Supplemental material

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Table 1. Characteristics of training samples vs. analytic samples

Characteristic	Training (N = 1,604) n (%)	Analytic (N = 6,449) n (%)
Age, mean (SD)	9.9 (0.6)	9.9 (0.6)
Sex		
Female	759 (47.3)	3,069 (47.6)
Income-to-needs ratio, mean (SD)	4.3 (3.3)	4.3 (3.3)
Family history of psychosis		
Yes	142 (8.9)	517 (8.0)
Parental education		
At least one parent have obtained a bachelor's degree	1,065 (66.4)	4,264 (66.1)
Race and ethnicity		
Non-Hispanic White	938 (58.5)	3,718 (57.7)
Non-Hispanic Black	173 (10.8)	730 (11.3)
Hispanic	290 (18.1)	1,174 (18.2)
Non-Hispanic Asian	35 (2.2)	133 (2.1)
Other	168 (10.5)	694 (10.8)
Genetic ancestry		
EUR	1,246 (77.7)	4,985 (77.3)
AFR	174 (10.8)	706 (10.9)
EAS	37 (2.3)	168 (2.6)
ADMIX	147 (9.2)	590 (9.1)
Persistent distressing psychotic-like experiences		
Yes	316 (19.7)	1,272 (19.7)

Table 2. Comparison between the analytic sample and excluded participants in the ABCD cohort

	Total: 11868		
	Analytic (N = 6,449)	Excluded (N = 5,419)	% Missing
A. Sample Characteristics			
Age (mean (SD))	9.92 (0.63)	9.91 (0.62)	0
Sex (%)[a]			0
Female	3380 (52.4)	2808 (51.8)	
Male	3069 (47.6)	2608 (48.1)	
Race/Ethnicity (%)			0
Non-Hispanic White	3718 (57.7)	2455 (45.3)	
Non-Hispanic Black	730 (11.3)	1054 (19.5)	
Non-Hispanic Asian	133 (2.1)	119 (2.2)	
Non-Hispanic Others[b]	694 (10.8)	553 (10.2)	
Hispanic Ethnicity	1174 (18.2)	1236 (22.8)	
Parent Bachelor's Degree (%)	4264 (66.1)	2791 (51.6)	0.1
INR (mean (SD))	4.33 (3.31)	3.89 (3.33)	10
Family History of Psychosis (%)	517 (8.0)	470 (8.7)	0
B. Area-level Deprivation Index (Median [IQR])			
% Single Parent Households	13.59 [8.65, 21.50]	13.24 [8.48, 21.03]	31.4
% Home Ownership	71.63 [54.30, 83.94]	72.64 [55.59, 83.94]	31.4
% Less Than 9 Years Education	2.19 [0.92, 5.09]	2.23 [0.93, 4.95]	31.4
% High School Education	92.91 [86.31, 96.40]	92.79 [86.07, 96.27]	31.4
% White Collar Occupation	94.51 [91.64, 96.65]	94.49 [91.74, 96.60]	31.4
Median Family Income	75,000.00 [54,368.00, 98,690.00]	75,768.50 [54,565.25, 98,546.00]	31.4
Income Disparity	1.97 [1.23, 2.79]	1.93 [1.24, 2.79]	31.4
Median Property Value	227,200.00 [154,600.00, 318,800.00]	227,100.00 [151,450.00, 329,000.00]	31.4
Median Gross Rent	1,057.00 [858.00, 1,326.00]	1,052.00 [849.75, 1,343.00]	31.4
Median Monthly Mortgage	1,403.00 [1,081.00, 1,719.00]	1,401.00 [1,096.00, 1,727.25]	31.4
Crowding	1.55 [0.48, 3.56]	1.43 [0.48, 3.31]	31.4
Unemployment	7.20 [4.88, 10.49]	7.25 [4.90, 10.34]	31.4
% Below Poverty Line	6.56 [3.07, 13.47]	6.30 [3.04, 12.95]	31.4
% Below 138% Poverty Line	15.03 [8.97, 26.68]	14.95 [8.53, 26.53]	31.4
% Households with No Car	4.68 [2.13, 9.61]	4.39 [1.99, 9.66]	31.4
% Poor Plumbing	0.00 [0.00, 0.30]	0.00 [0.00, 0.15]	31.4
C. Child Opportunity Index (Median [IQR])			
Industrial Pollutants	-0.40 [-0.71, 0.45]	-0.40 [-0.73, 0.42]	31.4
Hazardous Waste Dump Sites	0.27 [0.27, 0.27]	0.27 [0.27, 0.27]	31.4
Access to Food	0.38 [-0.17, 0.66]	0.39 [-0.16, 0.69]	31.4
Access to Green Space	-0.30 [-0.91, 0.56]	-0.30 [-0.88, 0.54]	31.4

Walkability	10.50 [7.17, 14.00]	10.42 [7.33, 14.00]	31.4
D. Crime (Median [IQR])			
Total Crime	22,761.33 [7,832.00, 53,399.67]	22,761.33 [7,832.00, 53,399.67]	31.4
E. Environmental Quality (Median [IQR])			
PM2.5 (μg/m3)	7.67 [6.54, 8.60]	7.76 [6.65, 8.57]	31.4
NO2 (ppb)	18.71 [14.76, 22.13]	18.93 [14.66, 22.40]	31.4
O3 (ppb)	40.47 [38.17, 45.20]	40.26 [38.16, 44.99]	31.4
Lead Risk	15.71 [6.90, 31.25]	15.93 [6.62, 31.49]	31.4
Proximity to Roadways	857.18 [396.70, 1,575.70]	848.52 [375.48, 1,572.78]	31.4
F. Social Vulnerability Index(Median [IQR])			
% Minority Population	46.60 [28.45, 70.55]	46.02 [28.63, 69.66]	31.4
% Non-English Speakers	48.57 [27.67, 71.35]	50.14 [27.67, 71.35]	31.4
G. Polygenic Risk Scores (mean (SD))			
PRS-csx	-0.04 (1.00)	0.17 (0.98)	34.1
PRS-SBayesRC	-0.03 (1.00)	0.13 (0.97)	34.1
H. Outcome			
Persistent distressing psychotic-like experiences (%)	1272 (19.7)	752 (21.7)	16.5

[a] sex=3 (n=3,0.4%) is excluded.
[b] Others included participants who reported a race that was not included in the list, did not know their race, or did not disclose.

Table 3. The association between polygenic risk score (calculated by SBayesRC), neighborhood exposome score, and persistent distressing psychotic-like experiences, additionally adjusting for self-reported race and ethnicity group

Association alone		
	OR (95% CI) [a]	**P**
SCZ-PRS	1.06 (0.97, 1.16)	0.187
NE score	1.15 (1.04, 1.26)	<0.001
Multiplicative interaction		
	OR (95% CI)	**P**
NE score*SCZ-PRS	0.93 (0.86, 1.00)	0.066
Additive interaction		
	RERI	**P**
NE score*SCZ-PRS	-0.05 (-0.14, 0.03)	0.224

Abbreviation: NE, neighborhood exposome; SCZ-PRS, schizophrenia polygenic risk score
[a]Models were adjusted for age, sex, income-to-needs ratio (INR), family history of psychosis, parental education levels, and four genetic principal components (PCs).

Table 4. The association between polygenic risk score (calculated by SBayesRC), neighborhood exposome score, and persistent distressing psychotic-like experiences, excluding the African ancestry population

Association alone		
	OR (95% CI) [a]	**P**
SCZ-PRS	1.07 (0.99, 1.16)	0.100
NE score	1.16 (1.05, 1.28)	0.004
Multiplicative interaction		
	OR (95% CI)	**P**
NE score* SCZ-PRS	0.95(0.88, 1.04)	0.255
Additive interaction		
	RERI	**P**
NE score*SCZ-PRS	-0.03 (-0.11, 0.06)	0.532

Abbreviation: NE, neighborhood exposome; SCZ-PRS, schizophrenia polygenic risk score

[a]Models were adjusted for age, sex, income-to-needs ratio (INR), family history of psychosis, parental education levels, and four genetic principal components (PCs).

Table 5. Training weights of each ancestral schizophrenia polygenic risk score

	$N_{summary\ statistics}$	N_{cases}	$N_{controls}$	Weight (SBayesRC)[a]	Weight (PRScsx)
EUR	127,906	52,017	75,889	0.29	0.35
AFR	9,824	5,998	3,826	0.16	0.15
EAS	27,363	12,305	15,058	-0.15	-0.16

Abbreviation: AFR, African ancestry; EAS, East Asian ancestry; EUR, European ancestry

[a]Weights were calculated by regressing the phenotype on polygenic risk scores calculated from EUR, AFR, and EAS summary statistics before being used to derive a multi-ancestral polygenic risk score.

Table 6 List of neighborhood exposure definitions and years measured

Index Domain/Exposure Component	Definition	Year(s) Measured
Area-level Deprivation Index		
% Single Parent Households	Percentage of single-parent households	2010-2014
% Home Ownership	Percentage of owner-occupied households	2010-2014
% Less Than 9 Years Education	Percentage of population aged >=25 years with <9 years of education	2010-2014
% At least High School Education	Percentage of population aged >=25 years with at least a high school diploma	2010-2014
% White Collar Occupation	Percentage of employed persons aged >=16 years in white-collar occupations	2010-2014
Median Family Income	Median family income	2010-2014
Income Disparity	Income disparity is defined by Singh (2003) as the log of 100 x ratio of the number of households with <10000 annual income to the number of households with >50000 annual income	2010-2014
Median Home Value	Median home value	2010-2014
Median Gross Rent	Median gross rent	2010-2014
Median Monthly Mortgage	Median monthly mortgage	2010-2014
Crowding	Percentage of occupied housing units with >1 person per room (crowding)	2010-2014
Unemployment	Percentage of civilian labor force population aged >=16 y unemployed (unemployment rate)	2010-2014
% Below Poverty Line	Percentage of families below the poverty level	2010-2014
% Below 138% Poverty Line	Percentage of population below 138% of the poverty threshold	2010-2014
% Households with No Car	Percentage of occupied housing units without a motor vehicle	2010-2014
% Poor Plumbing	Percentage of occupied housing units without complete plumbing (log)	2010-2014
Child Opportunity Index 2.0		
Industrial Pollutants	Index of toxic chemicals released by industrial facilities, converted to natural log units, transformed to z-scores and multiplied by -1	2015
Hazardous Waste Sites	Average number of Superfund sites within a 2-mile radius, converted to natural log units, transformed to z-scores and multiplied by -1	2015
Access to Food	Percentage households without a car located further than a half-mile from the nearest supermarket, transformed to z-scores and multiplied by -1	2015
Access to Green Space	Percentage impenetrable surface areas such as rooftops, roads or parking lots, transformed to z-scores and multiplied by -1	2015

Walkability	National Walkability Index from the Smart Location Database created by the United States Environmental Protection Agency (https://www.epa.gov/smartgrowth/smart-location-mapping#walkability)	2010
Crime		
Total Crime	County-level counts of arrests and offenses from Uniform Crime Reporting Program Data (https://doi.org/10.3886/ICPSR33523.v2).	average from 2010 -2012
Environmental Quality		
PM2.5 (µg/m3)	Spatio-temporal model predictions measured in µg/m3 at 1 km2 resolution	2016
NO2 (ppb)	Spatio-temporal model predictions measured in ppb (parts per billion) at 1 km2 resolution	2016
O3 (ppb)	Spatio-temporal model predictions measured in ppb (parts per billion) at 1 km2 resolution	2016
Lead Risk	Estimated percentage of homes at risk for lead exposure given lead-based paint in census tract of primary residential address	2010-2014
Proximity to Roadways	Number of meters away from major road or highway	2016
Social Vulnerability Index		
Percent Ethnoracial Minority	Percentage of ethnoracial minority population (i.e., all but white, non-Hispanic)	2014-2018
Percent Non-English Speakers	Percentage of persons at least 5 years old who speak English “less than well”	2014-2018

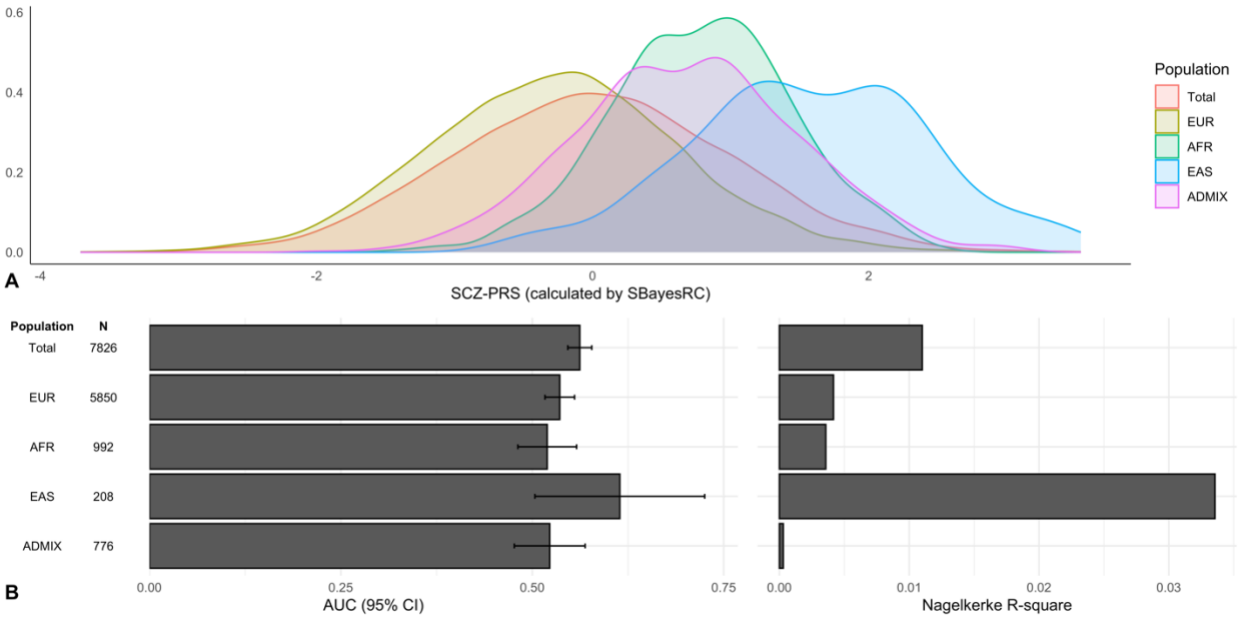


Figure 1. Schizophrenia polygenic risk score (calculated by SBayesRC) in the test set

(A) Distribution of polygenic risk score in total samples in the test set and across ancestry groups; (B) Performance of polygenic risk score in total samples and across ancestry group

Population	Persistent	Not Persistent	RERI (95% CI)	P
Total	1272	5177	-0.06 (-0.15, 0.03)	0.189
EUR	860	4125	-0.14 (-0.32, 0.05)	0.141
AFR	240	466	-0.10 (-0.35, 0.15)	0.441
EAS	24	144	3.98 (-17.43, 25.39)	0.716
ADMIX	148	442	0.07 (-0.06, 0.19)	0.294

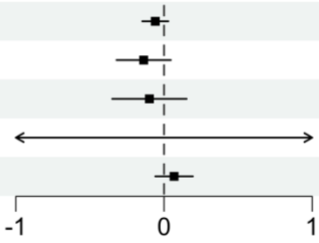


Figure 2. Additive interaction between schizophrenia polygenic risk score (calculated by SBayesRC) and neighborhood exposome score on persistent distressing psychotic-like experiences

Abbreviation: ADMIX, Admixed ancestry, AFR, African ancestry; EAS, East Asian ancestry; EUR, European ancestry; PLE, persistent distressing psychotic-like experience; RERI, relative excessive risk due to interaction

Note: Models were adjusted for age, sex, income-to-needs ratio (INR), family history of psychosis, parental education levels, and four genetic principal components (PCs).

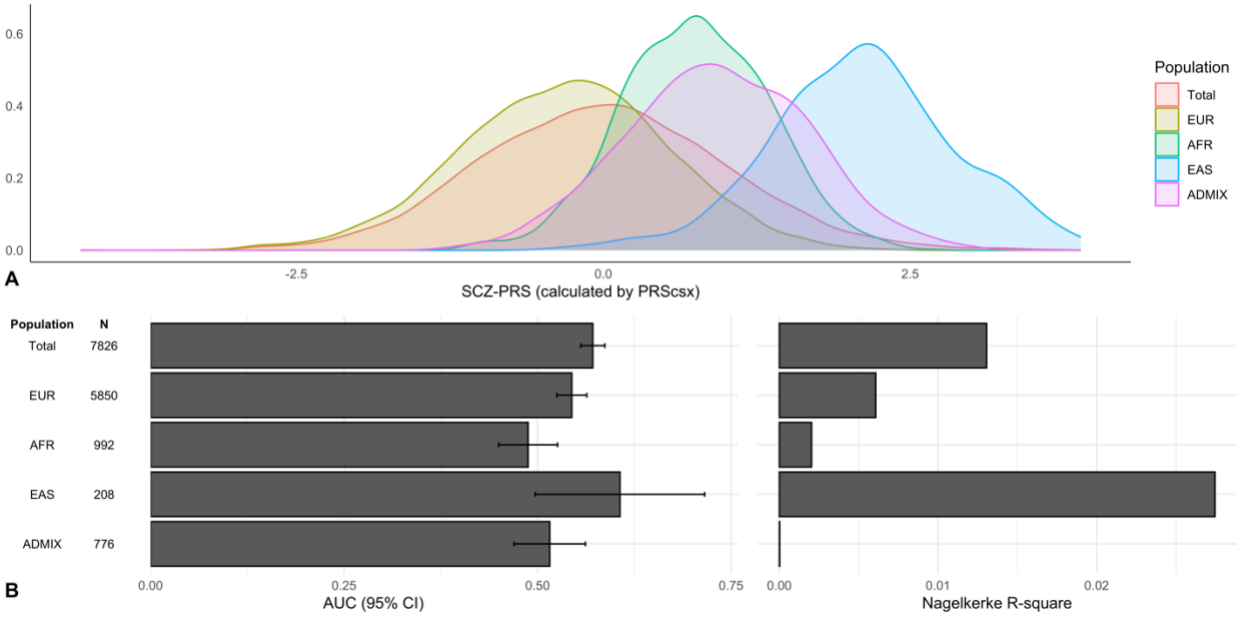


Figure 3. Schizophrenia polygenic risk score (calculated by PRScsx) in the test set

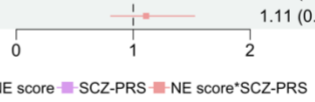
(A) Distribution of polygenic risk score in total samples in the test set and across ancestry groups; (B) Performance of polygenic risk score in total samples and across ancestry groups

A

Population	Persistent	Not Persistent	OR (95% CI)	P
Total	1272	5177	1.06 (0.97, 1.16)	0.182
EUR	860	4125	1.11 (1.02, 1.21)	0.013
AFR	240	466	0.85 (0.67, 1.09)	0.196
EAS	24	144	0.87 (0.43, 1.75)	0.687
ADMIX	148	442	1.08 (0.82, 1.42)	0.604

B

Population	Persistent	Not Persistent	OR (95% CI)	P
Total	1272	5177	1.16 (1.05, 1.27)	0.002
			1.28 (1.02, 1.60)	0.035
			0.93 (0.86, 1.01)	0.083
EUR	860	4125	1.09 (0.98, 1.22)	0.124
			1.47 (1.10, 1.96)	0.010
			0.89 (0.80, 0.99)	0.036
AFR	240	466	1.39 (0.94, 2.07)	0.100
			1.74 (0.45, 6.82)	0.424
			0.82 (0.56, 1.20)	0.299
EAS	24	144	7.42 (1.04, 52.70)	0.045
			5.11 (0.37, 70.14)	0.223
			0.55 (0.24, 1.27)	0.160
ADMIX	148	442	1.26 (0.85, 1.87)	0.253
			0.84 (0.28, 2.47)	0.745
			1.11 (0.81, 1.52)	0.518



C

Population	Persistent	Not Persistent	RERI (95% CI)	P
Total	1272	5177	-0.05 (-0.13, 0.04)	0.291
EUR	860	4125	-0.14 (-0.35, 0.07)	0.202
AFR	240	466	-0.10 (-0.39, 0.20)	0.508
EAS	24	144	22.18 (-101.15, 145.51)	0.724
ADMIX	148	442	0.04 (-0.07, 0.15)	0.475

Figure 4. Schizophrenia polygenic risk score (calculated by PRScsx), neighborhood exposome score, and persistent distressing psychotic-like experiences

Abbreviation: ADMIX, Admixed ancestry, AFR, African ancestry; EAS, East Asian ancestry; EUR, European ancestry; PLE, persistent distressing psychotic-like experience; RERI, related excessive risk due to interaction; SCZ-PRS, schizophrenia polygenic risk score

(A) The association between polygenic risk score and persistent distressing psychotic-like experiences; (B) Multiplicative interaction between polygenic risk score and neighborhood exposome score. The interpretation for each term would be (1) OR of persistent distressing PLE for a one-decile increase in NE among those with a population mean SCZ-PRS (NE score); OR of persistent distressing PLE for a one-SD increase in SCZ-PRS among those in the first decile of NE score (SCZ-PRS); interaction between NE score and SCZ-PRS (NE score*SCZ-PRS); (C) Additive interaction between polygenic risk score and neighborhood exposome score.

Note: Models were adjusted for age, sex, income-to-needs ratio (INR), family history of psychosis, parental education levels, and four genetic principal components (PCs)

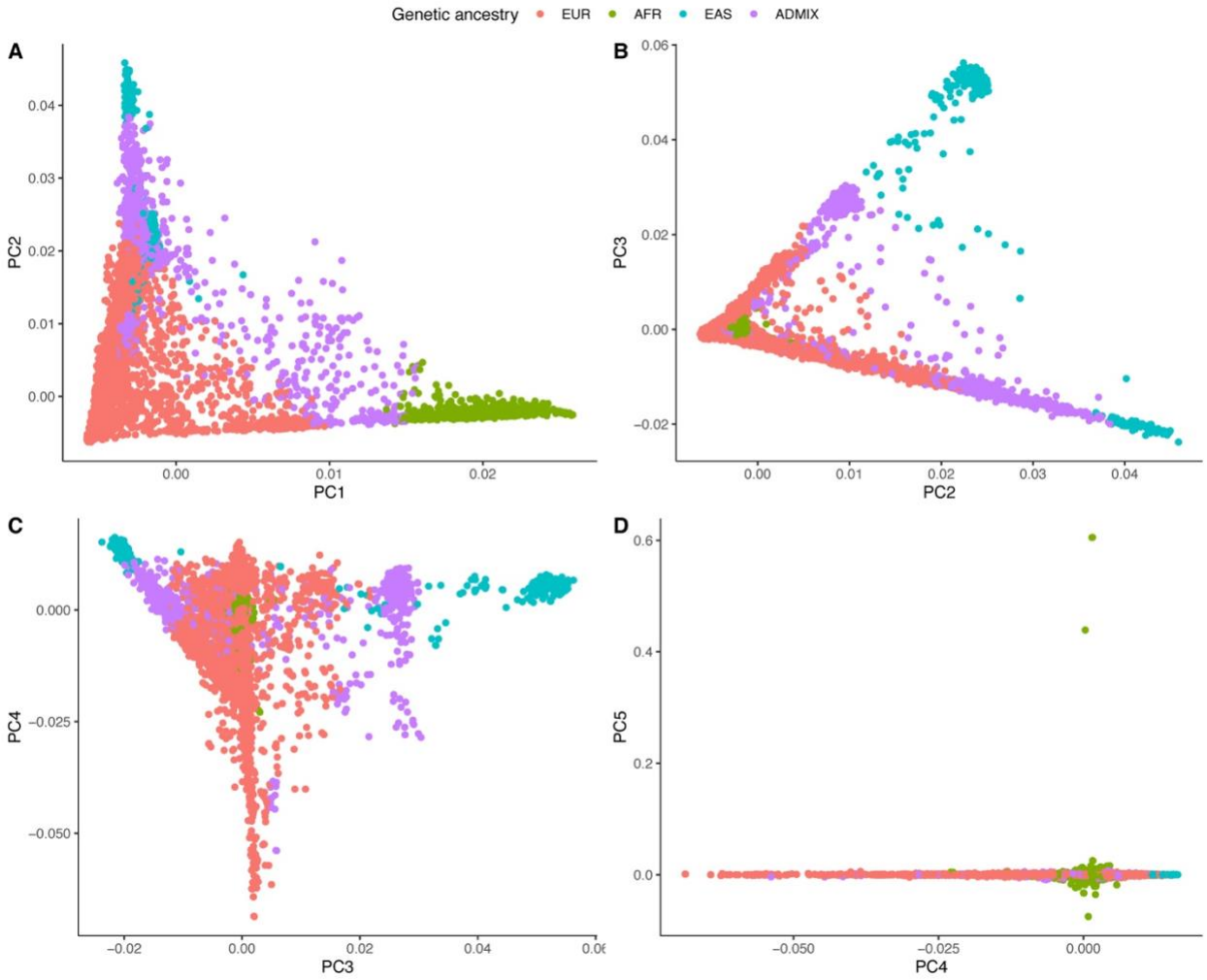


Figure 5. Principal component analysis on population stratification