Supplementary Material

A polygenic risk score for breast cancer in U.S. Latinas and Latin-American women

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Supplementary Methods

Participants

The San Francisco Bay Area Breast Cancer Study (SFBCS) is a population-based case-control study of breast cancer. The Greater Bay Area Cancer Registry was used to identify breast cancer cases newly diagnosed from 1995-2002 in self-identified Latinas. Random-digit dialing was used to identify controls matched on race/ethnicity and 5-year age group. The Northern California Breast Cancer Family Registry (NC-BCFR) is one of six international sites participating in the Breast Cancer Family Registry. Cases diagnosed from 1995-2009 were identified through the Greater Bay Area Cancer Registry, with controls also frequency matched on race/ethnicity and 5-year age group. We combined the SFBCS and NC-BCFR datasets given that they recruited from the same geographic region and in overlapping time frames. We used KING [1] to identify relative pairs between SFBCS/NC-BCFR using a kinship coefficient of > 0.2. We removed one individual from each relative pair while preferentially keeping cases. We also removed overlapping individuals with RPGEH, yielding a total of 942 cases and 589 controls.

The Kaiser Permanente Northern California Research Project on Genes, Environment, and Health (RPGEH) is a multiracial/multiethnic biobank comprised of consenting members of the Kaiser Permanente Health Plan. A subset of cohort members was genotyped, forming the Genetic Epidemiology Research on Adult health and Aging (GERA) cohort. We obtained genotype data for incident and prevalent cases of breast cancer in Latinas from the GERA cohort (total n = 222) plus non-breast cancer Latina controls (n = 3,563).

The Multiethnic Cohort (MEC) study is a prospective cohort study of cancer that recruited in California (predominantly Los Angeles County) and Hawaii. We analyzed a nested sample of 532 cases, representing all incident cases of breast cancer in women aged 45 and over at diagnosis who self-identified as Latina. We analyzed 1469 female controls matched on age (within 5 years) and self-identified ethnicity.

The Cancer de Mama (CAMA) study is a population-based case-control study of breast cancer in Mexico City, Monterrey, and Veracruz, Mexico. We analyzed 709 cases aged 35-69 years and diagnosed from 2005-2007 at one of eleven hospitals in the study region. We also included 702 controls frequency-matched by 5-year age group.

The Post-Columbian Study of Environmental and Heritable Causes of Breast Cancer (COLUMBUS) is a case-control study of breast cancer with individuals recruited throughout large cancer hospitals in central and

southern Colombia and Mexico City. From Colombia, we analyzed 954 cases aged 21-88 years and diagnosed 2011-2017. We included 768 cancer-free controls recruited from the same institutions as cases and matched on education, socioeconomic status, and local origin. Controls did not have a family history of breast cancer in a first-degree relative.

From Mexico City, Mexico, we analyzed data from 481 cases aged 25-89 and diagnosed 2010-2018 at the Social Security Hospital in Mexico City, the largest cancer hospital in the country. As controls, we included 453 blood donors without breast cancer recruited from the same hospital.

The Peru Genetics and Genomics of Breast Cancer Study (PEGEN-BC) is a case-series study. We recruited 1650 participants from the Instituto Nacional de Enfermedades Neoplásicas (INEN) in Lima, Peru. The initial inclusion criteria were an invasive breast cancer diagnosed between the ages of 21-79 years, and after 2010. In actuality, our sample included 79 women diagnosed before 2010 (5 of whom were diagnosed before the year 2000), and 4 women older than 79. A recruiter working locally at INEN identified eligible breast cancer patients who had upcoming appointments with their oncology provider. During appointment check-in, the recruiter approached eligible patients, provided the patients with information about the study, and obtained written informed consent if they showed interest in participating in the study. At the end of their clinic visit, blood was drawn by a certified phlebotomist at the INEN central laboratory. The participants were given a short questionnaire with questions on lifestyle, family history, and reproductive behavior. Clinical data including tumor characteristics, treatment, and disease progression was abstracted from medical records at INEN and from outside clinics, if necessary. The current analysis included 818 breast cancer cases for whom genome-wide genotypes were available. We analyzed 85 unrelated Peruvian samples from 1000 Genomes as controls.

From the City of Hope (COH), we included self-identified Latina participants in the Clinical Cancer Genetics Community Research Network (CCGCRN), a multi-site registry of cancer center and community-based clinics serving individuals with a personal or family history of breast cancer. Cases had a diagnosis of invasive breast cancer. Controls were recruited locally and primarily at community health fairs, with an additional 76 controls from the California Teachers Study [2]. We excluded first-degree relatives of MEC participants. We analyzed 1,039 cases and 305 controls.

Genotyping

We performed genotyping using the following arrays (**Table S1**): Affymetrix 6.0 for SFBCS/NC-BCFR samples; Affymetrix LAT for Kaiser Permanente RPGEH samples; Illumina 660 W-Quad for MEC cases and Illumina 2.5M for MEC controls; Illumina OncoArray for CAMA samples; Axiom GW LAT Axiom Custom for Colombian and Mexican controls, Axiom UK Biobank for COLUMBUS Colombian samples, and Affymetrix Axiom Precision Medicine Research Array (PMRA) for COLUMBUS Mexican cases and controls, and for the PEGEN-BC samples.

Sequence results were aligned using Burrows-Wheeler Aligner [3] and genotype calls were made using Genome Analysis Toolkit [4] as previously described [5].

We excluded samples with >5% missing genotypes and SNPs with >5% missingness. All genotype datasets were mapped to Genome Reference Consortium Human Build 37 (hg19). Each dataset (with the exception of COH/CCGCRN) was phased using EAGLE v2.3 [6] and imputed to the Haplotype Reference Consortium reference panel [7] using the Michigan Imputation Server [8]. Since the MEC datasets included both 660K and 2.5M arrays, we performed imputation using the overlapping SNPs (n = 192,795) given that pooling the separately-imputed datasets resulted in false positives.

Supplementary Table 1. Characteristics of 8 studies included in the analysis

Study	Recruitment area	Controls	Cases	Years of diagnosis (cases)	Age of cases, years	Control group composition	Genotyping Platform	Genotyping site	Imputation Reference
SFBCS/NC-BCFR	San Francisco Bay Area, USA	589	942	1995-2002 (SFBCS), 1995-2007 (NC-BCFR)	35-79 (SFBCS), 18-64 (NC-BCFR)	Identified through random digit-dialing and frequency matched on 5-year age groups (both)	Affymetrix 6.0	University of California, San Francisco (lab of Esteban Burchard)	1000 Genomes, HRC
Kaiser RPGEH	Northern California, USA	3563	222		>18	Overall cohort of self-identified Latinas without breast cancer	Affymetrix LAT	University of California, San Francisco (Institute of Human Genetics)	1000 Genomes, HRC
MEC	Los Angeles County and Hawaii, USA	1469	532		>45	Frequency matched on 5-year age groups and ethnicity.	Illumina 660 W-Quad (cases), Omni 2.5M (controls)	University of Southern California (cases), Broad Institute (controls)	1000 Genomes, HRC
CAMA	Mexico City, Monterrey, and Veracruz, Mexico	702	709	2005-2007	35-69	Frequency matched on 5-year age groups	Illumina OncoArray	Quebec Genome Center	HRC
COLUMBUS (Colombia)	Central and Southern Colombia	761	954	2011-2017	21-88	Recruited from same geographic region	Affymetrix Axiom GW LAT and Custom (controls), Axiom UKBiobank (cases)	University of North Carolina (cases), bioBANC (controls)	1000 Genomes, HRC
COLUMBUS (Mexico)	Mexico City, Mexico	453	481	2010-2018	25-89	Recruited from same geographical region	Affymetrix Axiom PMRA (cases, controls), Axiom GW LAT and Custom (controls)	Affymetrix (cases, controls), bioBANC (controls)	1000 Genomes, HRC
Peru	Lima, Peru	85	818	1985-2018	22-91	Unrelated individuals from 1000 Genomes recruited in Lima, Peru	Affymetrix Axiom PMRA (cases)	University of California, San Francisco	1000 Genomes
COH/ CCGCRN	Southern California, USA	305	1039	1998-present	18-85	Recruited from same geographic region	Next-generation sequencing with a targeted capture kit	City of Hope	N/A

Abbreviations: CAMA = Cancer de Mama; COH/CCGCRN = City of Hope/Clinical Cancer Genetics Community Research Network; COLUMBUS = Colombian Study of Environmental and Heritable Causes of Breast Cancer; HRC = Haplotype Reference Consortium; MEC = Multiethnic Cohort; NC-BCFR = Northern California Breast Cancer Family Registry; PEGEN-BC = Peru Genetics and Genomics of Breast Cancer Study; PRS = polygenic risk score; RPGEH = Research Project on Genes, Environment, and Health; SD = standard deviation; SFBCS = San Francisco Bay Area Breast Cancer Study

Supplementary Table 2. List of SNPs in the 180-SNP PRS with allele frequencies and associations from 7 pooled Hispanic datasets

SNP*	chr	pos	Risk	Other	COLUMBUS - Mexico			COLUMBUS - Colombia			All other studies†			Meta-analysis		
					RAF	OR (95% CI)‡	*P*‡	RAF	OR (95% CI)‡	*P*‡	RAF	OR (95% CI)‡	*P*‡	OR (95% CI)‡	*P*‡	P_{het}§
rs616488	1	10566215	A	G	0.48	1.11 (0.92-1.35)	0.28	0.57	1.12 (0.98-1.29)	0.10	0.56	1.08 (1.00-1.17)	0.05	1.09 (1.03-1.16)	0.006	0.88
rs2992756	1	18807339	T	C	0.38	0.91 (0.75-1.12)	0.37	0.42	1.00 (0.87-1.14)	0.94	0.40	0.98 (0.90-1.05)	0.54	0.97 (0.91-1.04)	0.41	0.78
rs4233486	1	41380440	T	C	0.76	0.89 (0.70-1.12)	0.32	0.76	1.03 (0.88-1.21)	0.67	0.71	1.06 (0.98-1.16)	0.16	1.04 (0.97-1.12)	0.29	0.36
rs79724016	1	42137311	T	G	0.99	1.78 (0.65-4.85)	0.26	0.98	1.24 (0.70-2.19)	0.46	0.98	0.99 (0.75-1.31)	0.94	1.07 (0.84-1.36)	0.60	0.46
rs1707302	1	46600917	G	A	0.62	0.93 (0.76-1.13)	0.47	0.61	1.13 (0.98-1.29)	0.09	0.65	1.05 (0.97-1.14)	0.23	1.05 (0.99-1.12)	0.12	0.29
rs140850326	1	50846032	CAAAGGGCAAGATCTCCTTTTT	C	0.27	0.99 (0.80-1.24)	0.94	0.42	1.05 (0.92-1.21)	0.45	0.37	0.98 (0.90-1.06)	0.62	1.00 (0.93-1.07)	0.96	0.66
rs17426269	1	88156923	A	G	0.07	0.62 (0.41-0.93)	0.02	0.09	1.11 (0.88-1.40)	0.39	0.09	1.06 (0.93-1.22)	0.37	1.03 (0.92-1.15)	0.59	0.04
rs11552449	1	114448389	T	C	0.47	0.84 (0.69-1.03)	0.09	0.38	0.99 (0.86-1.14)	0.88	0.35	0.92 (0.85-0.99)	0.03	0.92 (0.86-0.99)	0.02	0.41
rs7529522	1	118230221	C	T	0.44	0.98 (0.80-1.20)	0.85	0.40	0.98 (0.85-1.12)	0.77	0.37	1.06 (0.98-1.14)	0.16	1.03 (0.97-1.10)	0.34	0.56
rs11249433	1	121280613	G	A	0.16	0.99 (0.75-1.30)	0.93	0.24	1.24 (1.06-1.45)	6.8E-03	0.27	1.05 (0.96-1.15)	0.32	1.08 (1.01-1.17)	0.03	0.14
rs12405132	1	145644984	C	T	0.71	1.11 (0.91-1.37)	0.31	0.66	0.98 (0.85-1.14)	0.83	0.68	1.03 (0.95-1.12)	0.48	1.03 (0.96-1.10)	0.42	0.63
rs12048493	1	149927034	C	A	0.22	1.00 (0.79-1.27)	0.97	0.27	1.13 (0.97-1.31)	0.12	0.23	1.02 (0.92-1.12)	0.75	1.04 (0.96-1.13)	0.29	0.50
rs4971059	1	155148781	A	G	0.61	1.02 (0.83-1.25)	0.87	0.55	0.99 (0.87-1.14)	0.91	0.50	1.05 (0.97-1.14)	0.21	1.03 (0.97-1.10)	0.30	0.76
rs35383942	1	201437832	T	C	0.03	0.76 (0.38-1.53)	0.44	0.02	1.25 (0.83-1.89)	0.29	0.03	0.99 (0.78-1.25)	0.91	1.02 (0.84-1.24)	0.84	0.43
rs6678914	1	202187176	G	A	0.77	0.90 (0.72-1.14)	0.40	0.70	1.08 (0.93-1.26)	0.33	0.70	1.10 (1.01-1.20)	0.03	1.08 (1.00-1.15)	0.04	0.30
rs4951011	1	203766331	G	A	0.39	1.14 (0.94-1.39)	0.19	0.35	1.05 (0.91-1.21)	0.52	0.30	1.05 (0.97-1.14)	0.23	1.06 (0.99-1.13)	0.09	0.74
rs4245739	1	204518842	C	A	0.24	1.07 (0.86-1.34)	0.54	0.27	1.01 (0.87-1.19)	0.86	0.26	1.03 (0.94-1.12)	0.56	1.03 (0.96-1.10)	0.45	0.92
rs11117758	1	217220574	G	A	0.75	0.83 (0.66-1.04)	0.11	0.75	1.04 (0.89-1.22)	0.62	0.76	1.04 (0.96-1.14)	0.34	1.02 (0.95-1.09)	0.61	0.18
rs72755295	1	242034263	G	A	0.01	0.36 (0.07-1.92)	0.23	0.01	0.99 (0.39-2.52)	0.98	0.01	1.08 (0.69-1.70)	0.74	1.00 (0.67-1.49)	1.00	0.46
rs113577745	2	10135681	G	C	0.04	1.11 (0.70-1.77)	0.64	0.05	1.03 (0.76-1.40)	0.84	0.07	1.10 (0.94-1.28)	0.25	1.09 (0.95-1.24)	0.23	0.93
rs12710696	2	19320803	T	C	0.27	1.11 (0.90-1.38)	0.33	0.33	0.95 (0.82-1.10)	0.47	0.32	1.06 (0.98-1.15)	0.17	1.04 (0.97-1.11)	0.27	0.35
rs200648189	2	24739694	CT	C	0.86	1.16 (0.88-1.53)	0.29	0.82	1.13 (0.94-1.34)	0.19	0.85	1.04 (0.93-1.16)	0.49	1.07 (0.98-1.17)	0.12	0.63
rs6725517	2	25129473	A	G	0.75	1.02 (0.81-1.27)	0.88	0.71	1.13 (0.97-1.32)	0.12	0.68	1.08 (0.99-1.17)	0.09	1.08 (1.01-1.16)	0.03	0.74
rs4577244	2	29120733	T	C	0.62	1.05 (0.86-1.29)	0.61	0.45	0.89 (0.78-1.02)	0.11	0.48	1.03 (0.95-1.11)	0.45	1.00 (0.94-1.07)	0.97	0.18
rs71801447	2	111925731	C	CTTATGTT	0.05	1.15 (0.72-1.81)	0.56	0.06	0.99 (0.74-1.31)	0.92	0.07	1.06 (0.91-1.23)	0.46	1.05 (0.92-1.19)	0.45	0.85
rs4849887	2	121245122	C	T	0.90	0.88 (0.63-1.22)	0.43	0.88	1.19 (0.96-1.46)	0.11	0.88	1.01 (0.90-1.14)	0.82	1.04 (0.94-1.14)	0.48	0.25
rs2016394	2	172972971	G	A	0.55	0.95 (0.79-1.16)	0.64	0.52	1.03 (0.90-1.18)	0.66	0.56	1.13 (1.05-1.22)	0.001	1.09 (1.02-1.16)	0.007	0.19
rs1550623	2	174212894	A	G	0.74	0.93 (0.75-1.17)	0.55	0.77	1.23 (1.04-1.45)	0.02	0.78	1.02 (0.93-1.12)	0.70	1.05 (0.97-1.13)	0.22	0.08
rs1830298	2	202181247	C	T	0.47	1.12 (0.93-1.36)	0.23	0.48	0.97 (0.84-1.11)	0.62	0.42	1.02 (0.95-1.10)	0.58	1.02 (0.96-1.09)	0.53	0.45
rs4442975	2	217920769	G	T	0.27	1.03 (0.83-1.29)	0.76	0.36	1.08 (0.94-1.25)	0.26	0.36	1.16 (1.07-1.26)	2.5E-04	1.13 (1.06-1.21)	2.6E-04	0.49
rs34005590	2	217963060	C	A	0.99	0.61 (0.23-1.65)	0.33	0.99	1.44 (0.78-2.66)	0.25	0.98	1.14 (0.87-1.48)	0.35	1.14 (0.90-1.44)	0.30	0.35
rs16857609	2	218296508	T	C	0.44	1.14 (0.94-1.39)	0.20	0.34	1.03 (0.89-1.18)	0.71	0.38	1.03 (0.95-1.11)	0.50	1.04 (0.97-1.11)	0.25	0.62
rs12479355	2	227226952	A	G	0.72	0.92 (0.74-1.14)	0.44	0.74	1.03 (0.88-1.20)	0.75	0.76	1.02 (0.94-1.12)	0.58	1.01 (0.94-1.09)	0.72	0.65
rs6762644	3	4742276	G	A	0.22	0.99 (0.78-1.25)	0.93	0.29	1.10 (0.95-1.27)	0.20	0.26	1.04 (0.95-1.13)	0.38	1.05 (0.98-1.13)	0.19	0.71
rs4973768	3	27416013	T	C	0.57	0.88 (0.72-1.06)	0.18	0.59	1.20 (1.04-1.38)	0.01	0.56	1.06 (0.98-1.14)	0.13	1.06 (1.00-1.13)	0.05	0.04
rs12493607	3	30682939	C	G	0.35	0.98 (0.80-1.20)	0.87	0.24	1.12 (0.95-1.31)	0.17	0.33	1.00 (0.92-1.08)	1.00	1.02 (0.95-1.09)	0.61	0.44
rs6796502	3	46866866	G	A	0.71	1.04 (0.84-1.29)	0.73	0.79	1.02 (0.86-1.21)	0.83	0.79	0.99 (0.90-1.08)	0.75	1.00 (0.93-1.07)	0.96	0.88
rs1053338	3	63967900	G	A	0.23	0.88 (0.70-1.11)	0.29	0.21	0.90 (0.76-1.07)	0.23	0.19	1.00 (0.91-1.10)	0.98	0.96 (0.89-1.04)	0.36	0.43
rs6805189	3	71532113	T	C	0.83	1.05 (0.80-1.38)	0.73	0.71	1.10 (0.95-1.27)	0.22	0.71	0.93 (0.86-1.02)	0.14	0.98 (0.91-1.06)	0.60	0.17
rs13066793	3	87037543	A	G	0.97	1.13 (0.66-1.93)	0.66	0.93	1.18 (0.90-1.55)	0.23	0.95	1.00 (0.83-1.20)	0.98	1.06 (0.91-1.23)	0.45	0.58
rs9833888	3	99723580	T	G	0.22	1.12 (0.89-1.41)	0.33	0.23	1.02 (0.87-1.19)	0.84	0.23	1.07 (0.98-1.17)	0.11	1.07 (0.99-1.14)	0.09	0.77
rs34207738	3	141112859	C	CTT	0.19	1.53 (1.20-1.95)	5.8E-04	0.27	1.12 (0.96-1.30)	0.14	0.27	1.03 (0.95-1.13)	0.46	1.09 (1.01-1.17)	0.02	0.01

rs58058861	3	172285237	A	G	0.28	0.90 (0.73-1.12)	0.36	0.09	1.40 (1.13-1.74)	2.3E-03	0.23	1.00 (0.92-1.10)	0.93	1.03 (0.96-1.11)	0.41	0.01
rs6815814	4	38816338	C	A	0.33	1.08 (0.87-1.32)	0.49	0.37	1.05 (0.91-1.21)	0.50	0.37	0.95 (0.88-1.02)	0.17	0.98 (0.92-1.05)	0.54	0.29
chr4:84370124	4	84370124	TAA	TA	0.30	1.06 (0.85-1.31)	0.61	0.33	1.16 (1.00-1.34)	0.05	0.38	1.10 (1.01-1.19)	0.02	1.11 (1.04-1.18)	0.003	0.75
rs10022462	4	89243818	T	C	0.18	1.29 (1.01-1.66)	0.04	0.28	1.07 (0.92-1.25)	0.35	0.29	0.94 (0.86-1.03)	0.19	1.00 (0.93-1.07)	0.94	0.04
rs9790517	4	106084778	T	C	0.34	1.11 (0.91-1.37)	0.30	0.31	1.06 (0.92-1.22)	0.45	0.31	1.01 (0.93-1.09)	0.86	1.03 (0.96-1.10)	0.41	0.61
rs77528541	4	126843504	G	T	0.95	1.15 (0.74-1.79)	0.54	0.95	1.13 (0.82-1.55)	0.45	0.94	1.18 (1.00-1.39)	0.05	1.17 (1.01-1.34)	0.03	0.97
rs6828523	4	175846426	C	A	0.78	1.04 (0.82-1.32)	0.74	0.87	0.78 (0.65-0.95)	0.01	0.81	1.06 (0.96-1.16)	0.27	1.00 (0.92-1.08)	0.99	0.02
rs116095464	5	345109	C	T	0.06	1.00 (0.65-1.54)	1.00	0.08	0.86 (0.66-1.11)	0.24	0.07	1.15 (0.99-1.33)	0.06	1.06 (0.94-1.20)	0.32	0.15
rs10069690	5	1279790	T	C	0.18	0.86 (0.67-1.11)	0.26	0.20	1.09 (0.93-1.29)	0.29	0.21	1.10 (1.00-1.21)	0.06	1.07 (0.99-1.16)	0.08	0.22
rs3215401	5	1296255	A	AG	0.78	0.99 (0.79-1.25)	0.95	0.76	1.15 (0.98-1.36)	0.09	0.75	1.00 (0.92-1.10)	0.93	1.03 (0.96-1.11)	0.42	0.33
rs13162653	5	16187528	G	T	0.66	0.97 (0.78-1.19)	0.75	0.61	0.98 (0.85-1.12)	0.75	0.62	1.04 (0.96-1.12)	0.33	1.02 (0.95-1.09)	0.58	0.66
rs2012709	5	32567732	T	C	0.37	1.07 (0.88-1.31)	0.50	0.32	1.00 (0.86-1.16)	0.99	0.40	0.92 (0.85-1.00)	0.04	0.95 (0.89-1.02)	0.14	0.30
rs10941679	5	44706498	G	A	0.38	1.08 (0.88-1.32)	0.47	0.31	1.22 (1.05-1.41)	0.008	0.32	1.09 (1.00-1.18)	0.04	1.11 (1.04-1.19)	0.002	0.40
rs35951924	5	50195093	A	AT	0.81	0.92 (0.71-1.19)	0.54	0.84	0.87 (0.73-1.05)	0.16	0.76	1.02 (0.93-1.12)	0.61	0.99 (0.91-1.07)	0.72	0.28
rs62355902	5	56053723	T	A	0.25	1.04 (0.84-1.30)	0.70	0.24	1.06 (0.90-1.24)	0.49	0.23	1.10 (1.01-1.20)	0.03	1.09 (1.01-1.17)	0.02	0.84
rs10472076	5	58184061	C	T	0.30	1.08 (0.88-1.34)	0.46	0.32	0.88 (0.76-1.02)	0.08	0.32	1.01 (0.93-1.09)	0.84	0.99 (0.92-1.05)	0.68	0.18
rs1353747	5	58337481	T	G	0.89	0.94 (0.68-1.28)	0.68	0.90	0.92 (0.73-1.15)	0.46	0.91	1.01 (0.89-1.14)	0.92	0.98 (0.88-1.09)	0.69	0.76
rs7707921	5	81538046	A	T	0.91	0.98 (0.69-1.40)	0.93	0.84	1.06 (0.88-1.27)	0.54	0.85	1.01 (0.90-1.13)	0.90	1.02 (0.93-1.12)	0.70	0.88
rs10474352	5	90732225	C	T	0.78	0.94 (0.74-1.18)	0.58	0.79	1.06 (0.90-1.24)	0.51	0.80	1.14 (1.04-1.26)	0.007	1.10 (1.01-1.19)	0.02	0.26
rs6882649	5	111217786	T	G	0.43	0.82 (0.67-1.00)	0.05	0.51	0.91 (0.80-1.05)	0.20	0.50	1.08 (1.00-1.16)	0.07	1.01 (0.95-1.08)	0.78	0.01
rs6596100	5	132407058	C	T	0.91	1.20 (0.84-1.70)	0.31	0.87	1.09 (0.89-1.33)	0.41	0.86	1.10 (0.98-1.24)	0.10	1.11 (1.00-1.22)	0.04	0.89
rs1432679	5	158244083	C	T	0.55	0.83 (0.68-1.01)	0.07	0.64	1.09 (0.95-1.26)	0.22	0.53	1.08 (1.00-1.16)	0.05	1.05 (0.99-1.12)	0.10	0.05
rs4562056	5	169591487	T	G	0.48	1.02 (0.84-1.24)	0.83	0.38	1.06 (0.92-1.21)	0.43	0.44	1.02 (0.95-1.10)	0.53	1.03 (0.97-1.10)	0.35	0.92
rs11242675	6	1318878	T	C	0.48	1.04 (0.86-1.26)	0.71	0.52	0.95 (0.83-1.09)	0.47	0.55	1.05 (0.97-1.13)	0.21	1.03 (0.96-1.09)	0.41	0.46
rs204247	6	13722523	G	A	0.41	1.10 (0.91-1.33)	0.34	0.51	0.91 (0.79-1.04)	0.17	0.42	1.06 (0.99-1.15)	0.11	1.03 (0.97-1.10)	0.32	0.11
rs3819405	6	16399557	C	T	0.50	0.98 (0.81-1.19)	0.86	0.57	0.96 (0.84-1.10)	0.57	0.53	1.06 (0.98-1.14)	0.15	1.03 (0.97-1.10)	0.37	0.43
rs2223621	6	20621238	T	C	0.35	1.05 (0.86-1.28)	0.62	0.29	1.12 (0.97-1.30)	0.12	0.34	0.99 (0.92-1.07)	0.85	1.02 (0.96-1.09)	0.49	0.34
rs71557345	6	26680698	G	A	0.98	0.81 (0.39-1.67)	0.56	0.98	0.90 (0.53-1.54)	0.70	0.97	1.00 (0.76-1.30)	0.99	0.96 (0.76-1.20)	0.72	0.84
rs9257408	6	28926220	C	G	0.54	1.10 (0.91-1.33)	0.32	0.58	0.93 (0.81-1.07)	0.31	0.63	1.03 (0.94-1.13)	0.50	1.01 (0.95-1.09)	0.71	0.31
rs12207986	6	81094287	A	G	0.22	0.77 (0.60-0.98)	0.04	0.30	1.03 (0.89-1.19)	0.69	0.32	0.92 (0.85-1.01)	0.08	0.93 (0.87-1.00)	0.06	0.12
rs17529111	6	82128386	C	T	0.26	1.01 (0.82-1.25)	0.89	0.12	1.16 (0.95-1.43)	0.15	0.24	1.13 (1.03-1.23)	0.007	1.12 (1.04-1.20)	0.004	0.62
rs6569648	6	130349119	T	C	0.93	1.33 (0.92-1.94)	0.13	0.86	1.06 (0.87-1.30)	0.56	0.88	0.91 (0.81-1.03)	0.14	0.97 (0.88-1.08)	0.61	0.10
rs9485372	6	149608874	G	A	0.85	1.06 (0.82-1.37)	0.67	0.83	0.93 (0.78-1.11)	0.43	0.82	1.05 (0.96-1.16)	0.29	1.03 (0.95-1.12)	0.51	0.47
rs3757322	6	151942194	G	T	0.18	1.01 (0.78-1.30)	0.95	0.23	1.17 (1.00-1.37)	0.06	0.25	1.14 (1.04-1.25)	0.004	1.13 (1.05-1.22)	<0.001	0.62
rs9397437	6	151952332	A	G	0.03	1.52 (0.90-2.57)	0.12	0.04	1.40 (1.02-1.92)	0.04	0.05	1.17 (0.99-1.38)	0.06	1.24 (1.07-1.42)	0.003	0.46
rs140068132	6	151954834	A	G	0.86	1.02 (0.77-1.35)	0.90	0.89	1.45 (1.15-1.83)	0.002	0.90	1.70 (1.49-1.95)	5.6E-15	1.53 (1.37-1.70)	9.4E-15	0.005
rs851984	6	152023191	A	G	0.38	0.89 (0.73-1.09)	0.27	0.33	1.12 (0.97-1.30)	0.11	0.35	1.25 (1.15-1.35)	3.6E-08	1.18 (1.10-1.26)	8.4E-07	0.01
rs3778609	6	152133187	C	T	0.74	1.08 (0.86-1.35)	0.52	0.81	1.12 (0.94-1.34)	0.21	0.80	1.34 (1.21-1.47)	2.3E-09	1.26 (1.16-1.36)	1.1E-08	0.08
rs2747652	6	152437016	C	T	0.53	0.97 (0.80-1.17)	0.72	0.50	1.02 (0.89-1.16)	0.79	0.51	1.05 (0.97-1.13)	0.24	1.03 (0.97-1.10)	0.33	0.73
rs7971	7	21940960	A	G	0.76	1.08 (0.87-1.35)	0.49	0.68	0.95 (0.82-1.09)	0.45	0.71	0.97 (0.90-1.06)	0.53	0.98 (0.91-1.05)	0.51	0.61
rs17156577	7	28356889	C	T	0.20	0.81 (0.63-1.03)	0.08	0.15	0.85 (0.70-1.03)	0.10	0.17	0.96 (0.87-1.05)	0.37	0.92 (0.84-1.00)	0.04	0.31
rs6964587	7	91630620	T	G	0.30	1.12 (0.90-1.39)	0.30	0.37	0.96 (0.84-1.11)	0.60	0.35	1.01 (0.93-1.09)	0.77	1.01 (0.95-1.08)	0.75	0.51
rs17268829	7	94113799	C	T	0.35	1.10 (0.90-1.34)	0.35	0.28	1.03 (0.89-1.20)	0.67	0.33	1.00 (0.92-1.08)	0.92	1.01 (0.95-1.08)	0.68	0.64
rs71559437	7	101552440	G	A	0.94	0.78 (0.51-1.20)	0.26	0.91	1.03 (0.82-1.31)	0.79	0.92	0.99 (0.87-1.14)	0.94	0.99 (0.88-1.11)	0.82	0.52
rs4593472	7	130667121	C	T	0.85	0.97 (0.75-1.27)	0.85	0.85	1.11 (0.92-1.34)	0.27	0.79	0.98 (0.89-1.08)	0.68	1.00 (0.92-1.09)	0.94	0.49
rs11977670	7	139942304	A	G	0.63	0.97 (0.79-1.18)	0.75	0.54	1.01 (0.88-1.15)	0.94	0.55	1.01 (0.93-1.09)	0.83	1.00 (0.94-1.07)	0.91	0.93
rs720475	7	144074929	G	A	0.88	1.00 (0.75-1.33)	0.99	0.88	0.92 (0.75-1.12)	0.40	0.83	1.05 (0.95-1.17)	0.34	1.02 (0.93-1.12)	0.67	0.49

rs66823261	8	170692	C	T	0.20	0.92 (0.72-1.17)	0.50	0.22	0.97 (0.82-1.14)	0.71	0.22	1.19 (1.09-1.30)	1.7E-04	1.11 (1.03-1.20)	0.006	0.03
rs9693444	8	29509616	A	C	0.32	0.96 (0.78-1.18)	0.72	0.28	1.01 (0.87-1.18)	0.89	0.33	0.97 (0.90-1.05)	0.48	0.98 (0.91-1.05)	0.52	0.89
rs13365225	8	36858483	A	G	0.83	1.09 (0.84-1.42)	0.51	0.76	1.10 (0.94-1.29)	0.25	0.81	1.07 (0.97-1.18)	0.18	1.08 (1.00-1.17)	0.06	0.95
rs6472903	8	76230301	T	G	0.94	0.95 (0.64-1.40)	0.79	0.94	0.90 (0.67-1.19)	0.45	0.91	1.06 (0.92-1.22)	0.41	1.02 (0.91-1.15)	0.75	0.54
rs2943559	8	76417937	G	A	0.05	1.18 (0.77-1.79)	0.45	0.08	0.96 (0.74-1.23)	0.73	0.07	0.97 (0.84-1.12)	0.70	0.98 (0.87-1.11)	0.79	0.68
rs514192	8	102478959	A	T	0.41	1.04 (0.86-1.26)	0.69	0.41	1.02 (0.89-1.17)	0.81	0.39	1.05 (0.97-1.13)	0.25	1.04 (0.98-1.11)	0.24	0.94
rs12546444	8	106358620	A	T	0.90	1.05 (0.77-1.45)	0.75	0.93	0.97 (0.75-1.27)	0.85	0.90	1.09 (0.96-1.23)	0.20	1.06 (0.96-1.18)	0.26	0.77
rs13267382	8	117209548	A	G	0.69	0.93 (0.75-1.16)	0.53	0.62	1.04 (0.91-1.20)	0.55	0.61	1.07 (0.99-1.16)	0.11	1.05 (0.98-1.12)	0.15	0.52
rs58847541	8	124610166	A	G	0.07	1.00 (0.68-1.47)	0.98	0.09	0.99 (0.78-1.25)	0.92	0.08	1.00 (0.87-1.16)	0.95	1.00 (0.89-1.13)	1.00	0.99
rs17350191	8	124757661	T	C	0.29	1.10 (0.89-1.35)	0.39	0.27	1.01 (0.87-1.18)	0.89	0.31	1.08 (1.00-1.17)	0.06	1.07 (1.00-1.14)	0.06	0.73
rs13281615	8	128355618	G	A	0.67	0.91 (0.74-1.13)	0.39	0.54	1.12 (0.98-1.28)	0.10	0.59	1.12 (1.04-1.21)	0.004	1.10 (1.03-1.17)	0.004	0.19
rs11780156	8	129194641	T	C	0.18	0.94 (0.73-1.22)	0.64	0.15	1.31 (1.10-1.57)	0.003	0.17	1.06 (0.96-1.17)	0.24	1.10 (1.01-1.19)	0.03	0.06
rs1011970	9	22062134	T	G	0.43	1.15 (0.95-1.41)	0.16	0.34	1.13 (0.97-1.30)	0.11	0.34	1.06 (0.98-1.14)	0.17	1.08 (1.01-1.15)	0.02	0.60
rs10759243	9	110306115	A	C	0.49	1.03 (0.85-1.25)	0.77	0.41	0.89 (0.77-1.03)	0.11	0.41	1.12 (1.04-1.21)	0.003	1.06 (1.00-1.13)	0.06	0.02
rs10816625	9	110837073	G	A	0.19	1.14 (0.90-1.44)	0.29	0.13	1.01 (0.83-1.23)	0.93	0.15	1.10 (1.00-1.21)	0.06	1.09 (1.00-1.18)	0.05	0.70
rs13294895	9	110837176	T	C	0.11	0.78 (0.55-1.09)	0.14	0.08	0.95 (0.74-1.22)	0.70	0.12	1.10 (0.97-1.23)	0.13	1.04 (0.94-1.15)	0.48	0.13
rs676256	9	110895353	T	C	0.73	1.09 (0.88-1.36)	0.42	0.68	1.01 (0.87-1.16)	0.94	0.68	1.14 (1.05-1.24)	0.002	1.11 (1.03-1.18)	0.004	0.31
rs1895062	9	119313486	A	G	0.72	0.98 (0.79-1.22)	0.88	0.66	1.11 (0.96-1.28)	0.17	0.67	1.08 (0.99-1.17)	0.08	1.07 (1.00-1.15)	0.04	0.66
rs10760444	9	129396434	G	A	0.49	0.87 (0.72-1.06)	0.18	0.57	1.04 (0.91-1.20)	0.55	0.48	1.02 (0.94-1.10)	0.65	1.01 (0.95-1.07)	0.82	0.32
rs8176636	9	136151579	T	TGGTGCAGGCGCCAGGAAAAAATTGTGGCAATTCCTCA	0.11	1.09 (0.80-1.49)	0.56	0.15	0.80 (0.66-0.97)	0.03	0.15	1.11 (0.99-1.23)	0.06	1.03 (0.94-1.13)	0.48	0.02
rs2380205	10	5886734	C	T	0.75	1.09 (0.87-1.36)	0.47	0.69	1.03 (0.89-1.19)	0.73	0.67	0.98 (0.90-1.07)	0.65	1.00 (0.93-1.07)	1.00	0.66
rs67958007	10	9088113	T	TG	0.20	0.99 (0.78-1.26)	0.93	0.13	0.99 (0.81-1.21)	0.90	0.17	1.02 (0.92-1.12)	0.75	1.01 (0.93-1.09)	0.85	0.96
rs7072776	10	22032942	A	G	0.34	1.05 (0.85-1.29)	0.67	0.35	1.15 (1.00-1.32)	0.05	0.33	1.05 (0.97-1.14)	0.20	1.07 (1.00-1.15)	0.04	0.56
rs11814448	10	22315843	C	A	0.04	1.49 (0.89-2.50)	0.13	0.06	1.12 (0.84-1.50)	0.43	0.06	1.16 (0.99-1.37)	0.07	1.18 (1.02-1.35)	0.02	0.63
rs10995201	10	64299890	A	G	0.93	0.83 (0.56-1.22)	0.34	0.92	0.92 (0.72-1.18)	0.51	0.90	1.05 (0.92-1.21)	0.49	1.00 (0.89-1.12)	0.99	0.40
rs704010	10	80841148	T	C	0.41	1.16 (0.95-1.41)	0.15	0.44	0.99 (0.86-1.13)	0.86	0.41	1.06 (0.98-1.15)	0.13	1.05 (0.99-1.12)	0.10	0.42
rs140936696	10	95292187	CAA	C	0.10	1.14 (0.83-1.58)	0.43	0.12	0.97 (0.79-1.20)	0.80	0.13	0.98 (0.88-1.10)	0.79	1.00 (0.90-1.09)	0.92	0.69
rs7904519	10	114773927	G	A	0.27	0.94 (0.75-1.19)	0.63	0.30	0.93 (0.80-1.08)	0.33	0.35	1.08 (0.99-1.17)	0.08	1.03 (0.96-1.10)	0.38	0.17
rs11199914	10	123093901	C	T	0.48	0.84 (0.69-1.02)	0.08	0.59	1.02 (0.89-1.17)	0.77	0.56	0.99 (0.92-1.07)	0.88	0.98 (0.92-1.05)	0.59	0.24
rs35054928	10	123340431	GC	G	0.39	1.29 (1.06-1.57)	0.01	0.39	1.25 (1.09-1.43)	0.002	0.42	1.19 (1.10-1.28)	7.2E-06	1.21 (1.14-1.29)	2.3E-09	0.67
rs45631563	10	123349324	A	T	0.98	0.76 (0.35-1.65)	0.49	0.97	1.40 (0.89-2.20)	0.15	0.97	1.17 (0.93-1.47)	0.18	1.18 (0.96-1.43)	0.11	0.41
rs6597981	11	803017	G	A	0.66	0.86 (0.69-1.06)	0.17	0.58	0.98 (0.86-1.13)	0.81	0.59	1.05 (0.97-1.13)	0.27	1.01 (0.95-1.08)	0.70	0.22
rs3817198	11	1909006	C	T	0.18	0.89 (0.69-1.14)	0.35	0.19	1.17 (0.99-1.39)	0.07	0.21	1.13 (1.03-1.24)	0.01	1.11 (1.03-1.20)	0.009	0.17
rs3903072	11	65583066	G	T	0.77	1.15 (0.91-1.45)	0.26	0.71	0.99 (0.85-1.15)	0.91	0.68	1.01 (0.93-1.10)	0.87	1.02 (0.95-1.09)	0.67	0.56
rs75915166	11	69379161	A	C	0.01	1.78 (0.83-3.82)	0.14	0.01	1.51 (0.83-2.76)	0.18	0.03	1.30 (1.04-1.63)	0.02	1.35 (1.10-1.66)	0.004	0.69
rs11374964	11	108345515	G	GA	0.42	0.94 (0.77-1.15)	0.56	0.43	1.03 (0.90-1.18)	0.64	0.46	1.04 (0.97-1.12)	0.29	1.03 (0.97-1.10)	0.36	0.65
rs74911261	11	108357137	G	A	0.99	0.94 (0.35-2.56)	0.91	0.98	1.10 (0.69-1.76)	0.70	0.99	0.98 (0.68-1.40)	0.90	1.01 (0.77-1.33)	0.92	0.92
rs11820646	11	129461171	C	T	0.48	1.02 (0.84-1.24)	0.84	0.50	1.03 (0.90-1.18)	0.63	0.54	1.07 (0.99-1.15)	0.09	1.05 (0.99-1.12)	0.09	0.86
rs12422552	12	14413931	C	G	0.18	1.21 (0.94-1.55)	0.14	0.21	0.96 (0.81-1.13)	0.60	0.22	1.07 (0.98-1.18)	0.13	1.06 (0.98-1.14)	0.14	0.27
rs7297051	12	28174817	C	T	0.59	0.68 (0.55-0.84)	2.8E-04	0.75	1.10 (0.94-1.29)	0.24	0.65	1.15 (1.06-1.24)	6.2E-04	1.08 (1.01-1.15)	0.03	2.33E-05
rs202049448	12	85009437	T	C	0.66	1.13 (0.93-1.38)	0.22	0.65	0.96 (0.83-1.10)	0.54	0.64	1.00 (0.92-1.08)	1.00	1.00 (0.94-1.07)	0.91	0.39
rs17356907	12	96027759	A	G	0.59	1.04 (0.85-1.26)	0.72	0.61	1.07 (0.93-1.23)	0.34	0.64	1.06 (0.99-1.15)	0.11	1.06 (1.00-1.13)	0.06	0.97
rs1292011	12	115836522	A	G	0.65	0.89 (0.73-1.09)	0.25	0.61	1.14 (0.99-1.32)	0.06	0.63	1.00 (0.92-1.08)	0.95	1.01 (0.95-1.08)	0.65	0.10

rs206966	12	120832146	T	C	0.07	1.12 (0.75-1.67)	0.59	0.10	1.03 (0.81-1.29)	0.83	0.09	1.03 (0.90-1.18)	0.68	1.04 (0.92-1.16)	0.55	0.93
rs11571833	13	32972626	T	A	0.00	0.69 (0.04-11.14)	0.79	0.00	1.00 (0.37-2.70)	1.00	0.00	1.01 (0.54-1.89)	0.98	0.99 (0.59-1.67)	0.98	0.97
rs6562760	13	73957681	G	A	0.89	1.18 (0.86-1.62)	0.32	0.83	1.18 (0.99-1.42)	0.07	0.82	1.04 (0.94-1.16)	0.46	1.08 (0.99-1.18)	0.08	0.43
rs2236007	14	37132769	G	A	0.89	0.60 (0.42-0.86)	0.005	0.87	1.09 (0.89-1.34)	0.41	0.87	1.14 (1.01-1.29)	0.04	1.07 (0.97-1.19)	0.17	0.004
rs2588809	14	68660428	T	C	0.13	1.11 (0.83-1.47)	0.48	0.17	1.10 (0.92-1.32)	0.29	0.17	1.05 (0.94-1.16)	0.38	1.07 (0.98-1.16)	0.15	0.86
rs999737	14	69034682	C	T	0.86	1.09 (0.83-1.43)	0.53	0.85	1.04 (0.85-1.26)	0.70	0.83	0.98 (0.89-1.09)	0.76	1.00 (0.92-1.09)	0.91	0.74
rs941764	14	91841069	G	A	0.51	0.92 (0.76-1.11)	0.39	0.41	1.01 (0.88-1.16)	0.91	0.46	1.06 (0.98-1.14)	0.14	1.03 (0.97-1.10)	0.33	0.38
rs11627032	14	93104072	T	C	0.71	0.90 (0.73-1.12)	0.36	0.70	1.05 (0.91-1.22)	0.50	0.73	0.99 (0.91-1.08)	0.88	1.00 (0.93-1.07)	0.91	0.52
rs10623258	14	105212261	CTT	C	0.71	1.01 (0.81-1.27)	0.89	0.63	1.07 (0.93-1.23)	0.35	0.62	1.00 (0.92-1.08)	0.99	1.02 (0.95-1.08)	0.64	0.71
rs2290203	15	91512067	G	A	0.63	0.89 (0.72-1.10)	0.29	0.73	1.03 (0.89-1.20)	0.70	0.68	1.17 (1.08-1.27)	1.4E-04	1.11 (1.04-1.19)	0.003	0.03
rs11076805	16	4106788	C	A	0.91	1.18 (0.84-1.64)	0.34	0.85	1.25 (1.02-1.52)	0.03	0.85	1.13 (1.01-1.26)	0.04	1.16 (1.05-1.27)	0.003	0.68
rs4784227	16	52599188	T	C	0.31	1.53 (1.24-1.89)	7.0E-05	0.35	1.21 (1.05-1.39)	0.008	0.29	1.25 (1.15-1.36)	4.5E-08	1.27 (1.19-1.35)	2.4E-12	0.16
rs17817449	16	53813367	T	G	0.81	0.97 (0.76-1.25)	0.82	0.77	0.95 (0.81-1.11)	0.52	0.73	1.04 (0.96-1.14)	0.34	1.02 (0.94-1.09)	0.67	0.55
rs11075995	16	53855291	A	T	0.41	0.91 (0.75-1.10)	0.33	0.27	1.22 (1.05-1.41)	0.009	0.32	1.10 (1.02-1.19)	0.02	1.10 (1.03-1.17)	0.005	0.06
rs28539243	16	54682064	A	G	0.58	0.92 (0.76-1.11)	0.39	0.59	0.92 (0.80-1.06)	0.24	0.57	0.99 (0.91-1.06)	0.73	0.97 (0.91-1.03)	0.27	0.61
rs2432539	16	56420987	A	G	0.37	0.96 (0.79-1.17)	0.69	0.45	1.07 (0.94-1.23)	0.32	0.38	1.02 (0.95-1.10)	0.55	1.03 (0.96-1.09)	0.41	0.66
rs13329835	16	80650805	G	A	0.12	1.41 (1.05-1.91)	0.02	0.19	1.08 (0.91-1.27)	0.39	0.19	1.00 (0.90-1.10)	0.97	1.04 (0.96-1.13)	0.30	0.09
rs4496150	16	87085237	C	A	0.59	0.94 (0.77-1.15)	0.57	0.65	1.15 (1.00-1.33)	0.05	0.65	0.96 (0.89-1.04)	0.30	1.00 (0.93-1.06)	0.90	0.07
rs146699004	17	29230520	GGT	G	0.87	0.84 (0.62-1.13)	0.25	0.81	0.99 (0.84-1.18)	0.93	0.82	1.01 (0.91-1.11)	0.92	0.99 (0.91-1.08)	0.78	0.53
rs72826962	17	40836389	T	C	0.01	0.59 (0.10-3.55)	0.57	0.01	0.65 (0.24-1.75)	0.39	0.01	1.35 (0.87-2.10)	0.18	1.16 (0.78-1.72)	0.45	0.31
rs2532263	17	44252468	G	A	0.90	1.14 (0.82-1.59)	0.44	0.86	1.04 (0.85-1.27)	0.68	0.88	0.99 (0.86-1.13)	0.85	1.02 (0.91-1.13)	0.76	0.71
rs2787486	17	53209774	A	C	0.81	1.19 (0.92-1.54)	0.18	0.82	1.06 (0.89-1.27)	0.51	0.76	1.05 (0.96-1.15)	0.30	1.06 (0.98-1.15)	0.12	0.65
rs745570	17	77781725	A	G	0.27	0.88 (0.70-1.11)	0.28	0.33	1.13 (0.98-1.30)	0.10	0.35	1.01 (0.93-1.10)	0.77	1.02 (0.96-1.10)	0.48	0.17
rs527616	18	24337424	G	C	0.84	0.81 (0.62-1.06)	0.13	0.76	1.01 (0.87-1.19)	0.86	0.77	1.09 (0.99-1.20)	0.07	1.05 (0.97-1.13)	0.26	0.12
rs1436904	18	24570667	T	G	0.55	1.11 (0.92-1.35)	0.27	0.62	0.96 (0.83-1.10)	0.52	0.56	1.08 (1.00-1.17)	0.04	1.06 (0.99-1.13)	0.07	0.25
rs36194942	18	25401204	A	AT	0.76	0.96 (0.77-1.21)	0.75	0.72	1.11 (0.95-1.29)	0.20	0.71	1.15 (1.06-1.25)	0.001	1.12 (1.04-1.20)	0.002	0.35
rs117618124	18	29977689	T	C	1.00	0.72 (0.14-3.71)	0.69	0.99	1.39 (0.63-3.07)	0.42	0.98	1.49 (1.04-2.13)	0.03	1.43 (1.04-1.97)	0.03	0.70
rs6507583	18	42399590	A	G	0.92	0.92 (0.64-1.32)	0.65	0.92	1.17 (0.90-1.51)	0.25	0.91	1.05 (0.92-1.20)	0.49	1.06 (0.94-1.18)	0.34	0.57
rs322144	19	11423703	C	G	0.31	0.84 (0.68-1.04)	0.11	0.42	0.87 (0.76-1.00)	0.05	0.40	0.95 (0.88-1.03)	0.23	0.92 (0.86-0.98)	0.02	0.34
rs78269692	19	13158277	C	T	0.01	0.74 (0.28-1.96)	0.54	0.01	1.74 (0.89-3.40)	0.10	0.02	0.85 (0.61-1.21)	0.37	0.97 (0.72-1.29)	0.82	0.15
rs2594714	19	13954571	G	A	0.70	1.14 (0.92-1.41)	0.23	0.72	0.99 (0.86-1.15)	0.94	0.72	1.00 (0.92-1.08)	0.93	1.01 (0.94-1.08)	0.79	0.51
rs67397200	19	17401404	G	C	0.10	1.08 (0.79-1.49)	0.62	0.16	0.97 (0.80-1.17)	0.72	0.18	0.94 (0.85-1.05)	0.26	0.96 (0.88-1.04)	0.33	0.71
rs4808801	19	18571141	A	G	0.60	0.96 (0.78-1.17)	0.66	0.68	1.03 (0.89-1.19)	0.70	0.62	1.12 (1.03-1.21)	0.005	1.08 (1.01-1.15)	0.02	0.28
rs2965183	19	19545696	A	G	0.49	0.90 (0.74-1.09)	0.28	0.43	0.98 (0.86-1.13)	0.82	0.42	1.04 (0.97-1.12)	0.27	1.02 (0.95-1.08)	0.64	0.33
rs113701136	19	30277729	T	C	0.27	0.76 (0.60-0.96)	0.02	0.32	1.00 (0.87-1.15)	0.99	0.27	0.96 (0.88-1.04)	0.30	0.95 (0.88-1.02)	0.12	0.13
rs3760982	19	44286513	A	G	0.26	1.09 (0.87-1.37)	0.44	0.29	1.07 (0.92-1.25)	0.36	0.33	1.05 (0.97-1.14)	0.25	1.06 (0.99-1.13)	0.11	0.93
rs71338792	19	46183031	AT	A	0.10	1.25 (0.92-1.70)	0.15	0.12	1.13 (0.92-1.39)	0.24	0.13	1.05 (0.93-1.18)	0.42	1.09 (0.99-1.20)	0.09	0.52
rs16991615	20	5948227	A	G	0.05	0.77 (0.49-1.22)	0.27	0.06	0.99 (0.74-1.33)	0.96	0.05	1.05 (0.88-1.25)	0.60	1.00 (0.87-1.16)	0.96	0.47
rs2284378	20	32588095	T	C	0.39	0.79 (0.65-0.98)	0.03	0.31	0.96 (0.83-1.11)	0.59	0.31	1.09 (1.00-1.18)	0.04	1.03 (0.96-1.10)	0.45	0.01
rs6122906	20	48945911	G	A	0.40	0.87 (0.71-1.06)	0.18	0.33	1.06 (0.92-1.23)	0.39	0.30	1.02 (0.94-1.11)	0.58	1.01 (0.95-1.08)	0.69	0.26
rs2823093	21	16520832	G	A	0.70	1.06 (0.86-1.31)	0.57	0.74	1.00 (0.86-1.17)	0.98	0.70	1.00 (0.93-1.09)	0.94	1.01 (0.94-1.08)	0.79	0.88
rs132390	22	29621477	C	T	0.00	2.30 (0.45-11.83)	0.32	0.01	1.46 (0.73-2.91)	0.28	0.01	0.55 (0.36-0.86)	0.008	0.77 (0.54-1.11)	0.16	0.03
rs738321	22	38568833	C	G	0.55	0.92 (0.76-1.11)	0.39	0.53	1.24 (1.08-1.42)	0.003	0.57	1.01 (0.94-1.09)	0.71	1.05 (0.98-1.11)	0.16	0.02
chr22:39359355	22	39359355	<CN0>	C	0.26	1.00 (0.81-1.25)	0.99	0.19	1.06 (0.89-1.25)	0.52	0.18	1.09 (0.99-1.20)	0.08	1.07 (0.99-1.16)	0.09	0.79
rs6001930	22	40876234	C	T	0.08	1.17 (0.83-1.66)	0.36	0.10	1.21 (0.96-1.51)	0.10	0.09	1.06 (0.93-1.21)	0.35	1.10 (0.99-1.23)	0.07	0.59
rs73161324	22	42038786	T	C	0.01	0.55 (0.16-1.92)	0.35	0.02	0.71 (0.41-1.21)	0.20	0.02	0.77 (0.56-1.04)	0.09	0.74 (0.57-0.96)	0.02	0.86
rs28512361	22	46283297	A	G	0.06	0.98 (0.65-1.48)	0.92	0.07	1.01 (0.78-1.32)	0.92	0.08	0.85 (0.73-0.99)	0.04	0.90 (0.79-1.02)	0.09	0.48

Abbreviations: chr = chromosome; CI = confidence interval; COLUMBUS = Colombian Study of Environmental and Heritable Causes of Breast Cancer; OR = odds ratio; pos = position; RAF = risk allele frequency; SNP = single nucleotide polymorphism

* rs72749841 not included in meta-analysis due to imputation quality
† San Francisco Bay Area Breast Cancer Study/Northern California Breast Cancer Family Registry (SFBCS/NC-BCFR), Research Project on Genes, Environment, and Health (RPGEH), Multiethnic Cohort (MEC), Cancer de Mama (CAMA), the Peru Genetics and Genomics of Breast Cancer Study (PEGEN-BC)
‡ Odds ratio and p-value for association of risk versus other allele with breast cancer in multivariable logistic regression adjusted for genetic ancestry
§ Two-sided P-value from Cochran's Q-test for heterogeneity of estimates

Supplementary Table 3. Association of PRS constructed using different imputation r^2 cutoffs with breast cancer risk

Imputation r^2 cutoff	Number of SNPs	OR per SD (95% CI)*
$r^2 > 0$	180	1.57 (1.49 to 1.65)
$r^2 > 0.5$	166	1.57 (1.50 to 1.66)
$r^2 > 0.8$	134	1.53 (1.45 to 1.61)

Abbreviations: CI = confidence interval; OR = odds ratio; SD = standard deviation; SNPs = single nucleotide polymorphisms

* Odds ratio of breast cancer per standard deviation increment of PRS relative to the mean in controls. Calculated from multivariable logistic regression of PRS adjusted for study and genetic ancestry among participants of the San Francisco Bay Area Breast Cancer Study/Northern California Breast Cancer Family Registry (SFBCS/NC-BCFR), Research Project on Genes, Environment, and Health (RPGEH), Multiethnic Cohort (MEC), and Cancer de Mama (CAMA), total n = 8,728

Supplementary Table 4. Associations of the 180-SNP and 71-SNP PRS with genetic ancestry

PRS	Indigenous American		European		African	
	β (95% CI)*	*P*-value*	β (95% CI)*	*P*-value*	β (95% CI)*	*P*-value*
180-SNP†	-0.002 (-0.006 to 0.002)	0.40	0 (-0.005 to 0.004)	0.72	0.002 (0 to 0.004)	0.02
71-SNP‡	-0.018 (-0.023 to -0.013)	<0.001	0.013 (0.008 to 0.019)	<0.001	0.005 (0.003 to 0.007)	<0.001

Abbreviations: CI = confidence interval; PRS = polygenic risk score

* Beta coefficient, 95% CI, and two-sided p-value from linear regression of PRS (independent variable) on genetic ancestry (dependent variable), adjusted for study. Beta values correspond to change in genetic ancestry on 0 to 1 scale per standard deviation increase in PRS relative to the mean in controls
† Calculated in controls from 7 datasets, excluding City of Hope/Clinical Cancer Genetics Community Research Network (COH/CCGCRN) data (n = 7,622)
‡ Calculated in controls from all datasets (n = 7,927)

Supplementary Table 5. Association between 71-SNP PRS and breast cancer risk (COH/CCGCRN participants excluded)

PRS category	Controls	Cases	OR (95% CI)†	*P*-trend‡
Continuous (per standard deviation)	7622	4658	1.49 (1.43 to 1.55)	--
Percentiles of PRS				<0.001
<10	763	232	0.55 (0.46 to 0.65)	
10-20	762	292	0.69 (0.59 to 0.81)	
20-30	761	312	0.74 (0.63 to 0.86)	
30-40	763	353	0.83 (0.71 to 0.97)	
40-60	1525	849	1 (referent)	
60-70	762	536	1.26 (1.10 to 1.45)	
70-80	761	562	1.33 (1.16 to 1.52)	
80-90	763	646	1.52 (1.33 to 1.74)	
>90	762	876	2.06 (1.82 to 2.35)	

Abbreviations: CI = confidence interval; OR = odds ratio; SD = standard deviation

* Calculated in case-control analysis in 7 datasets, excluding City of Hope/Clinical Cancer Genetics Community Research Network (COH/CCGCRN) data (n = 12,280)
† Odds ratio from multivariable logistic regression of PRS adjusted for study and genetic ancestry. Referent group is 40-60th percentile.
‡ Two-sided P-value for test of linear trend between per-decile estimates

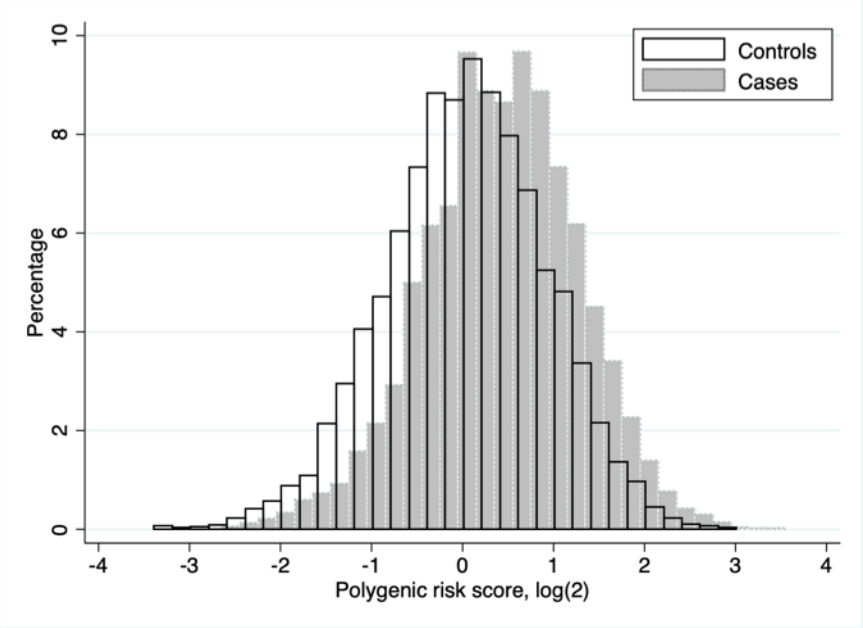
Supplementary Table 6. Areas under the receiver operating characteristic curve and odds ratios per standard deviation of the 180-SNP PRS in Hispanics by quartiles of Indigenous American ancestry, stratified by U.S. Latinas and Latin-American women

Indigenous American ancestry category	Controls	Cases	AUROC (95% CI)*	*P*-value†	OR (95% CI)‡	*P*-value§
U.S. Latinas‖						
All	5621	1696	0.63 (0.62 to 0.65)		1.62 (1.52 to 1.71)	
Quartiles of IA ancestry (%)				0.06		0.02
Q1, <0.22	1493	337	0.66 (0.63 to 0.69)		1.88 (1.65 to 2.13)	
Q2, 0.22-0.34	1412	417	0.61 (0.58 to 0.64)		1.51 (1.34 to 1.70)	
Q3, 0.34-0.45	1345	484	0.63 (0.60 to 0.66)		1.57 (1.40 to 1.75)	
Q4, >0.45	1371	458	0.62 (0.59 to 0.65)		1.53 (1.38 to 1.70)	
Latin-American women¶						
All	2001	2962	0.62 (0.61 to 0.64)		1.54 (1.45 to 1.63)	
Quartiles of IA ancestry (%)				0.35		0.49
Q1, <0.43	527	714	0.61 (0.58 to 0.65)		1.52 (1.35 to 1.71)	
Q2, 0.43-0.54	554	687	0.63 (0.60 to 0.66)		1.55 (1.37 to 1.74)	
Q3, 0.54-0.71	538	703	0.61 (0.58 to 0.64)		1.46 (1.30 to 1.64)	
Q4, >0.71	382	858	0.64 (0.60 to 0.67)		1.62 (1.43 to 1.82)	

Abbreviations: AUROC = area under receiver operating characteristic curve; CI = confidence interval; IA = Indigenous American

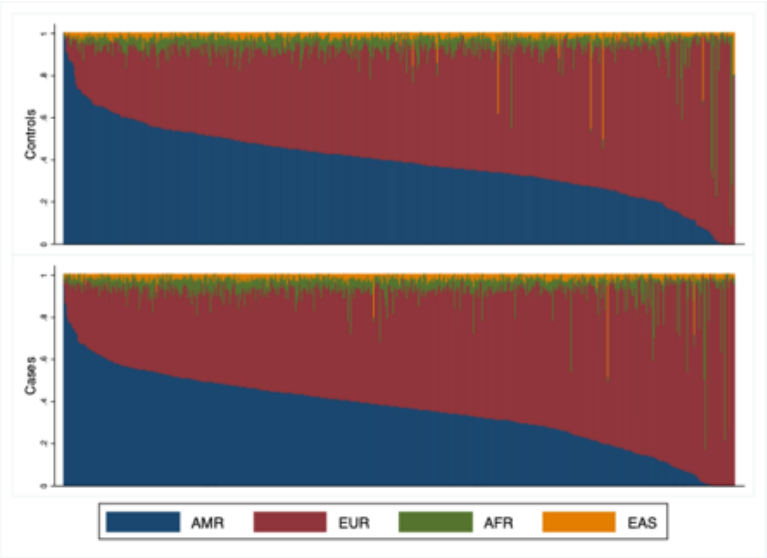
* AUROC from multivariable logistic regression of PRS adjusted for study and genetic ancestry
† Two-sided P-value for test of equality of AUROCs between Q1 and Q4 of IA ancestry
‡ Odds ratio of breast cancer per standard deviation increment of PRS relative to the mean in controls. Calculated from multivariable logistic regression adjusted for study and genetic ancestry
§ Two-sided P-value for comparison of OR of PRS between Q1 and Q4 of IA ancestry using Wald test of linear hypothesis
‖ Women from U.S. studies: SFBCS/NC-BCFR, RPGEH, MEC (total n = 7,317)
¶ Women from Latin-American studies: CAMA, Peru, COLUMBUS - Colombia, COLUMBUS – Mexico (total n = 4,963)

Supplementary Figure 1. Distribution of log-normalized polygenic risk score containing 180 single nucleotide polymorphisms in 4,658 cases and 7,622 controls.

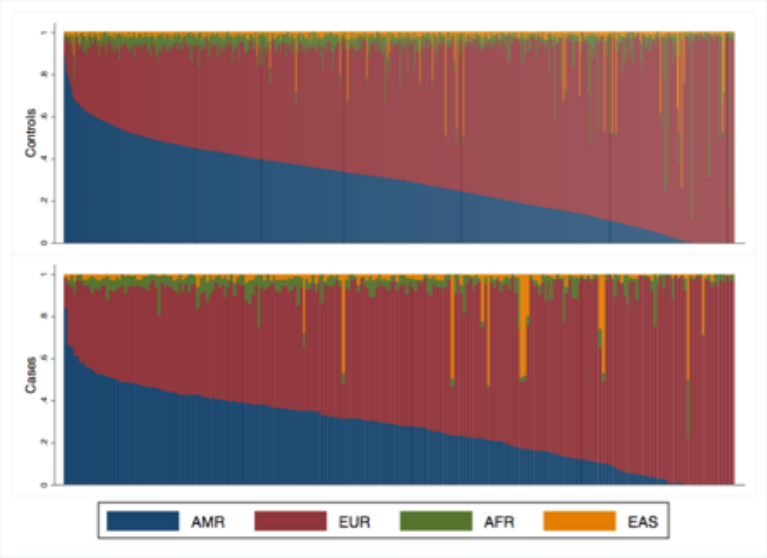


Supplementary Figure 2. Ancestry distribution by case/control status across eight studies included in this analysis: (A) San Francisco Bay Area Breast Cancer Study and Northern California Breast Cancer Family Registry (SFBCS/NC-BCFR), (B) Research Project on Genes, Environment, and Health (RPGEH), (C) Multiethnic Cohort (MEC), (D) Cancer de Mama (CAMA), (E) Colombian Study of Environmental and Heritable Causes of Breast Cancer (COLUMBUS)-Colombia, (F) COLUMBUS-Mexico, (G) Peru Genetics and Genomics of Breast Cancer Study (PEGEN-BC), and (H) City of Hope/Clinical Cancer Genetics Community Research Network (COH/CCGCRN). Each individual is represented by a vertical line with relative contributions of Indigenous American (AMR), European (EUR), African (AFR), and East Asian (EAS) genetic ancestry represented by the colors.

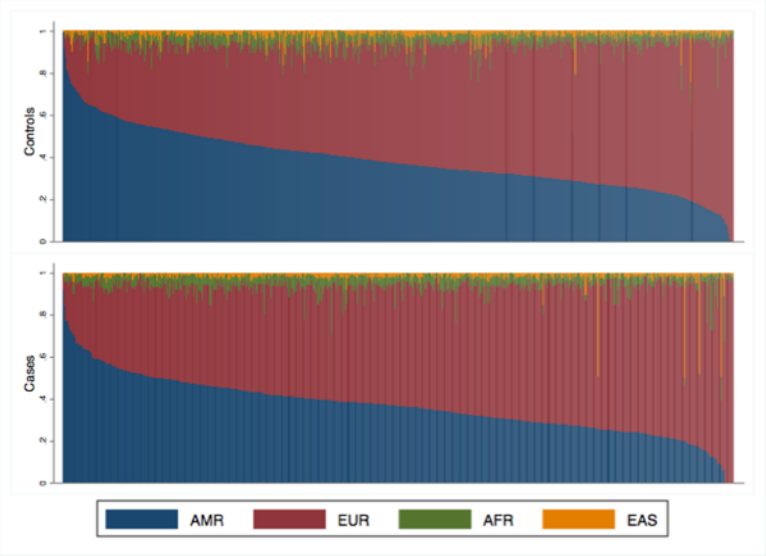
A. SFBCS/NC-BCFR



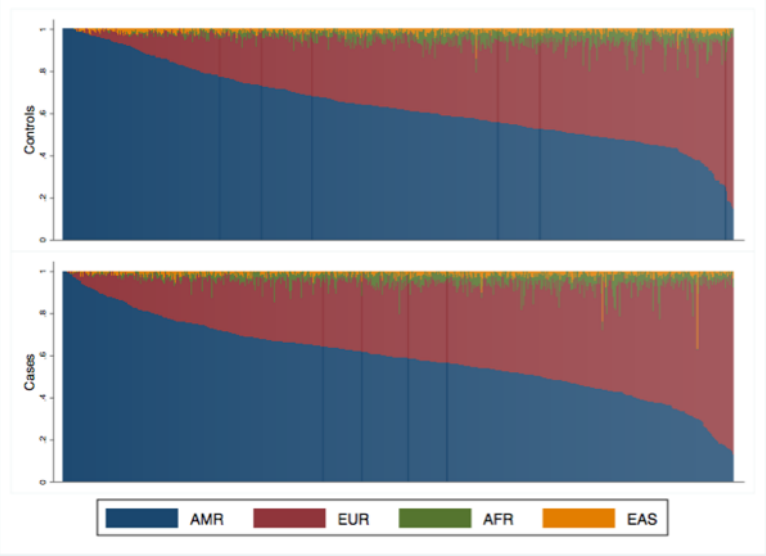
B. RPGEH



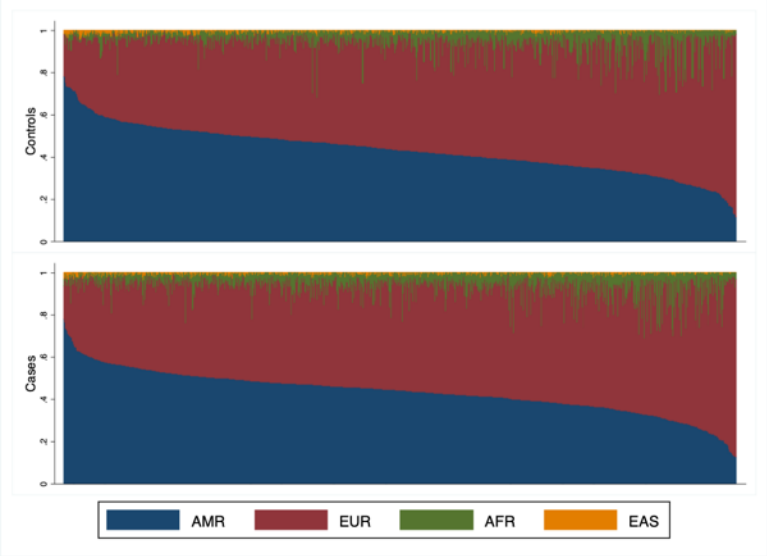
C. MEC



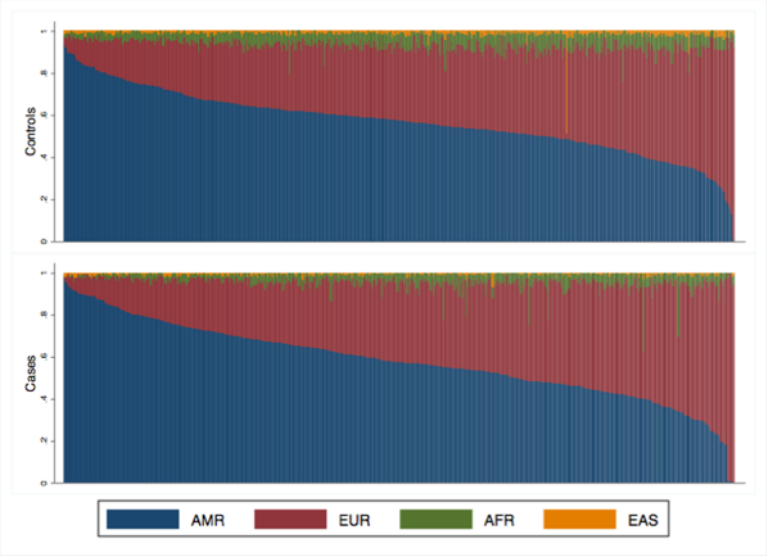
D. CAMA



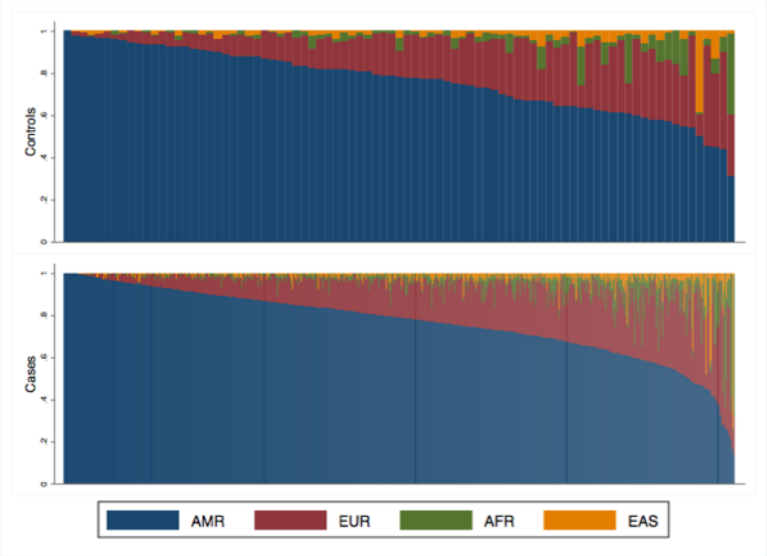
E. COLUMBUS - Colombia



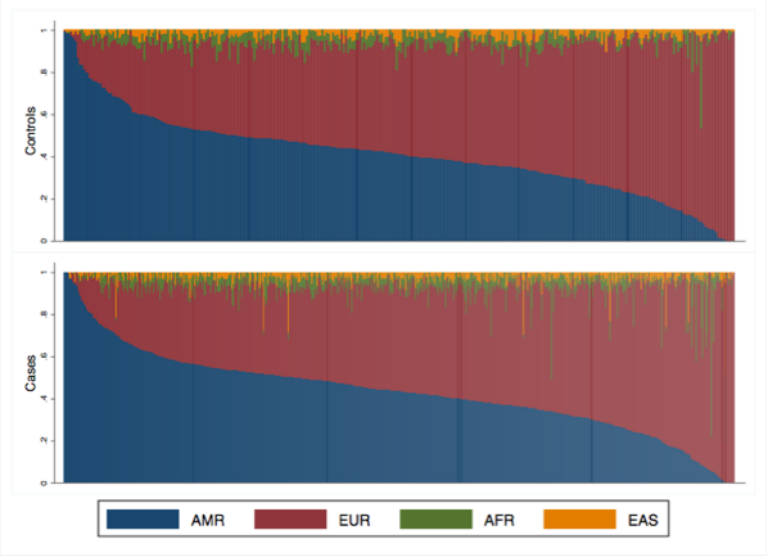
F. COLUMBUS - Mexico



G. PEGEN-BC



H. CCGRN



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