PS	0.702	0.20	0.721	0.663	0.783	0.831	0.795	0.872	0.721	0.663	0.783	0.750	0.693	0.809	0.735	0.688	0.781
AFR	TA-PS	0.702	0.20	0.647	0.510	0.783	0.855	0.776	0.921	0.647	0.510	0.783	0.705	0.558	0.837	0.674	0.550	0.771
AMR	TA-PS	0.702	0.20	0.760	0.670	0.838	0.798	0.728	0.866	0.760	0.670	0.838	0.760	0.679	0.835	0.760	0.692	0.819
EAS	TA-PS	0.702	0.20	0.625	0.412	0.824	0.935	0.833	1.000	0.625	0.412	0.824	0.875	0.667	1.000	0.727	0.526	0.872
EUR	TA-PS	0.702	0.20	0.798	0.780	0.814	0.800	0.781	0.817	0.798	0.780	0.814	0.818	0.802	0.832	0.808	0.795	0.820
SAS	TA-PS	0.702	0.20	0.769	0.635	0.887	0.822	0.725	0.903	0.769	0.635	0.887	0.744	0.608	0.846	0.753	0.637	0.837
MA	TA-PS (S)	-0.119	0.20	0.850	0.835	0.865	0.790	0.772	0.806	0.850	0.835	0.865	0.811	0.797	0.827	0.830	0.819	0.842
NonEUR	TA-PS (S)	-0.119	0.20	0.872	0.826	0.913	0.728	0.679	0.779	0.872	0.826	0.913	0.693	0.635	0.745	0.772	0.728	0.810
AFR	TA-PS (S)	-0.119	0.20	0.857	0.739	0.944	0.739	0.651	0.826	0.857	0.739	0.944	0.645	0.524	0.754	0.736	0.630	0.820
AMR	TA-PS (S)	-0.119	0.20	0.885	0.817	0.942	0.746	0.673	0.822	0.885	0.817	0.942	0.745	0.669	0.823	0.810	0.749	0.862
EAS	TA-PS (S)	-0.119	0.20	0.769	0.571	0.933	0.600	0.428	0.783	0.769	0.571	0.933	0.576	0.371	0.769	0.667	0.444	0.806
EUR	TA-PS (S)	-0.119	0.20	0.848	0.832	0.863	0.800	0.781	0.819	0.848	0.832	0.863	0.826	0.811	0.843	0.837	0.825	0.849
SAS	TA-PS (S)	-0.119	0.20	0.918	0.830	0.980	0.738	0.629	0.831	0.918	0.830	0.980	0.696	0.586	0.803	0.792	0.704	0.863
MA	TA-PS (M)	9.502	0.20	0.847	0.833	0.860	0.789	0.772	0.806	0.847	0.833	0.860	0.811	0.794	0.825	0.828	0.817	0.839
NonEUR	TA-PS (M)	9.502	0.20	0.840	0.791	0.890	0.724	0.676	0.773	0.840	0.791	0.890	0.680	0.625	0.738	0.752	0.708	0.793

AFR	TA-PS (M)	9.502	0.20	0.813	0.692	0.915	0.787	0.698	0.867	0.813	0.692	0.915	0.673	0.545	0.794	0.738	0.630	0.819
AMR	TA-PS (M)	9.502	0.20	0.876	0.804	0.932	0.733	0.647	0.811	0.876	0.804	0.932	0.734	0.652	0.812	0.797	0.735	0.851
EAS	TA-PS (M)	9.502	0.20	0.769	0.571	0.941	0.364	0.200	0.538	0.769	0.571	0.941	0.459	0.294	0.629	0.576	0.400	0.714
EUR	TA-PS (M)	9.502	0.20	0.848	0.832	0.863	0.800	0.780	0.818	0.848	0.832	0.863	0.827	0.811	0.843	0.837	0.825	0.849
SAS	TA-PS (M)	9.502	0.20	0.833	0.718	0.932	0.792	0.698	0.877	0.833	0.718	0.932	0.723	0.596	0.839	0.772	0.667	0.852
MA	GRS2x	0.453	0.25	0.794	0.778	0.810	0.749	0.731	0.768	0.794	0.778	0.810	0.771	0.754	0.789	0.782	0.769	0.795
NonEUR	GRS2x	0.453	0.25	0.790	0.741	0.844	0.742	0.693	0.788	0.790	0.741	0.844	0.681	0.623	0.739	0.731	0.685	0.777
AFR	GRS2x	0.453	0.25	0.709	0.574	0.826	0.845	0.767	0.916	0.709	0.574	0.826	0.714	0.583	0.827	0.710	0.600	0.804
AMR	GRS2x	0.453	0.25	0.794	0.717	0.874	0.665	0.581	0.748	0.794	0.717	0.874	0.664	0.581	0.743	0.723	0.654	0.787
EAS	GRS2x	0.453	0.25	0.762	0.563	0.938	0.733	0.563	0.882	0.762	0.563	0.938	0.667	0.462	0.842	0.711	0.537	0.836
EUR	GRS2x	0.453	0.25	0.794	0.777	0.811	0.750	0.729	0.770	0.794	0.777	0.811	0.782	0.763	0.798	0.788	0.775	0.801
SAS	GRS2x	0.453	0.25	0.878	0.771	0.957	0.750	0.645	0.841	0.878	0.771	0.957	0.692	0.576	0.800	0.772	0.682	0.848
MA	TA-PS	0.320	0.25	0.838	0.824	0.852	0.755	0.735	0.773	0.838	0.824	0.852	0.784	0.768	0.800	0.810	0.798	0.822
NonEUR	TA-PS	0.320	0.25	0.796	0.736	0.845	0.787	0.740	0.829	0.796	0.736	0.845	0.724	0.667	0.776	0.757	0.712	0.797
AFR	TA-PS	0.320	0.25	0.674	0.531	0.804	0.845	0.762	0.911	0.674	0.531	0.804	0.702	0.565	0.825	0.686	0.564	0.779
AMR	TA-PS	0.320	0.25	0.837	0.758	0.908	0.718	0.636	0.798	0.837	0.758	0.908	0.712	0.633	0.793	0.769	0.704	0.829
EAS	TA-PS	0.320	0.25	0.667	0.450	0.867	0.875	0.739	0.969	0.667	0.450	0.867	0.780	0.562	0.947	0.714	0.514	0.857
EUR	TA-PS	0.320	0.25	0.843	0.826	0.859	0.749	0.730	0.770	0.843	0.826	0.859	0.791	0.775	0.809	0.816	0.804	0.829
SAS	TA-PS	0.320	0.25	0.895	0.805	0.977	0.806	0.704	0.895	0.895	0.805	0.977	0.754	0.630	0.865	0.817	0.727	0.889
MA	TA-PS (S)	-0.377	0.25	0.883	0.869	0.896	0.739	0.721	0.757	0.883	0.869	0.896	0.784	0.768	0.798	0.830	0.819	0.842
NonEUR	TA-PS (S)	-0.377	0.25	0.879	0.833	0.921	0.682	0.627	0.733	0.879	0.833	0.921	0.659	0.599	0.712	0.752	0.708	0.793
AFR	TA-PS (S)	-0.377	0.25	0.877	0.778	0.958	0.693	0.591	0.789	0.877	0.778	0.958	0.606	0.486	0.725	0.718	0.617	0.803
AMR	TA-PS (S)	-0.377	0.25	0.894	0.832	0.952	0.702	0.615	0.777	0.894	0.832	0.952	0.714	0.634	0.790	0.794	0.733	0.848
EAS	TA-PS (S)	-0.377	0.25	0.773	0.571	0.933	0.529	0.346	0.700	0.773	0.571	0.933	0.533	0.345	0.710	0.627	0.439	0.767
EUR	TA-PS (S)	-0.377	0.25	0.883	0.869	0.897	0.749	0.731	0.769	0.883	0.869	0.897	0.799	0.783	0.814	0.839	0.827	0.850
SAS	TA-PS (S)	-0.377	0.25	0.919	0.826	0.980	0.697	0.583	0.790	0.919	0.826	0.980	0.662	0.550	0.776	0.768	0.673	0.850
MA	TA-PS (M)	9.244	0.25	0.882	0.869	0.895	0.739	0.721	0.756	0.882	0.869	0.895	0.782	0.767	0.797	0.829	0.818	0.840
NonEUR	TA-PS (M)	9.244	0.25	0.877	0.833	0.917	0.675	0.620	0.726	0.877	0.833	0.917	0.654	0.598	0.706	0.749	0.705	0.789
AFR	TA-PS (M)	9.244	0.25	0.880	0.780	0.958	0.742	0.644	0.825	0.880	0.780	0.958	0.648	0.531	0.761	0.745	0.648	0.829
AMR	TA-PS (M)	9.244	0.25	0.895	0.833	0.952	0.682	0.603	0.762	0.895	0.833	0.952	0.702	0.625	0.780	0.785	0.725	0.846
EAS	TA-PS (M)	9.244	0.25	0.810	0.632	0.957	0.324	0.167	0.500	0.810	0.632	0.957	0.453	0.313	0.615	0.579	0.428	0.716
EUR	TA-PS (M)	9.244	0.25	0.883	0.869	0.897	0.750	0.730	0.769	0.883	0.869	0.897	0.799	0.782	0.815	0.839	0.827	0.850
SAS	TA-PS (M)	9.244	0.25	0.875	0.772	0.957	0.722	0.617	0.821	0.875	0.772	0.957	0.673	0.559	0.786	0.762	0.667	0.844

159 **ESM Table 11:** Comparison of sensitivity, specificity and F1 score between GRS2x and trans-ancestral scores (TA-PS), based on the Z-test.
160

		Sensitivity		Specificity		F1-score	
Z-test	Ancestry	p_sen	z_sen	p_spe	z_spe	p_f1	z_f1
GRS2x vs TA-PS	MA	2.17E-09	-5.985	3.82E-01	-0.874	3.13E-08	-5.534
GRS2x vs TA-PS	NonEUR	4.36E-01	0.778	1.77E-02	-2.371	9.98E-01	-0.002
GRS2x vs TA-PS	AFR	8.75E-01	0.157	7.23E-01	0.354	8.55E-01	0.183
GRS2x vs TA-PS	AMR	9.43E-01	-0.072	1.87E-02	-2.352	3.80E-01	-0.878
GRS2x vs TA-PS	EAS	1.65E-01	1.390	8.29E-02	-1.734	3.84E-01	0.871
GRS2x vs TA-PS	EUR	7.17E-12	-6.854	9.21E-01	0.100	2.24E-10	-6.344
GRS2x vs TA-PS	SAS	3.46E-01	0.942	7.49E-01	-0.320	4.71E-01	0.721
GRS2x vs TA-PS (S)	MA	9.64E-51	-14.982	5.73E-01	0.563	1.00E-35	-12.477
GRS2x vs TA-PS (S)	NonEUR	2.07E-10	-6.356	1.43E-01	1.465	7.99E-07	-4.936
GRS2x vs TA-PS (S)	AFR	1.09E-10	-6.454	1.59E-04	3.776	8.22E-05	-3.938
GRS2x vs TA-PS (S)	AMR	4.61E-04	-3.503	1.16E-01	-1.571	7.62E-04	-3.366
GRS2x vs TA-PS (S)	EAS	2.57E-02	-2.231	5.46E-01	0.603	1.06E-01	-1.614
GRS2x vs TA-PS (S)	EUR	3.84E-47	-14.421	9.89E-01	0.013	1.85E-37	-12.791
GRS2x vs TA-PS (S)	SAS	1.44E-01	-1.463	1.11E-01	1.593	5.42E-01	-0.610

161

162
163

ESM Table 12: AUROC of the various PRS tested in the validation cohorts.

Cohort	Ancestry	PRS	AUROC	CI lower (95%)	CI upper (95%)
CHOP-CAG	AFR	GRS2x	0.726	0.696	0.756
CHOP-CAG	AFR	TA-PS	0.720	0.690	0.750
CHOP-CAG	AFR	TA-PS (S)	0.729	0.699	0.759
CHOP-CAG	AFR	TA-PS (M)	0.729	0.234	0.681
CHOP-CAG	EUR	GRS2x	0.777	0.753	0.800
CHOP-CAG	EUR	TA-PS	0.781	0.758	0.804
CHOP-CAG	EUR	TA-PS (S)	0.777	0.754	0.800
CHOP-CAG	EUR	TA-PS (M)	0.779	0.684	0.767
CHOP-CAG	SAS	GRS2x	0.724	0.625	0.823
CHOP-CAG	SAS	TA-PS	0.765	0.671	0.860
CHOP-CAG	SAS	TA-PS (S)	0.736	0.644	0.829
CHOP-CAG	SAS	TA-PS (M)	0.747	0.756	0.802
CHOP-CAG	other	GRS2x	0.705	0.662	0.748
CHOP-CAG	other	TA-PS	0.728	0.686	0.769
CHOP-CAG	other	TA-PS (S)	0.720	0.678	0.762
CHOP-CAG	other	TA-PS (M)	0.726	0.699	0.759
GRACE-T1D	EAS	GRS2x	0.777	0.740	0.815
GRACE-T1D	EAS	TA-PS	0.777	0.740	0.814
GRACE-T1D	EAS	TA-PS (S)	0.810	0.775	0.844
GRACE-T1D	EAS	TA-PS (M)	0.806	0.771	0.841
AoU	AFR	GRS2x	0.617	0.574	0.617
AoU	AFR	TA-PS	0.666	0.626	0.666
AoU	AFR	TA-PS (S)	0.652	0.610	0.652
AoU	AFR	TA-PS (M)	0.647	0.604	0.647

AoU	AMR	GRS2x	0.693	0.659	0.693
AoU	AMR	TA-PS	0.679	0.645	0.679
AoU	AMR	TA-PS (S)	0.688	0.654	0.688
AoU	AMR	TA-PS (M)	0.687	0.653	0.687
AoU	EUR	GRS2x	0.821	0.800	0.821
AoU	EUR	TA-PS	0.801	0.781	0.801
AoU	EUR	TA-PS (S)	0.821	0.800	0.821
AoU	EUR	TA-PS (M)	0.819	0.798	0.819
AoU	MA	GRS2x	0.731	0.713	0.749
AoU	MA	TA-PS	0.741	0.725	0.758
AoU	MA	TA-PS (S)	0.752	0.735	0.769
AoU	MA	TA-PS (M)	0.750	0.734	0.767
UKB	MA	GRS2x	0.812	0.795	0.828
UKB	MA	TA-PS	0.843	0.827	0.858
UKB	MA	TA-PS (S)	0.857	0.842	0.873
UKB	MA	TA-PS (M)	0.856	0.840	0.871

165
166

ESM Table 13: Delong Test in the validation cohorts.

Cohort	Ancestry	PRS1	PRS2	AUROC1	AUROC2	p-value	Delta (AUROC1 - AUROC2)	CI lower (95%)	CI upper (95%)
CHOP-CAG	EUR	GRS2x	TA-PS	0.777	0.781	0.341	-0.004	-0.013	0.004
CHOP-CAG	EUR	GRS2x	TA-PS (S)	0.777	0.777	0.859	-0.001	-0.007	0.006
CHOP-CAG	EUR	GRS2x	TA-PS (M)	0.777	0.779	0.455	-0.002	-0.008	0.004
CHOP-CAG	EUR	TA-PS	TA-PS (S)	0.781	0.777	0.309	0.004	-0.003	0.011
CHOP-CAG	EUR	TA-PS	TA-PS (M)	0.781	0.779	0.523	0.002	-0.004	0.008
CHOP-CAG	EUR	TA-PS (S)	TA-PS (M)	0.777	0.779	0.039	-0.002	-0.003	0.000
CHOP-CAG	other	GRS2x	TA-PS	0.705	0.728	0.003	-0.023	-0.038	-0.008
CHOP-CAG	other	GRS2x	TA-PS (S)	0.705	0.720	0.020	-0.015	-0.028	-0.002
CHOP-CAG	other	GRS2x	TA-PS (M)	0.705	0.726	0.002	-0.021	-0.033	-0.008
CHOP-CAG	other	TA-PS	TA-PS (S)	0.728	0.720	0.175	0.008	-0.003	0.019
CHOP-CAG	other	TA-PS	TA-PS (M)	0.728	0.726	0.305	0.002	-0.002	0.006
CHOP-CAG	other	TA-PS (S)	TA-PS (M)	0.720	0.726	0.137	-0.006	-0.013	0.002
CHOP-CAG	AFR	GRS2x	TA-PS	0.726	0.720	0.468	0.006	-0.010	0.021
CHOP-CAG	AFR	GRS2x	TA-PS (S)	0.726	0.729	0.588	-0.003	-0.015	0.009
CHOP-CAG	AFR	GRS2x	TA-PS (M)	0.726	0.729	0.601	-0.003	-0.015	0.008
CHOP-CAG	AFR	TA-PS	TA-PS (S)	0.720	0.729	0.059	-0.009	-0.018	0.000
CHOP-CAG	AFR	TA-PS	TA-PS (M)	0.720	0.729	0.006	-0.009	-0.015	-0.003
CHOP-CAG	AFR	TA-PS (S)	TA-PS (M)	0.729	0.729	0.906	0.000	-0.003	0.004
CHOP-CAG	SAS	GRS2x	TA-PS	0.724	0.765	0.032	-0.041	-0.079	-0.004
CHOP-CAG	SAS	GRS2x	TA-PS (S)	0.724	0.736	0.387	-0.013	-0.041	0.016
CHOP-CAG	SAS	GRS2x	TA-PS (M)	0.724	0.747	0.083	-0.023	-0.050	0.003
CHOP-CAG	SAS	TA-PS	TA-PS (S)	0.765	0.736	0.102	0.029	-0.006	0.063
CHOP-CAG	SAS	TA-PS	TA-PS (M)	0.765	0.747	0.135	0.018	-0.006	0.041
CHOP-CAG	SAS	TA-PS (S)	TA-PS (M)	0.736	0.747	0.087	-0.011	-0.023	0.002
GRACE-T1D	EAS	GRS2x	TA-PS	0.777	0.777	0.251	0.000	0.001	0.001
GRACE-T1D	EAS	GRS2x	TA-PS (S)	0.777	0.810	0.005	-0.032	-0.054	-0.010
GRACE-T1D	EAS	GRS2x	TA-PS (M)	0.777	0.806	0.032	-0.029	-0.055	-0.002
GRACE-T1D	EAS	TA-PS	TA-PS (S)	0.777	0.810	0.004	-0.033	-0.055	-0.010
GRACE-T1D	EAS	TA-PS	TA-PS (M)	0.777	0.806	0.030	-0.029	-0.055	-0.003
GRACE-T1D	EAS	TA-PS (S)	TA-PS (M)	0.810	0.806	0.016	0.007	0.001	0.012
AoU	MA	GRS2x	TA-PS	0.731	0.741	0.048	-0.010	-0.020	0.000
AoU	MA	GRS2x	TA-PS (S)	0.731	0.752	0.000	-0.021	-0.027	-0.015
AoU	MA	GRS2x	TA-PS (M)	0.731	0.750	0.000	-0.019	-0.025	-0.013
AoU	MA	TA-PS	TA-PS (S)	0.741	0.752	0.001	-0.011	-0.017	-0.005

AoU	MA	TA-PS	TA-PS (M)	0.741	0.750	0.015	-0.009	-0.016	-0.002
AoU	MA	TA-PS (S)	TA-PS (M)	0.752	0.750	0.003	0.002	0.001	0.003
AoU	AFR	GRS2x	TA-PS	0.617	0.666	0.000	-0.049	-0.071	-0.027
AoU	AFR	GRS2x	TA-PS (S)	0.617	0.652	0.000	-0.034	-0.047	-0.022
AoU	AFR	GRS2x	TA-PS (M)	0.617	0.647	0.000	-0.030	-0.042	-0.017
AoU	AFR	TA-PS	TA-PS (S)	0.666	0.652	0.052	0.015	0.000	0.029
AoU	AFR	TA-PS	TA-PS (M)	0.666	0.647	0.028	0.019	0.002	0.037
AoU	AFR	TA-PS (S)	TA-PS (M)	0.652	0.647	0.001	0.005	0.002	0.008
AoU	AMR	GRS2x	TA-PS	0.693	0.679	0.136	0.014	-0.004	0.032
AoU	AMR	GRS2x	TA-PS (S)	0.693	0.688	0.345	0.005	-0.005	0.015
AoU	AMR	GRS2x	TA-PS (M)	0.693	0.687	0.246	0.006	-0.004	0.016
AoU	AMR	TA-PS	TA-PS (S)	0.679	0.688	0.180	-0.009	-0.022	0.004
AoU	AMR	TA-PS	TA-PS (M)	0.679	0.687	0.307	-0.008	-0.024	0.007
AoU	AMR	TA-PS (S)	TA-PS (M)	0.688	0.687	0.472	0.001	-0.002	0.003
AoU	EUR	GRS2x	TA-PS	0.821	0.801	0.000	0.020	0.009	0.030
AoU	EUR	GRS2x	TA-PS (S)	0.821	0.821	0.861	0.000	-0.005	0.006
AoU	EUR	GRS2x	TA-PS (M)	0.821	0.819	0.432	0.002	-0.003	0.007
AoU	EUR	TA-PS	TA-PS (S)	0.801	0.821	0.000	-0.019	-0.027	-0.011
AoU	EUR	TA-PS	TA-PS (M)	0.801	0.819	0.000	-0.018	-0.027	-0.009
AoU	EUR	TA-PS (S)	TA-PS (M)	0.821	0.819	0.067	0.001	0.000	0.003
UKB	MA	GRS2x	TA-PS	0.812	0.843	0.000	-0.031	-0.041	-0.021
UKB	MA	GRS2x	TA-PS (S)	0.812	0.857	0.000	-0.046	-0.054	-0.038
UKB	MA	GRS2x	TA-PS (M)	0.812	0.856	0.000	-0.044	-0.051	-0.037
UKB	MA	TA-PS	TA-PS (S)	0.843	0.857	0.000	-0.015	-0.021	-0.008
UKB	MA	TA-PS	TA-PS (M)	0.843	0.856	0.000	-0.013	-0.020	-0.006
UKB	MA	TA-PS (S)	TA-PS (M)	0.857	0.856	0.000	0.002	0.001	0.003

168 **ESM Table 14:** Metrics (sensitivity, specificity, F1) of the PRS by cutoff in the validation cohorts.
169

					Sensitivity			Specificity			F1		
Cohort	PRS	Ancestry	Cutoff (%)	Cutoff (Score)	Value	CI lower (95%)	CI upper (95%)	Value	CI lower (95%)	CI upper (95%)	Value	CI lower (95%)	CI upper (95%)
GRACE-T1D	GRS2x	EAS	5	3.027	0.191	0.149	0.237	0.948	0.921	0.970	0.306	0.249	0.366
GRACE-T1D	TA-PS	EAS	5	2.973	0.190	0.147	0.238	0.948	0.922	0.971	0.306	0.244	0.368
GRACE-T1D	TA-PS (M)	EAS	5	11.493	0.348	0.292	0.404	0.947	0.919	0.971	0.496	0.435	0.556
GRACE-T1D	TA-PS (S)	EAS	5	1.762	0.363	0.310	0.424	0.948	0.922	0.971	0.513	0.454	0.574
GRACE-T1D	GRS2x	EAS	10	2.367	0.502	0.442	0.561	0.899	0.863	0.931	0.624	0.568	0.675
GRACE-T1D	TA-PS	EAS	10	2.311	0.500	0.447	0.560	0.898	0.863	0.930	0.623	0.572	0.672
GRACE-T1D	TA-PS (M)	EAS	10	11.011	0.492	0.433	0.547	0.898	0.862	0.931	0.616	0.562	0.661
GRACE-T1D	TA-PS (S)	EAS	10	1.263	0.527	0.464	0.585	0.897	0.863	0.931	0.646	0.587	0.697
GRACE-T1D	GRS2x	EAS	15	1.701	0.564	0.509	0.622	0.849	0.807	0.888	0.656	0.606	0.704
GRACE-T1D	TA-PS	EAS	15	1.636	0.565	0.513	0.619	0.849	0.806	0.887	0.656	0.608	0.701
GRACE-T1D	TA-PS (M)	EAS	15	10.603	0.631	0.578	0.688	0.849	0.809	0.887	0.707	0.663	0.748
GRACE-T1D	TA-PS (S)	EAS	15	0.860	0.619	0.565	0.673	0.848	0.806	0.889	0.698	0.652	0.738
GRACE-T1D	GRS2x	EAS	20	1.663	0.627	0.572	0.681	0.799	0.750	0.841	0.683	0.637	0.727
GRACE-T1D	TA-PS	EAS	20	1.598	0.618	0.562	0.676	0.799	0.749	0.842	0.677	0.628	0.723
GRACE-T1D	TA-PS (M)	EAS	20	10.305	0.696	0.647	0.745	0.800	0.754	0.843	0.733	0.692	0.770
GRACE-T1D	TA-PS (S)	EAS	20	0.413	0.712	0.662	0.763	0.798	0.753	0.841	0.742	0.701	0.782
GRACE-T1D	GRS2x	EAS	25	1.601	0.651	0.599	0.702	0.748	0.698	0.797	0.681	0.639	0.721
GRACE-T1D	TA-PS	EAS	25	1.531	0.645	0.593	0.698	0.750	0.700	0.795	0.678	0.632	0.723
GRACE-T1D	TA-PS (M)	EAS	25	10.078	0.732	0.681	0.782	0.749	0.699	0.794	0.734	0.695	0.772
GRACE-T1D	TA-PS (S)	EAS	25	0.169	0.733	0.681	0.782	0.751	0.698	0.797	0.736	0.696	0.776
CHOP-CAG	GRS2x	AFR	5	11.694	0.081	0.054	0.109	0.997	0.994	0.999	0.148	0.102	0.195
CHOP-CAG	TA-PS	AFR	5	2.782	0.235	0.190	0.278	0.965	0.954	0.975	0.345	0.290	0.397
CHOP-CAG	TA-PS (S)	AFR	5	3.385	0.218	0.179	0.259	0.975	0.966	0.983	0.333	0.281	0.385

CHOP-CAG	TA-PS (M)	AFR	5	11.775	0.159	0.125	0.195	0.986	0.979	0.992	0.262	0.211	0.314
CHOP-CAG	GRS2x	EUR	5	11.694	0.287	0.247	0.327	0.950	0.941	0.958	0.373	0.326	0.419
CHOP-CAG	TA-PS	EUR	5	2.782	0.288	0.246	0.330	0.950	0.940	0.959	0.374	0.329	0.421
CHOP-CAG	TA-PS (S)	EUR	5	3.385	0.282	0.245	0.323	0.950	0.941	0.958	0.369	0.327	0.411
CHOP-CAG	TA-PS (M)	EUR	5	11.775	0.289	0.251	0.330	0.950	0.940	0.958	0.376	0.333	0.419
CHOP-CAG	GRS2x	other	5	11.694	0.192	0.136	0.248	0.970	0.960	0.979	0.284	0.209	0.353
CHOP-CAG	TA-PS	other	5	2.782	0.252	0.197	0.315	0.951	0.938	0.964	0.334	0.267	0.398
CHOP-CAG	TA-PS (S)	other	5	3.385	0.277	0.212	0.343	0.950	0.937	0.963	0.358	0.284	0.426
CHOP-CAG	TA-PS (M)	other	5	11.775	0.182	0.130	0.237	0.983	0.974	0.990	0.286	0.211	0.358
CHOP-CAG	GRS2x	SAS	5	11.694	0.194	0.069	0.353	0.972	0.951	0.990	0.269	0.105	0.438
CHOP-CAG	TA-PS	SAS	5	2.782	0.362	0.200	0.546	0.958	0.934	0.979	0.407	0.233	0.578
CHOP-CAG	TA-PS (S)	SAS	5	3.385	0.194	0.063	0.345	0.959	0.933	0.980	0.240	0.087	0.401
CHOP-CAG	TA-PS (M)	SAS	5	11.775	0.229	0.091	0.387	0.959	0.937	0.979	0.280	0.118	0.452
CHOP-CAG	GRS2x	AFR	10	10.827	0.116	0.084	0.150	0.991	0.986	0.996	0.202	0.150	0.255
CHOP-CAG	TA-PS	AFR	10	2.108	0.334	0.287	0.382	0.923	0.906	0.936	0.414	0.365	0.465
CHOP-CAG	TA-PS (S)	AFR	10	2.554	0.310	0.262	0.360	0.941	0.928	0.954	0.409	0.359	0.461
CHOP-CAG	TA-PS (M)	AFR	10	11.057	0.248	0.205	0.292	0.964	0.955	0.974	0.360	0.309	0.411
CHOP-CAG	GRS2x	EUR	10	10.827	0.433	0.387	0.475	0.900	0.888	0.911	0.448	0.409	0.485
CHOP-CAG	TA-PS	EUR	10	2.108	0.425	0.380	0.469	0.899	0.888	0.912	0.441	0.400	0.480
CHOP-CAG	TA-PS (S)	EUR	10	2.554	0.409	0.365	0.453	0.900	0.887	0.911	0.428	0.388	0.466
CHOP-CAG	TA-PS (M)	EUR	10	11.057	0.421	0.374	0.467	0.900	0.887	0.911	0.438	0.395	0.479
CHOP-CAG	GRS2x	other	10	10.827	0.301	0.241	0.368	0.940	0.925	0.954	0.370	0.307	0.445
CHOP-CAG	TA-PS	other	10	2.108	0.395	0.330	0.465	0.899	0.880	0.915	0.408	0.350	0.466
CHOP-CAG	TA-PS (S)	other	10	2.554	0.366	0.300	0.433	0.913	0.894	0.928	0.399	0.333	0.459
CHOP-CAG	TA-PS (M)	other	10	11.057	0.273	0.206	0.332	0.945	0.931	0.959	0.348	0.272	0.412
CHOP-CAG	GRS2x	SAS	10	10.827	0.365	0.194	0.548	0.924	0.894	0.951	0.349	0.197	0.492
CHOP-CAG	TA-PS	SAS	10	2.108	0.500	0.323	0.676	0.875	0.833	0.912	0.364	0.230	0.500

CHOP-CAG	TA-PS (S)	SAS	10	2.554	0.333	0.172	0.519	0.883	0.843	0.916	0.270	0.139	0.410
CHOP-CAG	TA-PS (M)	SAS	10	11.057	0.469	0.286	0.667	0.885	0.844	0.918	0.364	0.222	0.500
CHOP-CAG	GRS2x	AFR	15	10.131	0.159	0.125	0.197	0.984	0.976	0.990	0.261	0.210	0.314
CHOP-CAG	TA-PS	AFR	15	1.629	0.412	0.361	0.462	0.862	0.843	0.880	0.433	0.388	0.478
CHOP-CAG	TA-PS (S)	AFR	15	1.807	0.417	0.365	0.470	0.871	0.855	0.888	0.444	0.398	0.492
CHOP-CAG	TA-PS (M)	AFR	15	10.483	0.345	0.296	0.400	0.923	0.908	0.937	0.426	0.376	0.479
CHOP-CAG	GRS2x	EUR	15	10.131	0.531	0.486	0.576	0.850	0.836	0.865	0.467	0.431	0.501
CHOP-CAG	TA-PS	EUR	15	1.629	0.540	0.492	0.583	0.850	0.836	0.865	0.471	0.434	0.507
CHOP-CAG	TA-PS (S)	EUR	15	1.807	0.530	0.483	0.574	0.851	0.835	0.865	0.466	0.428	0.501
CHOP-CAG	TA-PS (M)	EUR	15	10.483	0.527	0.481	0.570	0.850	0.836	0.865	0.465	0.424	0.497
CHOP-CAG	GRS2x	other	15	10.131	0.362	0.298	0.430	0.898	0.880	0.914	0.379	0.318	0.438
CHOP-CAG	TA-PS	other	15	1.629	0.486	0.416	0.549	0.848	0.827	0.868	0.420	0.363	0.472
CHOP-CAG	TA-PS (S)	other	15	1.807	0.444	0.374	0.522	0.849	0.826	0.871	0.394	0.337	0.453
CHOP-CAG	TA-PS (M)	other	15	10.483	0.395	0.326	0.466	0.903	0.885	0.920	0.413	0.349	0.473
CHOP-CAG	GRS2x	SAS	15	10.131	0.439	0.261	0.613	0.870	0.830	0.910	0.323	0.184	0.460
CHOP-CAG	TA-PS	SAS	15	1.629	0.500	0.324	0.680	0.835	0.790	0.875	0.324	0.206	0.451
CHOP-CAG	TA-PS (S)	SAS	15	1.807	0.500	0.333	0.667	0.795	0.748	0.841	0.289	0.178	0.400
CHOP-CAG	TA-PS (M)	SAS	15	10.483	0.469	0.300	0.640	0.822	0.781	0.864	0.295	0.174	0.408
CHOP-CAG	GRS2x	AFR	20	9.590	0.234	0.191	0.276	0.973	0.964	0.981	0.352	0.295	0.403
CHOP-CAG	TA-PS	AFR	20	1.230	0.501	0.451	0.555	0.801	0.780	0.823	0.455	0.412	0.501
CHOP-CAG	TA-PS (S)	AFR	20	1.324	0.520	0.471	0.567	0.803	0.781	0.824	0.469	0.424	0.507
CHOP-CAG	TA-PS (M)	AFR	20	10.047	0.430	0.383	0.480	0.856	0.838	0.875	0.444	0.400	0.488
CHOP-CAG	GRS2x	EUR	20	9.590	0.609	0.567	0.651	0.799	0.784	0.815	0.467	0.431	0.503
CHOP-CAG	TA-PS	EUR	20	1.230	0.616	0.573	0.660	0.800	0.784	0.816	0.472	0.438	0.505
CHOP-CAG	TA-PS (S)	EUR	20	1.324	0.605	0.563	0.648	0.800	0.784	0.817	0.465	0.430	0.500
CHOP-CAG	TA-PS (M)	EUR	20	10.047	0.614	0.571	0.658	0.800	0.785	0.817	0.471	0.436	0.504
CHOP-CAG	GRS2x	other	20	9.590	0.455	0.386	0.524	0.852	0.831	0.873	0.405	0.348	0.463

CHOP-CAG	TA-PS	other	20	1.230	0.555	0.491	0.625	0.798	0.774	0.820	0.420	0.368	0.472
CHOP-CAG	TA-PS (S)	other	20	1.324	0.547	0.483	0.613	0.792	0.768	0.814	0.411	0.363	0.460
CHOP-CAG	TA-PS (M)	other	20	10.047	0.479	0.410	0.550	0.847	0.824	0.868	0.416	0.358	0.468
CHOP-CAG	GRS2x	SAS	20	9.590	0.500	0.308	0.680	0.807	0.762	0.851	0.297	0.184	0.412
CHOP-CAG	TA-PS	SAS	20	1.230	0.571	0.393	0.758	0.769	0.722	0.817	0.304	0.195	0.411
CHOP-CAG	TA-PS (S)	SAS	20	1.324	0.600	0.417	0.778	0.753	0.700	0.800	0.303	0.186	0.423
CHOP-CAG	TA-PS (M)	SAS	20	10.047	0.600	0.414	0.781	0.769	0.720	0.816	0.315	0.202	0.433
CHOP-CAG	GRS2x	AFR	25	9.160	0.290	0.240	0.336	0.952	0.940	0.962	0.397	0.340	0.448
CHOP-CAG	TA-PS	AFR	25	0.882	0.558	0.508	0.610	0.743	0.720	0.767	0.452	0.411	0.490
CHOP-CAG	TA-PS (S)	AFR	25	0.934	0.583	0.534	0.636	0.743	0.720	0.766	0.467	0.425	0.506
CHOP-CAG	TA-PS (M)	AFR	25	9.731	0.510	0.461	0.556	0.802	0.780	0.822	0.461	0.419	0.502
CHOP-CAG	GRS2x	EUR	25	9.160	0.671	0.632	0.710	0.749	0.731	0.764	0.459	0.429	0.488
CHOP-CAG	TA-PS	EUR	25	0.882	0.694	0.651	0.735	0.749	0.732	0.768	0.472	0.438	0.504
CHOP-CAG	TA-PS (S)	EUR	25	0.934	0.646	0.600	0.686	0.750	0.731	0.767	0.447	0.412	0.482
CHOP-CAG	TA-PS (M)	EUR	25	9.731	0.670	0.625	0.711	0.750	0.730	0.768	0.460	0.426	0.492
CHOP-CAG	GRS2x	other	25	9.160	0.504	0.433	0.571	0.815	0.794	0.837	0.403	0.348	0.460
CHOP-CAG	TA-PS	other	25	0.882	0.610	0.542	0.678	0.734	0.707	0.759	0.400	0.356	0.449
CHOP-CAG	TA-PS (S)	other	25	0.934	0.605	0.535	0.677	0.742	0.717	0.769	0.403	0.357	0.453
CHOP-CAG	TA-PS (M)	other	25	9.731	0.551	0.482	0.619	0.795	0.771	0.818	0.415	0.365	0.467
CHOP-CAG	GRS2x	SAS	25	9.160	0.500	0.308	0.667	0.741	0.688	0.789	0.254	0.147	0.350
CHOP-CAG	TA-PS	SAS	25	0.882	0.605	0.407	0.772	0.692	0.634	0.746	0.262	0.166	0.360
CHOP-CAG	TA-PS (S)	SAS	25	0.934	0.633	0.440	0.800	0.685	0.631	0.740	0.271	0.168	0.366
CHOP-CAG	TA-PS (M)	SAS	25	9.731	0.600	0.414	0.774	0.716	0.662	0.769	0.275	0.182	0.374
AoU	GRS2x	AFR	5	12.077	0.170	0.120	0.218	0.952	0.951	0.952	0.072	0.049	0.097
AoU	GRS2x	AMR	5	14.346	0.225	0.180	0.263	0.952	0.952	0.953	0.098	0.076	0.115
AoU	GRS2x	EUR	5	14.165	0.451	0.422	0.481	0.954	0.954	0.955	0.160	0.147	0.174
AoU	GRS2x	MA	5	14.049	0.331	0.311	0.356	0.953	0.953	0.954	0.126	0.117	0.138

AoU	TA-PS	AFR	5	1.783	0.170	0.130	0.216	0.952	0.951	0.952	0.072	0.055	0.093
AoU	TA-PS	AMR	5	2.254	0.213	0.179	0.263	0.952	0.952	0.953	0.093	0.076	0.112
AoU	TA-PS	EUR	5	2.535	0.345	0.320	0.381	0.953	0.953	0.954	0.122	0.110	0.136
AoU	TA-PS	MA	5	2.329	0.285	0.263	0.305	0.953	0.953	0.953	0.108	0.100	0.117
AoU	TA-PS (S)	AFR	5	2.550	0.195	0.154	0.245	0.952	0.951	0.953	0.083	0.065	0.106
AoU	TA-PS (S)	AMR	5	3.677	0.252	0.212	0.287	0.953	0.952	0.953	0.110	0.091	0.127
AoU	TA-PS (S)	EUR	5	3.530	0.426	0.398	0.458	0.954	0.954	0.955	0.151	0.138	0.164
AoU	TA-PS (S)	MA	5	3.397	0.334	0.311	0.362	0.953	0.953	0.954	0.127	0.117	0.137
AoU	TA-PS (M)	AFR	5	10.083	0.195	0.153	0.245	0.952	0.951	0.953	0.083	0.065	0.104
AoU	TA-PS (M)	AMR	5	11.042	0.244	0.206	0.290	0.953	0.952	0.953	0.106	0.088	0.124
AoU	TA-PS (M)	EUR	5	10.867	0.430	0.402	0.451	0.954	0.954	0.955	0.153	0.140	0.164
AoU	TA-PS (M)	MA	5	10.774	0.338	0.316	0.364	0.953	0.953	0.954	0.128	0.119	0.139
AoU	GRS2x	AFR	10	11.356	0.275	0.220	0.321	0.902	0.902	0.903	0.066	0.049	0.079
AoU	GRS2x	AMR	10	13.668	0.360	0.312	0.402	0.904	0.903	0.904	0.088	0.076	0.102
AoU	GRS2x	EUR	10	13.382	0.587	0.560	0.617	0.905	0.905	0.906	0.114	0.104	0.125
AoU	GRS2x	MA	10	13.244	0.444	0.422	0.469	0.904	0.904	0.905	0.093	0.087	0.101
AoU	TA-PS	AFR	10	1.369	0.295	0.231	0.338	0.903	0.902	0.903	0.070	0.053	0.083
AoU	TA-PS	AMR	10	1.767	0.322	0.282	0.373	0.903	0.902	0.904	0.078	0.065	0.092
AoU	TA-PS	EUR	10	1.952	0.522	0.490	0.562	0.905	0.904	0.905	0.102	0.094	0.112
AoU	TA-PS	MA	10	1.785	0.412	0.387	0.433	0.904	0.903	0.904	0.086	0.080	0.093
AoU	TA-PS (S)	AFR	10	1.936	0.335	0.284	0.386	0.903	0.902	0.904	0.080	0.066	0.097
AoU	TA-PS (S)	AMR	10	2.979	0.329	0.284	0.375	0.903	0.903	0.904	0.080	0.069	0.094
AoU	TA-PS (S)	EUR	10	2.765	0.597	0.568	0.627	0.905	0.905	0.906	0.116	0.106	0.127
AoU	TA-PS (S)	MA	10	2.684	0.460	0.437	0.484	0.904	0.904	0.905	0.096	0.090	0.103
AoU	TA-PS (M)	AFR	10	9.604	0.350	0.298	0.399	0.903	0.903	0.904	0.084	0.068	0.099
AoU	TA-PS (M)	AMR	10	10.499	0.322	0.279	0.364	0.903	0.902	0.904	0.078	0.066	0.092
AoU	TA-PS (M)	EUR	10	10.251	0.599	0.571	0.628	0.905	0.905	0.906	0.117	0.107	0.127

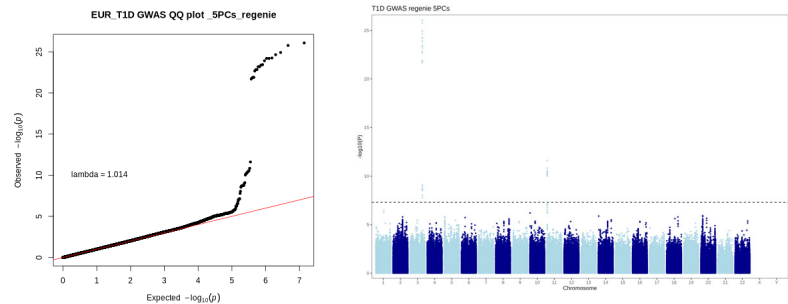
AoU	TA-PS (M)	MA	10	10.211	0.460	0.434	0.485	0.904	0.904	0.905	0.096	0.090	0.104
AoU	GRS2x	AFR	15	10.856	0.355	0.298	0.407	0.853	0.852	0.854	0.059	0.048	0.070
AoU	GRS2x	AMR	15	13.167	0.422	0.372	0.471	0.854	0.853	0.855	0.072	0.062	0.081
AoU	GRS2x	EUR	15	12.869	0.659	0.631	0.685	0.856	0.855	0.856	0.088	0.080	0.096
AoU	GRS2x	MA	15	12.706	0.501	0.479	0.524	0.854	0.854	0.855	0.073	0.067	0.078
AoU	TA-PS	AFR	15	1.051	0.365	0.318	0.421	0.853	0.852	0.854	0.061	0.051	0.072
AoU	TA-PS	AMR	15	1.460	0.388	0.345	0.431	0.853	0.853	0.854	0.066	0.057	0.075
AoU	TA-PS	EUR	15	1.571	0.599	0.567	0.634	0.855	0.854	0.855	0.080	0.073	0.089
AoU	TA-PS	MA	15	1.428	0.498	0.471	0.524	0.854	0.854	0.854	0.072	0.067	0.077
AoU	TA-PS (S)	AFR	15	1.466	0.390	0.332	0.442	0.853	0.852	0.854	0.065	0.053	0.078
AoU	TA-PS (S)	AMR	15	2.565	0.399	0.349	0.446	0.854	0.853	0.854	0.068	0.057	0.077
AoU	TA-PS (S)	EUR	15	2.238	0.661	0.634	0.689	0.856	0.855	0.856	0.089	0.082	0.096
AoU	TA-PS (S)	MA	15	2.187	0.533	0.501	0.553	0.855	0.854	0.855	0.077	0.072	0.083
AoU	TA-PS (M)	AFR	15	9.228	0.390	0.332	0.442	0.853	0.853	0.854	0.065	0.053	0.078
AoU	TA-PS (M)	AMR	15	10.172	0.399	0.346	0.439	0.854	0.853	0.854	0.068	0.057	0.078
AoU	TA-PS (M)	EUR	15	9.844	0.653	0.628	0.685	0.855	0.855	0.856	0.088	0.081	0.096
AoU	TA-PS (M)	MA	15	9.827	0.528	0.495	0.549	0.854	0.854	0.855	0.076	0.071	0.082
AoU	GRS2x	AFR	20	10.461	0.390	0.333	0.454	0.803	0.802	0.803	0.050	0.041	0.058
AoU	GRS2x	AMR	20	12.771	0.477	0.419	0.517	0.804	0.803	0.805	0.062	0.052	0.070
AoU	GRS2x	EUR	20	12.444	0.708	0.678	0.739	0.806	0.805	0.806	0.072	0.067	0.079
AoU	GRS2x	MA	20	12.266	0.555	0.533	0.580	0.804	0.804	0.805	0.061	0.058	0.066
AoU	TA-PS	AFR	20	0.824	0.435	0.375	0.486	0.803	0.802	0.804	0.055	0.046	0.066
AoU	TA-PS	AMR	20	1.226	0.422	0.377	0.463	0.803	0.802	0.804	0.055	0.047	0.063
AoU	TA-PS	EUR	20	1.271	0.662	0.631	0.697	0.805	0.805	0.806	0.068	0.063	0.074
AoU	TA-PS	MA	20	1.150	0.553	0.530	0.579	0.804	0.804	0.805	0.061	0.058	0.065
AoU	TA-PS (S)	AFR	20	1.099	0.445	0.378	0.495	0.803	0.802	0.804	0.057	0.047	0.066
AoU	TA-PS (S)	AMR	20	2.209	0.469	0.420	0.517	0.804	0.803	0.804	0.061	0.053	0.069

AoU	TA-PS (S)	EUR	20	1.819	0.706	0.683	0.735	0.806	0.805	0.806	0.072	0.067	0.078
AoU	TA-PS (S)	MA	20	1.788	0.583	0.555	0.603	0.805	0.804	0.805	0.064	0.060	0.069
AoU	TA-PS (M)	AFR	20	8.931	0.425	0.357	0.482	0.803	0.802	0.804	0.054	0.046	0.064
AoU	TA-PS (M)	AMR	20	9.880	0.465	0.413	0.508	0.804	0.803	0.805	0.060	0.051	0.068
AoU	TA-PS (M)	EUR	20	9.508	0.706	0.680	0.733	0.806	0.805	0.806	0.072	0.066	0.078
AoU	TA-PS (M)	MA	20	9.502	0.583	0.558	0.603	0.805	0.804	0.805	0.064	0.060	0.068
AoU	GRS2x	AFR	25	10.110	0.440	0.385	0.500	0.753	0.752	0.753	0.045	0.037	0.053
AoU	GRS2x	AMR	25	12.406	0.512	0.458	0.557	0.754	0.753	0.754	0.054	0.046	0.060
AoU	GRS2x	EUR	25	12.056	0.755	0.731	0.784	0.755	0.755	0.756	0.062	0.058	0.068
AoU	GRS2x	MA	25	11.892	0.603	0.576	0.629	0.754	0.754	0.755	0.054	0.051	0.058
AoU	TA-PS	AFR	25	0.628	0.485	0.418	0.550	0.753	0.752	0.754	0.050	0.042	0.059
AoU	TA-PS	AMR	25	1.002	0.484	0.432	0.537	0.753	0.753	0.754	0.051	0.043	0.058
AoU	TA-PS	EUR	25	1.020	0.727	0.704	0.757	0.755	0.755	0.756	0.060	0.056	0.065
AoU	TA-PS	MA	25	0.915	0.616	0.591	0.641	0.754	0.754	0.755	0.055	0.052	0.059
AoU	TA-PS (S)	AFR	25	0.785	0.475	0.409	0.531	0.753	0.752	0.754	0.049	0.041	0.057
AoU	TA-PS (S)	AMR	25	1.878	0.508	0.460	0.554	0.754	0.753	0.754	0.053	0.046	0.061
AoU	TA-PS (S)	EUR	25	1.449	0.751	0.728	0.776	0.755	0.755	0.756	0.062	0.057	0.067
AoU	TA-PS (S)	MA	25	1.417	0.628	0.604	0.652	0.754	0.754	0.755	0.056	0.053	0.059
AoU	TA-PS (M)	AFR	25	8.668	0.475	0.410	0.529	0.753	0.752	0.754	0.049	0.040	0.057
AoU	TA-PS (M)	AMR	25	9.629	0.512	0.459	0.554	0.754	0.753	0.754	0.054	0.046	0.061
AoU	TA-PS (M)	EUR	25	9.216	0.747	0.723	0.775	0.755	0.755	0.756	0.062	0.057	0.067
AoU	TA-PS (M)	MA	25	9.220	0.622	0.599	0.645	0.754	0.754	0.755	0.056	0.053	0.059
UKB	GRS2x	MA	5	0.000	0.409	0.376	0.447	0.950	0.949	0.951	0.028	0.025	0.032
UKB	TA-PS	MA	5	0.000	0.461	0.425	0.495	0.950	0.949	0.951	0.032	0.029	0.035
UKB	TA-PS (S)	MA	5	0.000	0.533	0.501	0.563	0.950	0.949	0.951	0.037	0.033	0.040
UKB	TA-PS (M)	MA	5	0.000	0.528	0.496	0.563	0.950	0.949	0.951	0.036	0.033	0.040
UKB	GRS2x	MA	10	0.000	0.533	0.496	0.569	0.900	0.899	0.901	0.019	0.017	0.021

UKB	TA-PS	MA	10	0.000	0.606	0.569	0.638	0.900	0.899	0.901	0.021	0.019	0.023
UKB	TA-PS (S)	MA	10	0.000	0.669	0.634	0.702	0.900	0.899	0.901	0.024	0.022	0.026
UKB	TA-PS (M)	MA	10	0.000	0.658	0.626	0.694	0.900	0.899	0.901	0.023	0.021	0.025
UKB	GRS2x	MA	15	0.000	0.611	0.579	0.642	0.850	0.849	0.851	0.015	0.013	0.016
UKB	TA-PS	MA	15	0.000	0.693	0.661	0.723	0.850	0.849	0.851	0.016	0.015	0.018
UKB	TA-PS (S)	MA	15	0.000	0.736	0.704	0.768	0.850	0.849	0.851	0.017	0.016	0.019
UKB	TA-PS (M)	MA	15	0.000	0.737	0.705	0.767	0.850	0.849	0.851	0.018	0.016	0.019
UKB	GRS2x	MA	20	0.000	0.683	0.652	0.715	0.800	0.799	0.801	0.012	0.011	0.013
UKB	TA-PS	MA	20	0.000	0.739	0.708	0.772	0.800	0.799	0.801	0.013	0.012	0.014
UKB	TA-PS (S)	MA	20	0.000	0.783	0.752	0.809	0.800	0.799	0.801	0.014	0.013	0.015
UKB	TA-PS (M)	MA	20	0.000	0.785	0.755	0.814	0.800	0.799	0.801	0.014	0.013	0.015
UKB	GRS2x	MA	25	0.000	0.732	0.702	0.761	0.750	0.749	0.751	0.011	0.010	0.011
UKB	TA-PS	MA	25	0.000	0.785	0.757	0.813	0.750	0.749	0.751	0.010	0.012	0.012
UKB	TA-PS (S)	MA	25	0.000	0.826	0.801	0.851	0.750	0.749	0.751	0.012	0.011	0.013
UKB	TA-PS (M)	MA	25	0.000	0.827	0.799	0.852	0.750	0.749	0.751	0.012	0.011	0.013

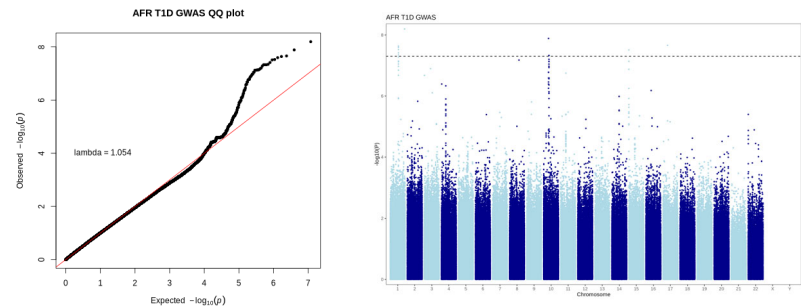
a EUR T1D GWAS

N=2113 cases and N= 1877 controls (all from CaCo)



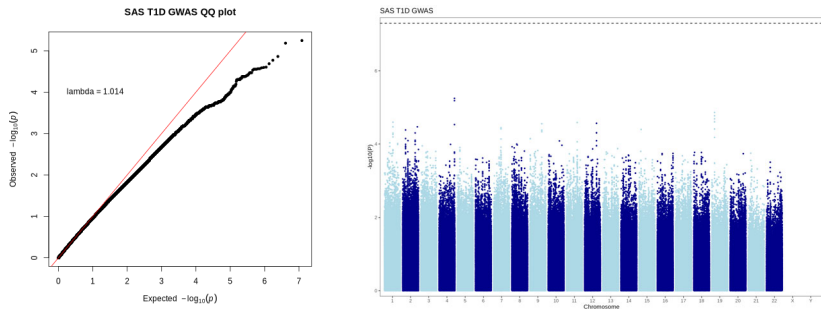
b AFR T1D GWAS

N=48 cases and N=88 controls (43 from CaCo and 45 from 1KG)



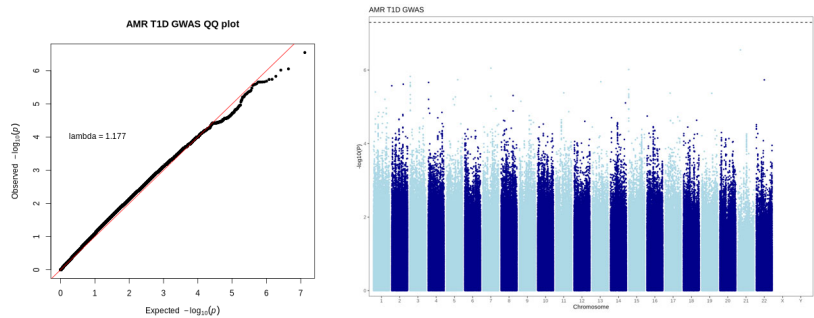
c SAS T1D GWAS

N=47 cases and N=72 controls (48 from CaCo and 24 from 1KG)



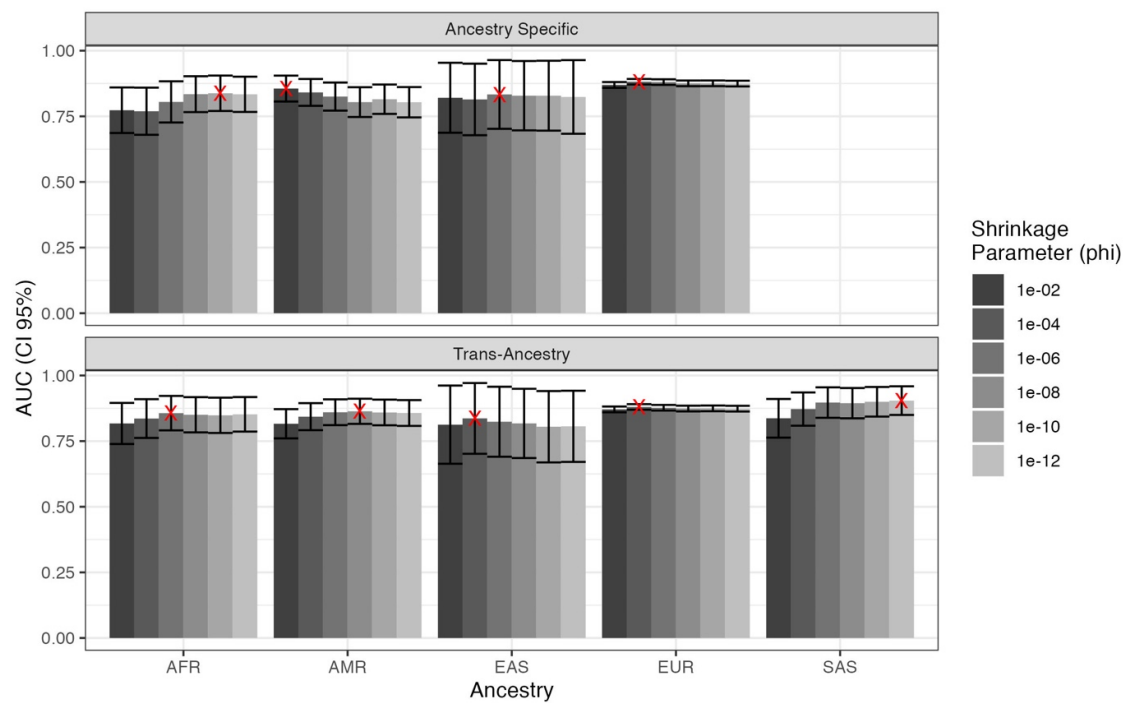
d AMR T1D GWAS

N=103 cases and N=123 controls (23 from CaCo and 100 from 1KG)



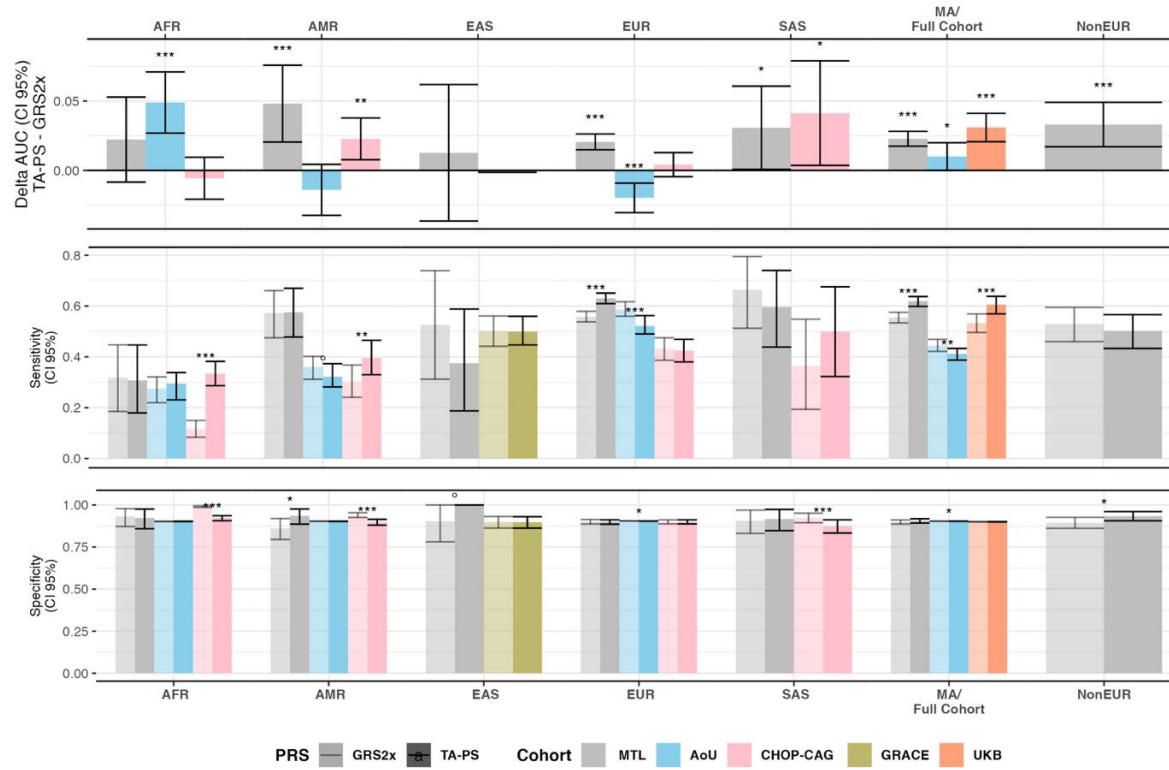
174 **ESM Fig. 1:** Manhattan plot and QQ plot of a pseudo-genome-wide association studies (GWAS) for type 1 diabetes in various ancestries included
175 in the Montreal-based cohort. a. Pseudo-GWAS results including cases of European ancestry of the Montreal-based cohort and ancestry-matched
176 controls. The genomic inflation factor (λ) was 1.014. b. Pseudo-GWAS results including cases of African ancestry of the Montreal-based
177 cohort and ancestry-matched controls. The genomic inflation factor (λ) was 1.054. c. Pseudo-GWAS results including cases of South Asian
178 ancestry of the Montreal-based cohort and ancestry-matched controls. The genomic inflation factor (λ) was 1.014. d. Pseudo-GWAS results
179 including cases of Hispanic ancestry of the Montreal-based cohort and ancestry-matched controls. The genomic inflation factor (λ) was
180 1.177.
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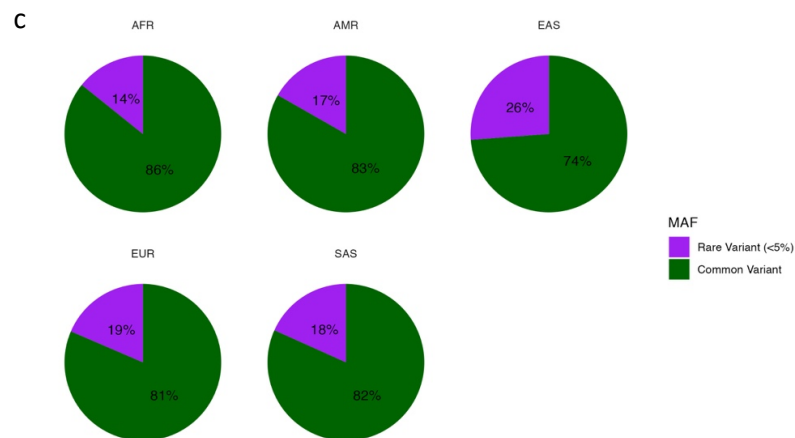
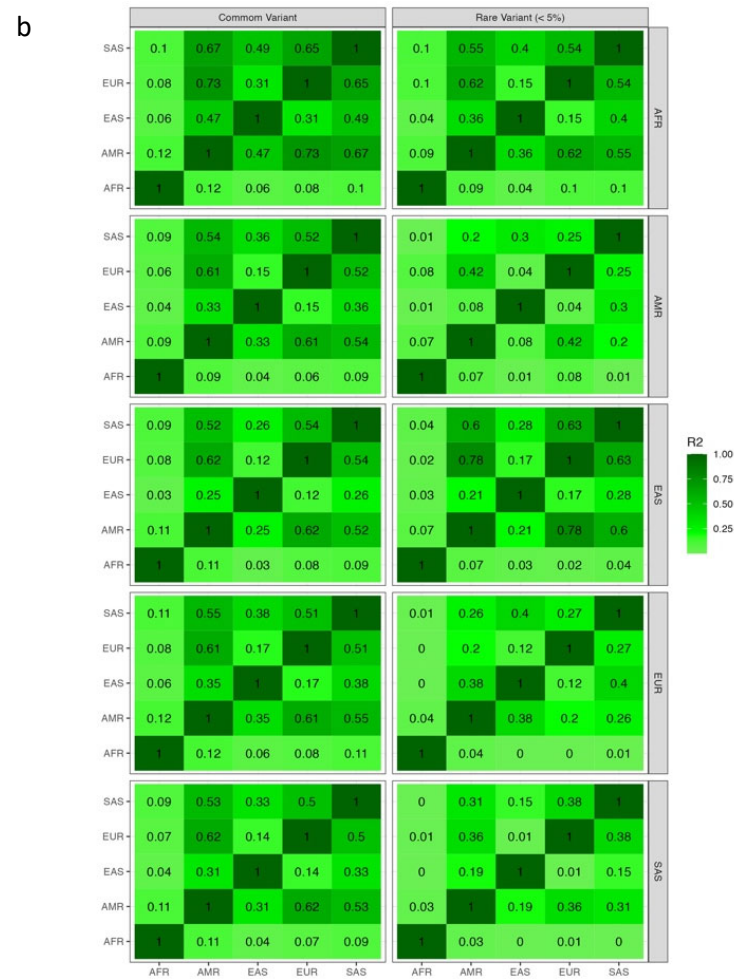
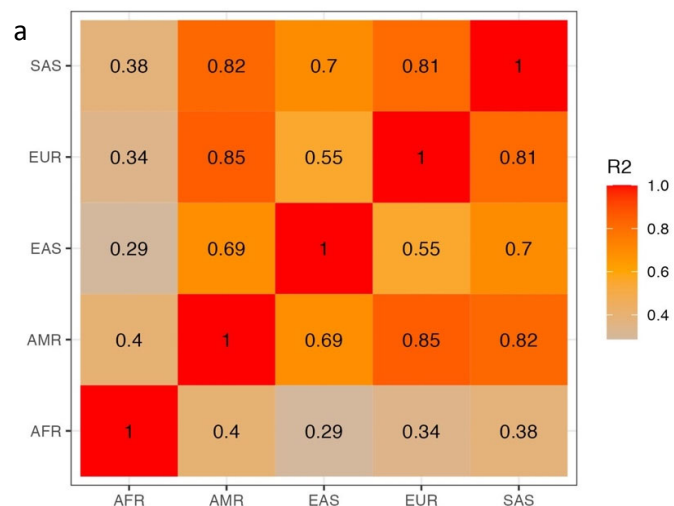
183

184 **ESM Fig. 2.** AUROC of the various PRS by ancestry and their 95% confidence intervals. Set of PRSs developed with PRS-CSx combined with the
 185 HLA portion of GRS2x. Six shrinkage parameters (phi) tested for each ancestry-specific PRS or for the trans-ancestry PRS. The red cross marks the
 186 best PRS.
 187



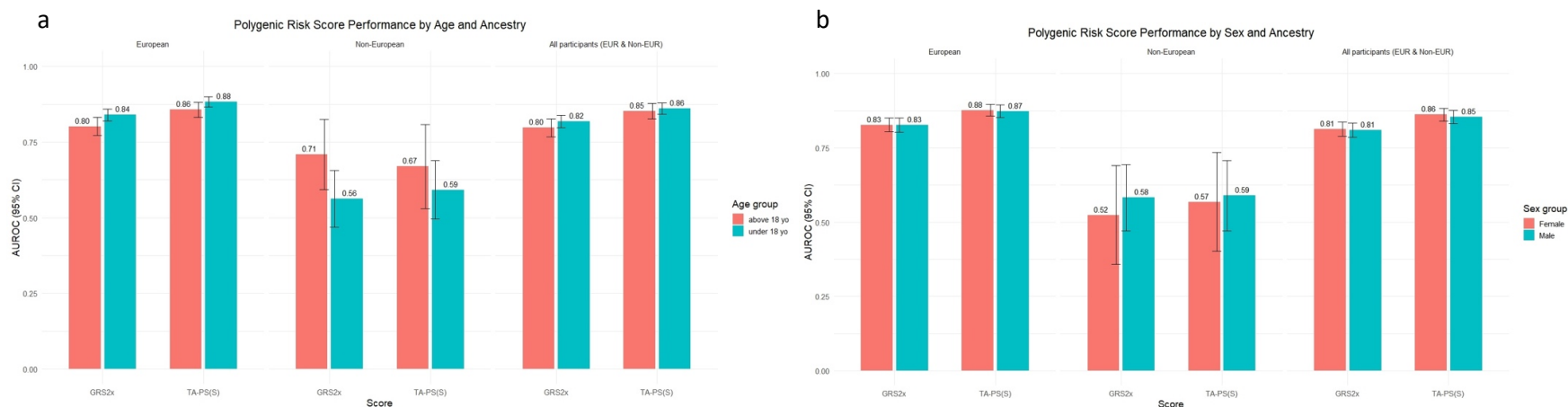
188

189 **ESM Fig. 3.** Performance of TA-PS versus GRS2x by cohorts and ancestry. Upper panel: AUROC difference between GRS2x and TA-PS and Delongs
 190 test (95% CI). Comparison between GRS2x and TA-PS of sensitivity (center panel) and specificity (bottom panel) at the 10% threshold (90th
 191 percentile). Threshold estimated on controls for case/control cohorts and for population cohorts the threshold was estimated on the whole
 192 population. Confidence intervals (95% CI) estimated by bootstrap and comparison made with Z-test. Significance threshold: $p < 0.001$: ***, $p <$
 193 0.01 : **, $p < 0.05$: *, $p < 0.10$: °. MA for Multi-Ancestry.

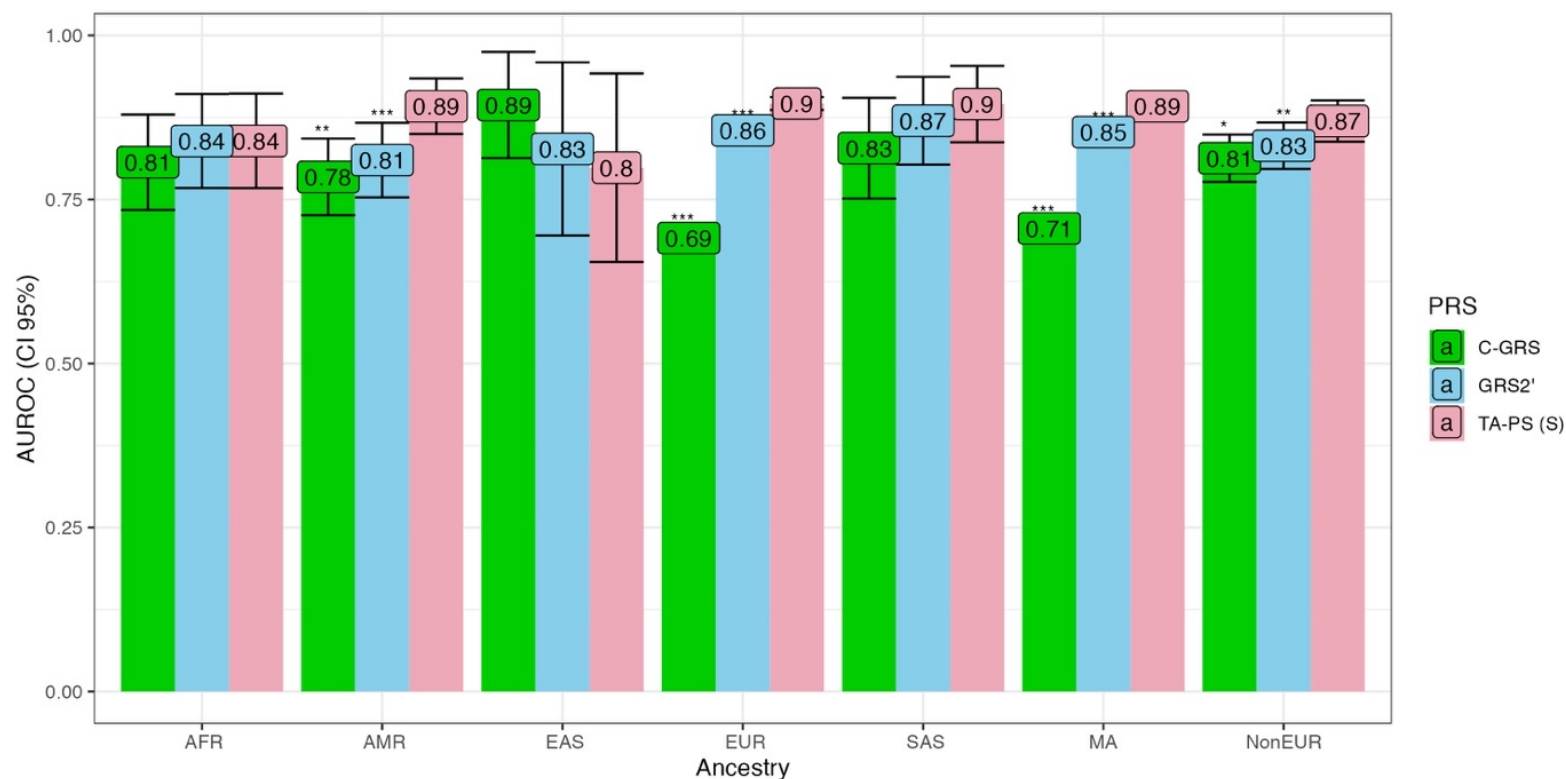


ESM Fig. 4. a) Comparison of the minor allele frequency (MAF) of the SNPs included in TA-PS across ancestries in the 1000 Genomes project. European (EUR) MAFs are highly correlated with those of Hispanics (AMR) and South Asians (SAS), while less so with East Asians (EAS) and even

198 less with those in African populations (AFR). b) Comparison of the MAF of the common (MAF>5%) versus rare (MAF<5%) SNPs included in TA-PS
 199 across ancestries c) Pie-charts with the percentages of common/low frequency/rare SNPs in TA-PS across ancestries.
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 201
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203 **ESM Fig. 5.** Performance of TA-PS (S) vs GRS2x in UKB (European, Non-European and all ancestries) in a) differentiating cases with type 1 Diabetes
 204 diagnosed before ($N_{all}=542$; $N_{EUR}=499$; $N_{non-EUR}=43$) and after age 18y ($N_{all}=236$; $N_{EUR}=234$; $N_{non-EUR}=2$) from controls and in b) differentiating type
 205 1 diabetes cases versus controls in females ($N_{all}=367$; $N_{EUR}=350$; $N_{non-EUR}=17$) versus males ($N_{all}=411$; $N_{EUR}=383$; $N_{non-EUR}=28$). The DeLong test
 206 results ($p < 1.2 \times 10^{-13}$) indicate that TA-PS(S) significantly outperforms GRS2x among European participants and in the combined dataset,
 207 regardless of age at diagnosis or sex. Among Non-European groups, there is no significant difference between the two scores, likely reflecting
 208 smaller number of cases. Also, there is no significant difference in the performance of TA-PS (S) in differentiating individuals diagnosed before vs
 209 after age 18y from controls and in differentiating male vs female cases from controls.
 210



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212 **ESM Fig. 6.** Comparison of the AUROC of ancestry-specific PRS to TA-PS across various ancestries using data from the MTL cohort. In the African
 213 (AFR) subset, TA-PS (S) shows similar performance to the African-specific GRS2'; in East Asians (EAS), the Chinese C-GRS is superior to TA-PS (S),
 214 but this difference is not significant (Delong test $p = 0.26$). In Hispanics (AMR), Europeans (EUR), as well as in the entire multi-ancestry (MA) and
 215 in the entire non-European (NonEUR) datasets, TA-PS (S) outperformed both C-GRS and GRS2'.

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218 References

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