SUPPLEMENTAL MATERIAL

Table S1. ICD codes used to determine cases and controls for cardiometabolic and female health phenotypes

Phenotype	Cases	Controls
Cardiometabolic Phenotypes		
Coronary Artery Disease	414.0*, I25.1*	Females without codes from cases
Hypertension	401*, I10*	Females without codes from cases
Type 2 Diabetes	250*, E11*	Females without codes from cases
Women's Health Phenotypes		
Placenta abruption, previa	O44.*, O45.*, 641.0, 641.1, 641.2, 667, 762.0, 762.1, 762.2	Z32.01, O80.*, 650, V72.42 (ICD-9)but no code 632.* or O02.* and no codes from cases
Gestational Hypertension	O13.*, 642.4, 642.5, 642.6, 642.7	Z32.01, O80.*, 650, V72.42 (ICD-9), O09.*, V23.*(ICD-9), Z33.1, V22.2 (ICD-9)but no code 632.* or O02.* and no codes from cases
PreEclampsia	O14.*, O11.*, 642.4, 642.5, 642.6, 642.7	Z32.01, O80.*, 650, V72.42 (ICD-9), O09.*, V23.*(ICD-9), Z33.1, V22.2 (ICD-9)but no code 632.* or O02.* and no codes from cases
Poor fetal growth	O36.5*	Females with codes O80.*, 650.* but not the code in cases
Excessive fetal growth	036.6*, 656.6, 656.60, 656.63, 656.61	Females with codes O80.*, 650.* but not the code in cases
Intrauterine Death	656.4, 656.41, 656.43, O31.2, O36.4. O36.4XX0,O36.4XX1, O36.4XX2, O36.4XX3, O36.4XX4, O36.4XX5, O36.4XX9, 656.4,656.41.656.43 but not with any of codes O35.9XX0, Q95.0, Q95.1, Q95.8,Q95.9	Females with codes O80.*, 650.* but not the code in cases
Stillbirth	P95, Z37.1, V27.1 (ICD-10), V27.4 (ICD-10), Z37.4, V27.7(ICD-10), V35 (ICD-9) Z37.7 but not with any of codes O35.9XX0, Q95.0, Q95.1, Q95.8,Q95.9	Females with codes O80.*, 650.* but not the code in cases also no code Z35.208

Gestational Diabetes	O24.*, 648.8*	Z32.01, O80.*, 650, V72.42 (ICD-9), O09.*, V23.*(ICD-9), Z33.1, V22.2 (ICD-9) but no code 632.* or O02.* and no codes from cases
Ectopic Pregnancy	633.*, O00.*, V32.42(ICD-9), 761.4, O08.105,O08.806, O08.006, O008.104, O009, P01.4, CPT-codes: 59130, 59140, 59135, 59136, 59120, 59121	Z32.01, O80.*, 650, V72.42 (ICD-9), O09.*, V23.*(ICD-9), Z33.1, V22.2 (ICD-9)but no code 632.* or O02.* and no codes from cases and no codes O09.1, O09.11, O09.12, O09.13, O09.10
Miscarriage	632,O02.1,O31.10X0 but not with any of codes O35.9XX0, Q95.0, Q95.1, Q95.8,Q95.9	Z32.01, O80.*, 650, V72.42 (ICD-9), O09.*, V23.*(ICD-9), Z33.1, V22.2 (ICD-9)but no codes from cases
Uterine fibroid	D25.9, 218.9	Females without codes from cases
Endometriosis	N80.*, 617.*	Females without codes from cases
Polycystic Ovarian Syndrome	E28.2, 256.4	Females without codes from cases
Breast Cancer	C50.*, 174,175,233.0	Females without codes from cases
Vulvar Cancer	C51.*, 184.4	Females without codes from cases
Vaginal Cancer	C52.*, 184.0	Females without codes from cases
Cervical Cancer	C53.*, 180.*	Females without codes from cases
Endometrial cancer	C54.*, 182.*	Females without codes from cases
Uterine cancer	C55.*, 179	Females without codes from cases
Ovarian Cancer	C56.*, 183,186,220,220.0	Females without codes from cases
Postpartum depression	F53.*, O90.6, 648.4*	Females with codes O80.*, 650.* but not the code in cases
Preterm birth	O60.1*, 644.765	Females with codes O80.*, 650.* but not the code in cases
Postpartum hemorrhage	O72.*, 666.0,666.1,666.2	Females with codes O80.*, 650.* but not the code in cases

Table S2. Publicly available female health condition GWAS used in two-sample MR

Phenotype	Ancestry	Source	Sample Size (N cases)	Reference or PMID
Breast Cancer	EUR	BCAC	33832 (15748)	25751625
Endometrial Cancer	EUR	ECAC, E2C2, UKBB	121885 (12906)	30093612
Gestational Diabetes	EUR	FinnGen	116363 (6033)	https://r5.finngen.fi/
Gestational Hypertension	EUR	FinnGen	118990 (4255)	https://r5.finngen.fi/
Preeclampsia	EUR	FinnGen	123579 (8844)	https://r5.finngen.fi/
Polycystic Ovarian Syndrome	EUR	FinnGen	118870 (642)	https://r5.finngen.fi/
Postpartum Depression	EUR	FinnGen	67205 (7604)	https://r5.finngen.fi/

Table S3. PGS performance on cardiometabolic phenotypes in PMBB using LD panels of different ancestries

PRS	LD Panel	R^2/AUC in PMBB All	R^2/AUC in PMBB EUR	R^2/AUC in PMBB AFR
BMI	Multi	0.1542	0.07977	0.03556
	EUR	0.1528	0.7888	0.3381
	AFR	0.1538	0.07575	0.03663
CAD	Multi	0.8235	0.8303	0.799
	EUR	0.8237	0.8303	0.7992
	AFR	0.8238	0.8303	0.7994
DBP	Multi	0.0425	0.01555	0.04545
	EUR	0.0412	0.01425	0.04429
	AFR	0.0427	0.01564	0.04597
PP	Multi	0.8125	0.7797	0.839
	EUR	0.8123	0.7796	0.8387
	AFR	0.8124	0.7795	0.839
SBP	Multi	0.8144	0.7817	0.8416
	EUR	0.8143	0.7818	0.8413
	AFR	0.8144	0.7815	0.8415
T2D	Multi	0.754	0.7133	0.7366
	EUR	0.7544	0.7148	0.7364
	AFR	0.7529	0.7089	0.7369

Table S4. Direct tests for pleiotropy using MR Egger for two-sample Mendelian randomization

Exposure	Outcome	Intercept	SE	P value
BMI	Breast Cancer	0.015	0.0056	0.0089
	Endometrial Cancer	0.0033	0.0064	0.6
	Gestational Diabetes	0.035	0.011	0.0016
	Polycystic Ovarian Syndrome	-0.0048	0.03	0.88
CAD	Breast Cancer	0.0025	0.0026	0.34
PP	Gestational Hypertension	0.009	0.0094	0.338
	Preeclampsia	0.0034	0.0075	0.66
SBP	Gestational Hypertension	-7.86E-05	0.013	0.99
	Preeclampsia	-0.002	0.0093	0.83
T2D	Breast Cancer	0.00035	0.0016	0.83
	Gestational Diabetes	0.0021	0.0033	0.53
	Gestational Hypertension	0.011	0.0027	9.61E-05
	Polycystic Ovarian Syndrome	0.01	0.007	0.14
	Postpartum Depression	0.0037	0.0021	0.082

Table S5. Two-sample Mendelian randomization using female-specific health conditions as exposures and cardiometabolic phenotypes as outcomes

Exposure	Outcome	Method	Beta	SE	P value
Breast Cancer	BMI	IVW	-0.024	0.023	0.3
		Weighted median	-0.01	0.012	0.39
		MR Egger	0.028	0.06	0.64
	CAD	IVW	0.0095	0.01	0.34
		Weighted median	0.014	0.013	0.27
		MR Egger	0.0084	0.023	0.72
	T2D	IVW	0.0023	0.17	0.89
		Weighted median	0.0011	0.009	0.91
		MR Egger	0.026	0.039	0.51
Endometrial Cancer	BMI	IVW	0.034	0.022	0.13
		Weighted median	0.03	0.018	0.1
		MR Egger	0.021	0.12	0.87
Gestational Diabetes	BMI	IVW	-0.021	0.022	0.37
		Weighted median	0.0096	0.01	0.35
		MR Egger	0.0037	0.0099	0.71
	T2D	IVW	0.2	0.049	3.00E-05
		Weighted median	0.12	0.011	3.00E-31
		MR Egger	0.13	0.11	0.26
Polycystic Ovarian Syndrome	T2D	Wald ratio	-0.01	0.016	0.51
Preeclampsia	PP	IVW	0.91	0.27	0.00065
		Weighted median	0.84	0.25	0.00093
		MR Egger	5.75	4	0.39

	SBP	IVW	3.46	0.65	1.12E-07
		Weighted median	3.41	0.41	6.06E-17
		MR Egger	7.5	14.9	0.7

*No SNPs were left after filtering for genome-wide significance and pruning for the postpartum depression GWAS. PCOS had no overlapping SNPs with the BMI GWAS. SNPs could not be extracted for the gestational hypertension GWAS.
**Wald ratio was used for the PCOS and T2D MR since there was only one genome-wide significant SNP in the PCOS GWAS.

Table S6. Mean F-statistic of SNPs used in each two-sample MR analysis

Exposure	Outcome	Mean F-statistic
BMI	Breast Cancer	64.968
	Endometrial Cancer	64.968
	Gestational Diabetes	64.775
	Polycystic Ovarian Syndrome	64.775
CAD	Breast Cancer	67.841
PP	Gestational Hypertension	57.511
	Preeclampsia	57.511
SBP	Gestational Hypertension	57.848
	Preeclampsia	57.848
T2D	Breast Cancer	84.601
	Gestational Diabetes	83.931
	Gestational Hypertension	83.931
	Polycystic Ovarian Syndrome	83.931

Table S7. PRS PC associations in PMBB and eMERGE

PRS	Group	R^2
eMERGE		
BMI	All	0.503
	EUR	0.0727
	AFR	0.27
CAD	All	0.11
	EUR	0.0156
	AFR	0.0361
DBP	All	0.352
	EUR	0.135
	AFR	0.182
PP	All	0.346
	EUR	0.0469
	AFR	0.176
SBP	All	0.572
	EUR	0.271
	AFR	0.395
T2D	All	0.598
	EUR	0.174
	AFR	0.374
PMBB		
BMI	All	0.602
	EUR	0.00334
	AFR	0.227

CAD	All	0.163
	EUR	0.0106
	AFR	0.0158
DBP	All	0.451
	EUR	0.0423
	AFR	0.102
PP	All	0.517
	EUR	0.0117
	AFR	0.16
SBP	All	0.58
	EUR	0.0284
	AFR	0.198
T2D	All	0.647
	EUR	0.0428
	AFR	0.292

Table S8. One-sample Mendelian randomization using only PRS with no other covariates

Exposure	Outcome	Group	Beta	SE	P value
BMI	Breast Cancer	All	-0.00737	0.0027	0.00629
	Endometrial Cancer	All	6.94E-07	0.000402	0.999
		EUR	0.0014	0.000362	0.000112
	Gestational Diabetes	All	0.0097	0.00731	0.185
		EUR	0.0144	0.00373	0.000108
	Polycystic Ovarian Syndrome	All	0.00264	0.000678	9.79E-05
		EUR	0.00275	0.000387	1.18E-12
CAD	Breast Cancer	All	-0.427	0.0451	3.24E-21
		EUR	-0.2	0.0356	1.75E-08
	Postpartum Depression	EUR	2.62	1.61	0.104
HT (PP)	Gestational Hypertension	All	0.911	0.564	0.106
		EUR	1.73	0.671	0.00976
	Preeclampsia	All	0.915	0.369	0.0132
SBP	Gestational Hypertension	All	0.743	0.287	0.00978
		EUR	0.987	0.432	0.0223
		AFR	0.722	0.296	0.0149
	Preeclampsia	All	0.779	0.0176	9.35E-06
		EUR	0.637	0.165	0.000119
		AFR	0.853	0.314	0.00658
T2D	Breast Cancer	All	-0.182	0.0506	0.000315
		EUR	-0.114	0.0223	3.06E-07
	Gestational Diabetes	All	1.05	0.165	2.11E-10
		EUR	1.59	0.252	2.59E-10

	Gestational Hypertension	All	0.976	0.251	0.000102
		EUR	0.865	0.272	0.00146
	Polycystic Ovarian Syndrome	All	0.058	0.00717	5.67E-16
		EUR	0.0625	0.0108	5.95E-09
		AFR	0.0246	0.0244	0.312
	Postpartum Depression	All	1.33	0.77	0.0839

Figure S1. Genetic correlations between multi-ancestry cardiometabolic phenotypes and female-specific health conditions using European (left) and African (right) ancestry-derived GWASs

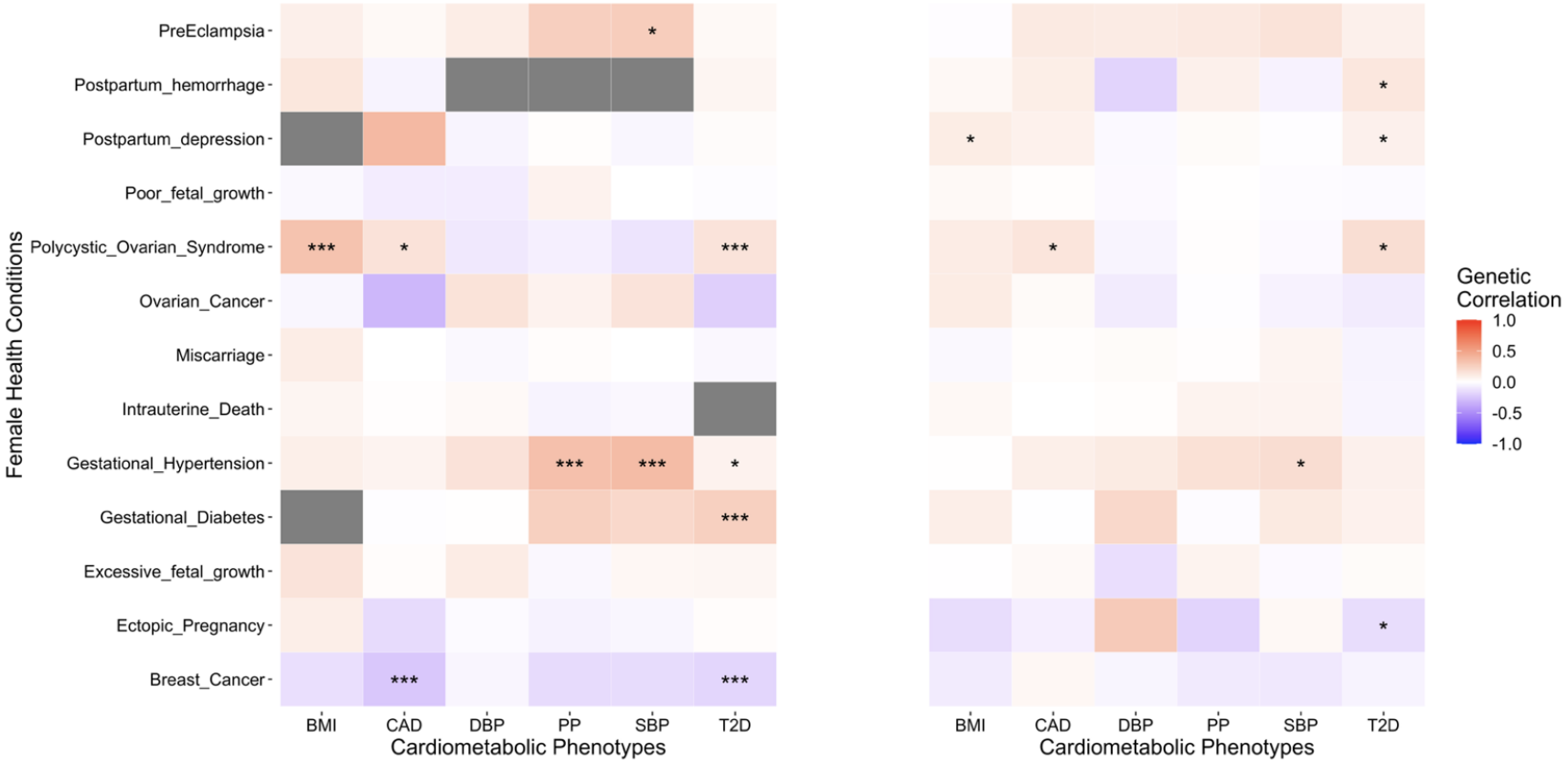


Figure S2. PRS_{BMI} distribution (eMERGE on left and PMBB on right)

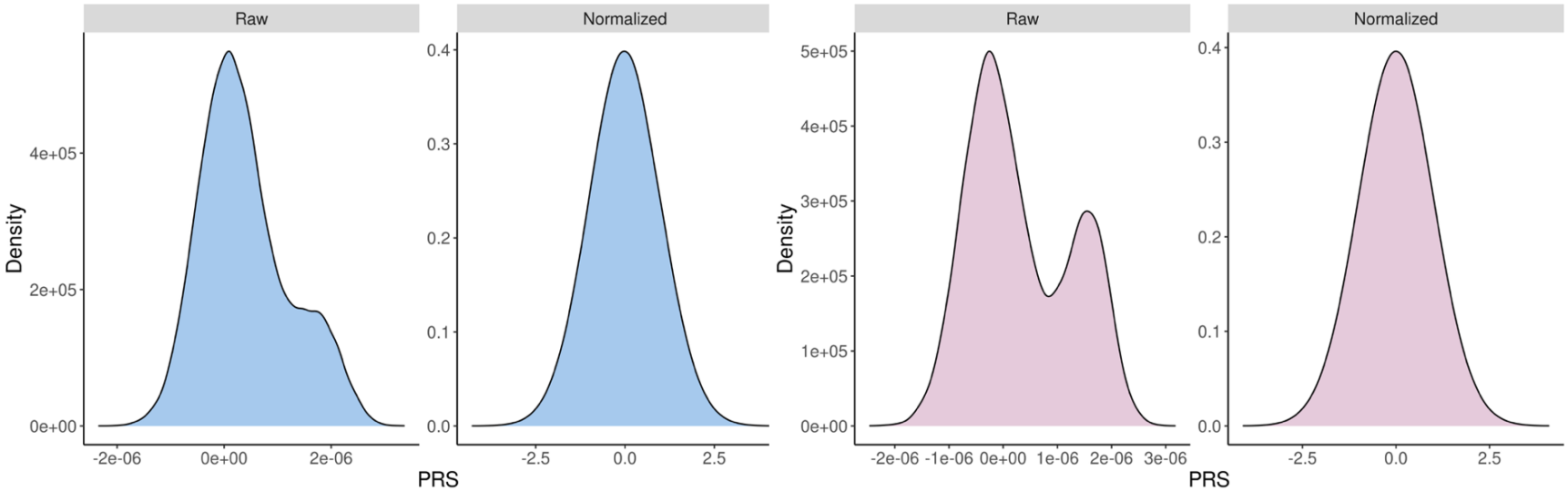


Figure S3. PRS_{CAD} distribution (eMERGE on left and PMBB on right)

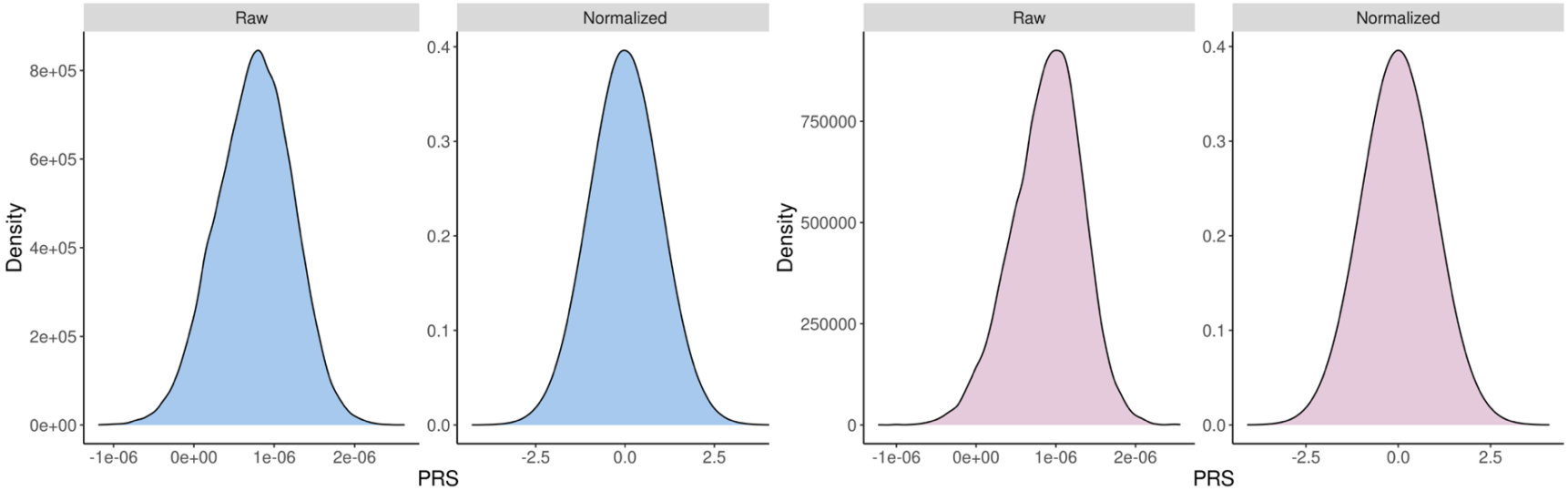


Figure S4. PRS_{DBP} distribution (eMERGE on left and PMBB on right)

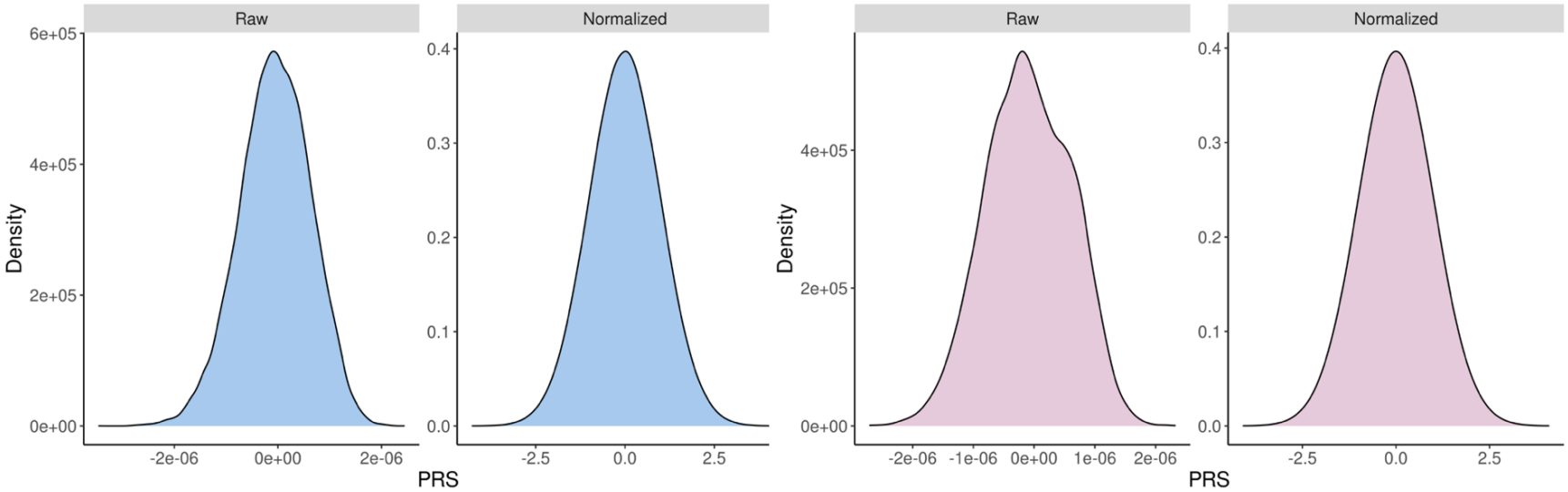


Figure S5. PRS_{PP} distribution (eMERGE on left and PMBB on right)

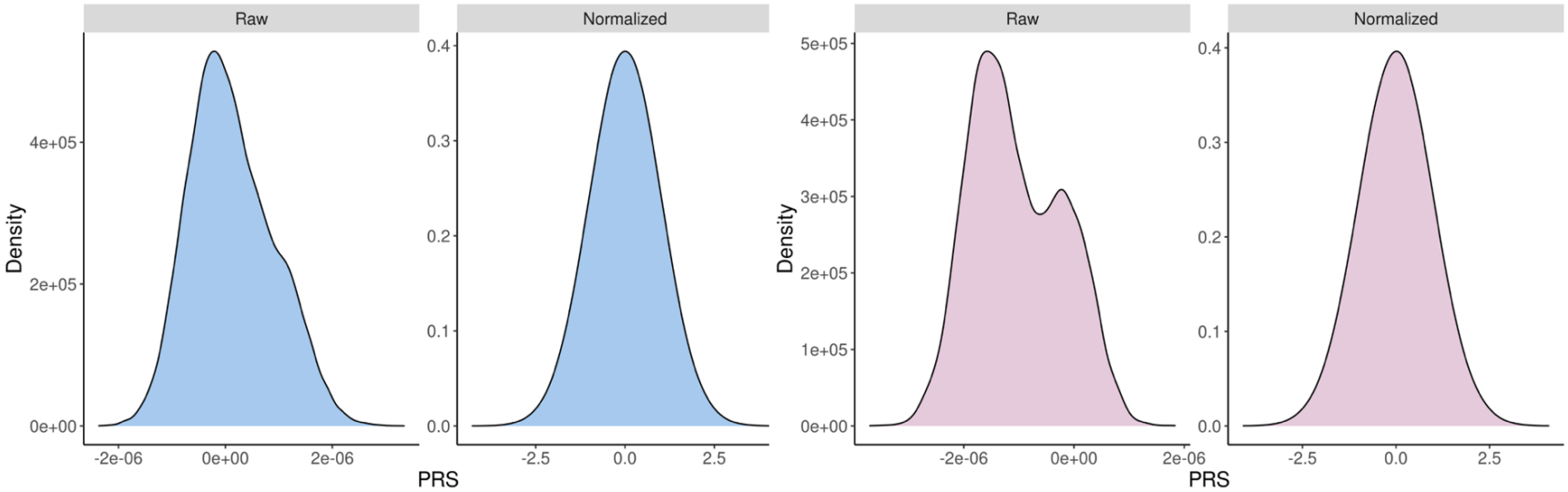


Figure S6. PRS_{SBP} distribution (eMERGE on left and PMBB on right)

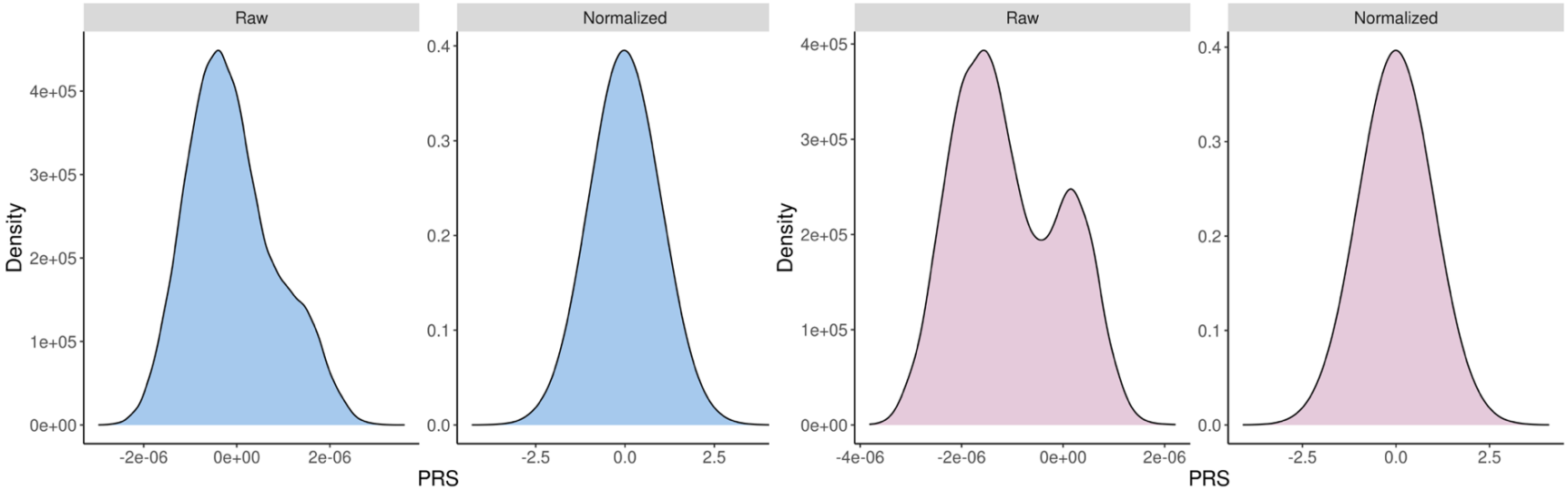


Figure S7. PRS_{T2D} distribution (eMERGE on left and PMBB on right)

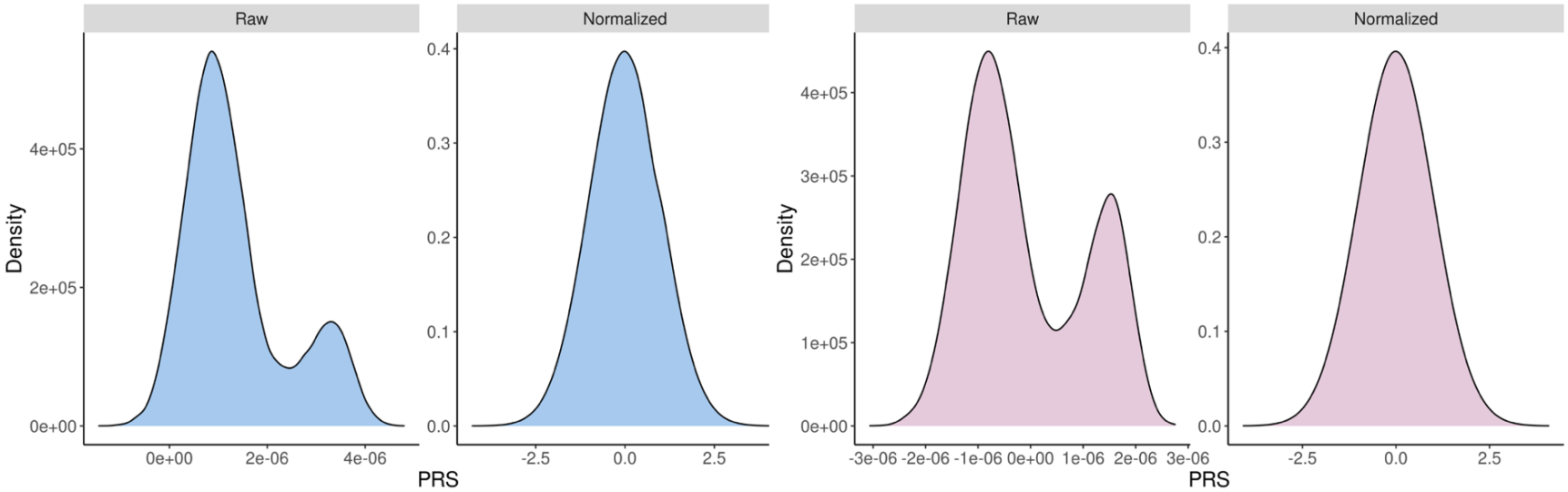


Figure S8. Prevalence by PRS quintile plot (PRS_{BMI} and breast cancer and PRS_{BMI} and endometrial cancer)

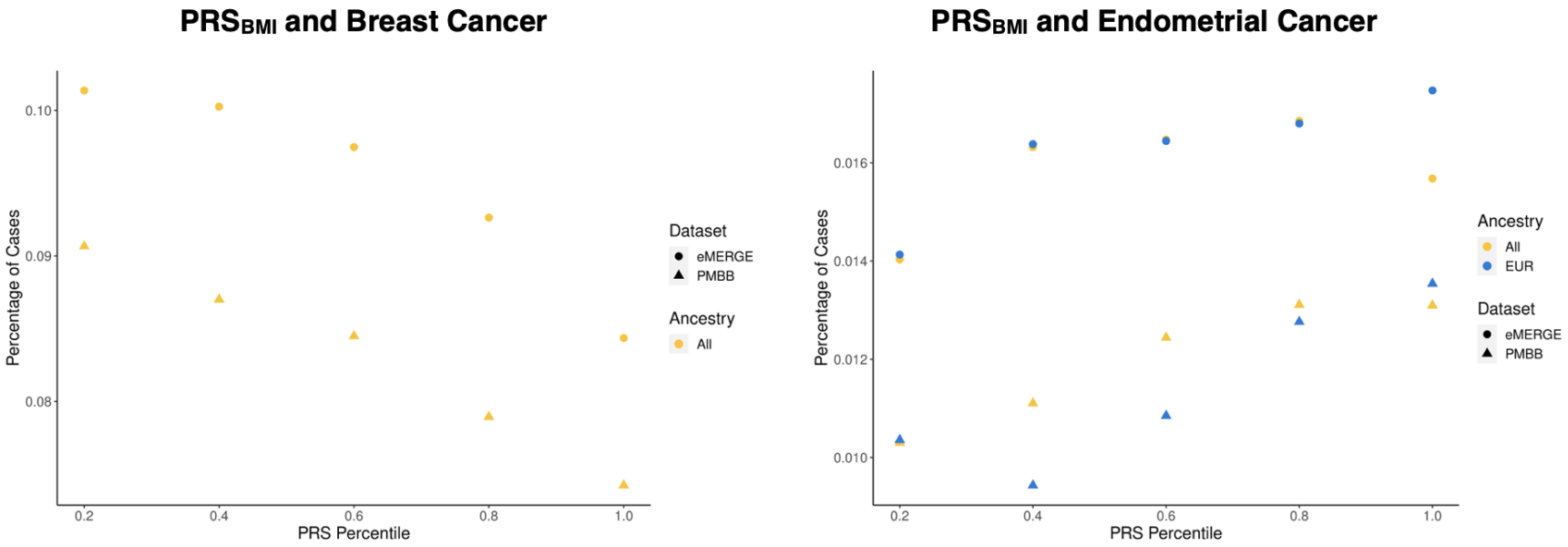


Figure S9. Prevalence by PRS quintile plot (PRS_{BMI} and gestational diabetes and PRS_{BMI} and PCOS)

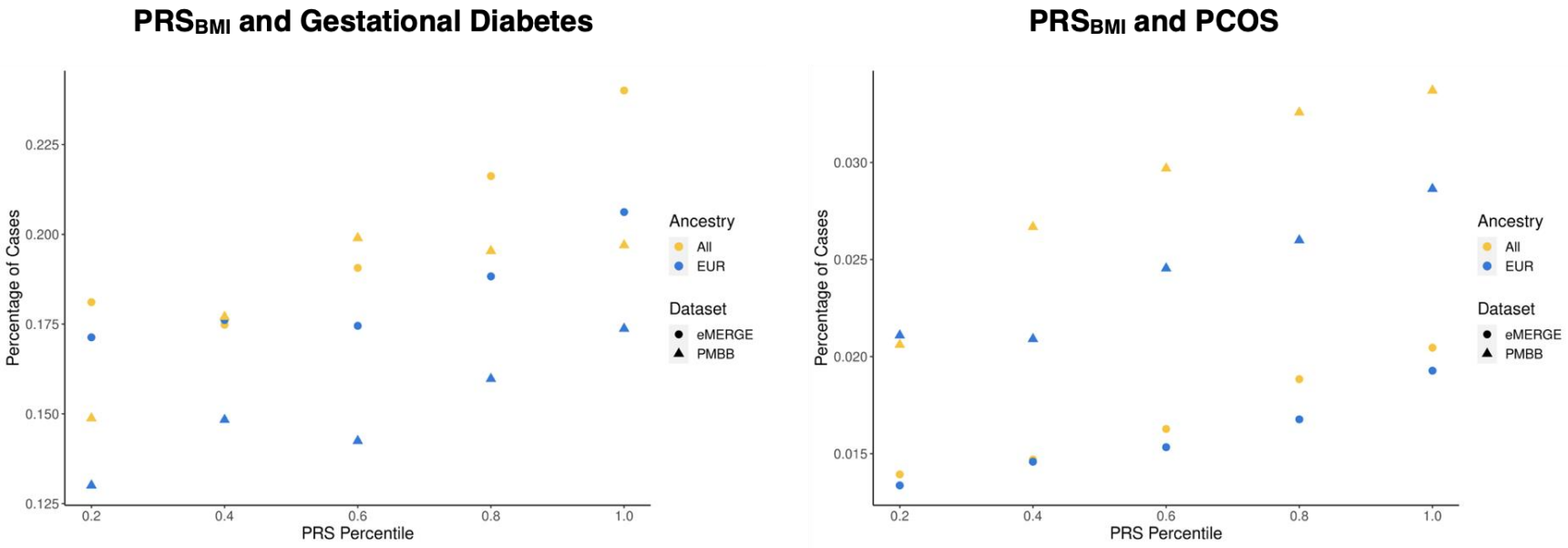


Figure S10. Prevalence by PRS quintile plot (PRS_{DBP} and excessive fetal growth and PRS_{DBP} and gestational hypertension)

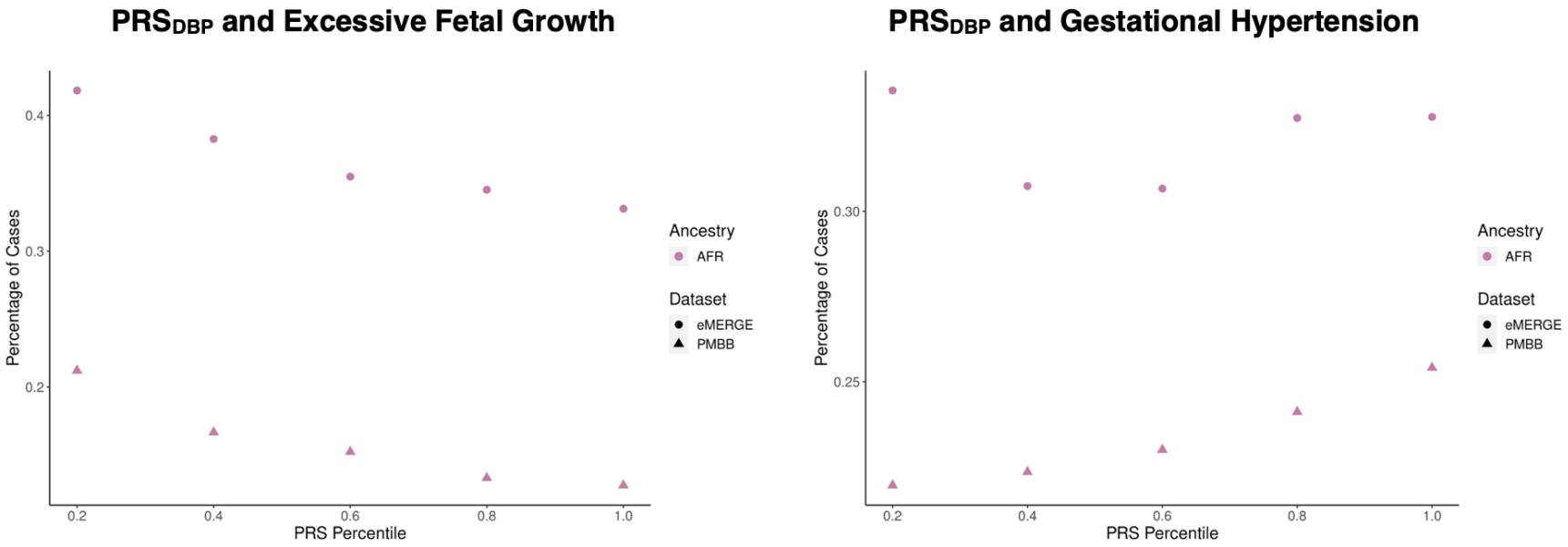


Figure S11. Prevalence by PRS quintile plot (PRS_{PP} and gestational hypertension and PRS_{PP} and preeclampsia)

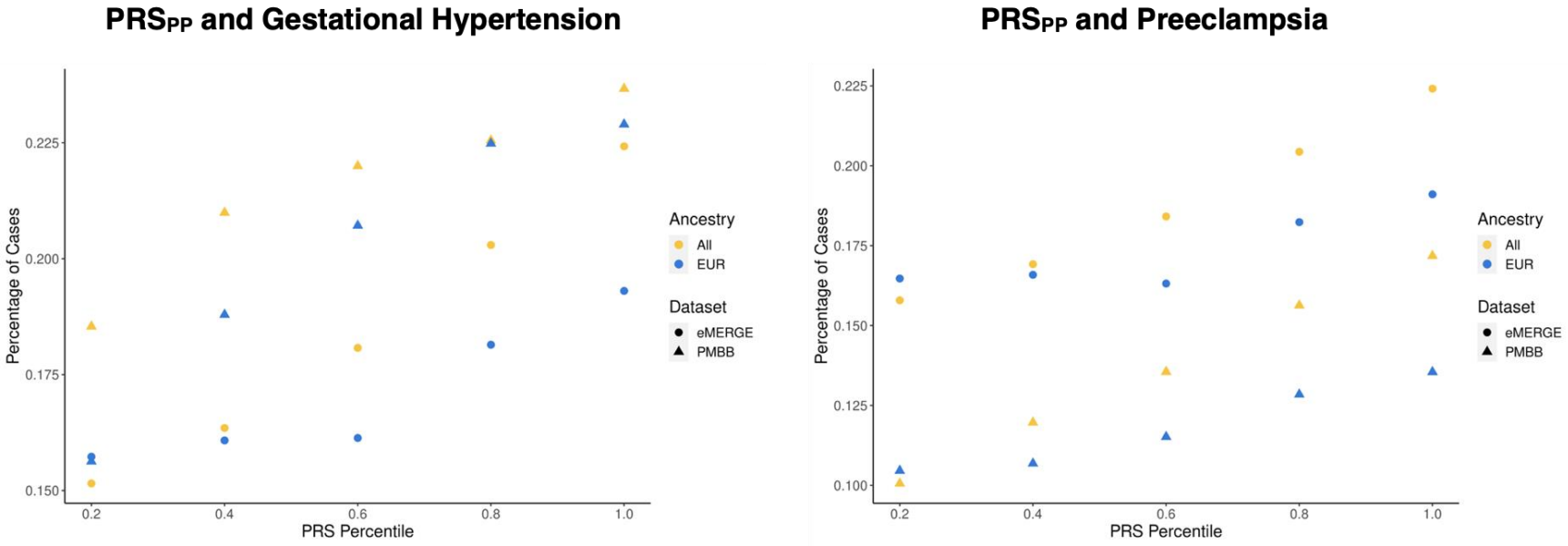


Figure S12. Prevalence by PRS quintile plot (PRS_{SBP} and gestational hypertension and PRS_{SBP} and preeclampsia)

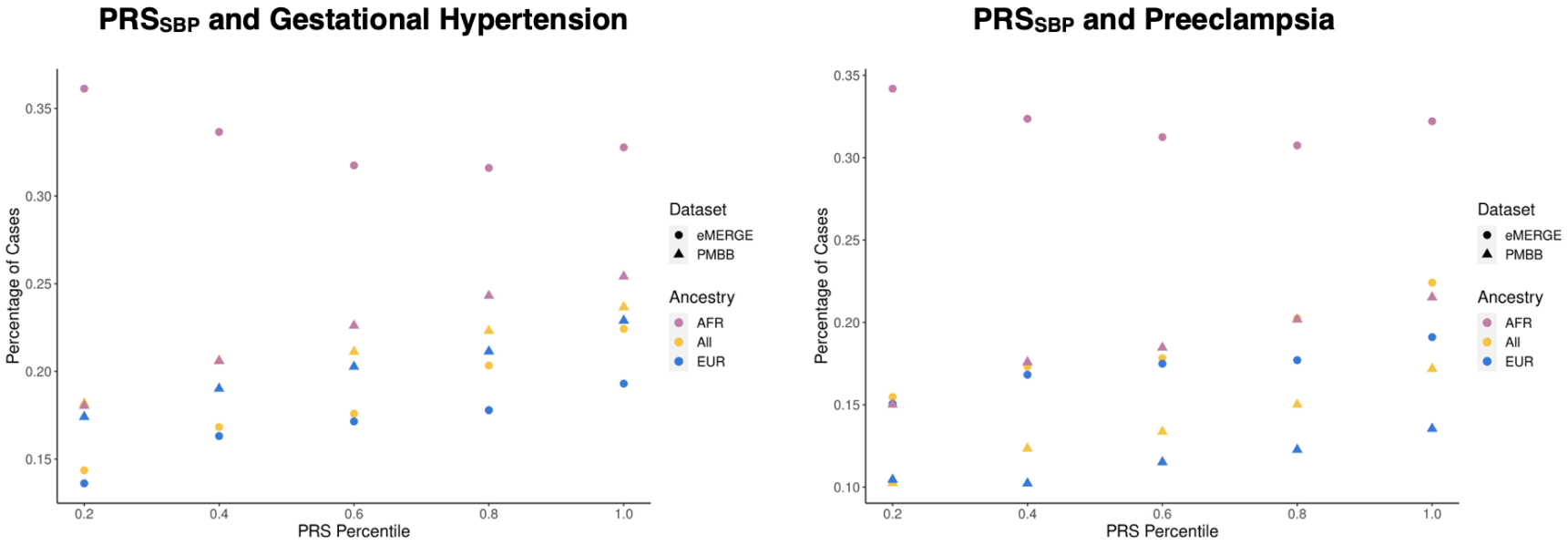


Figure S13. Prevalence by PRS quintile plot (PRS_{T2D} and breast cancer and PRS_{T2D} and gestational diabetes)

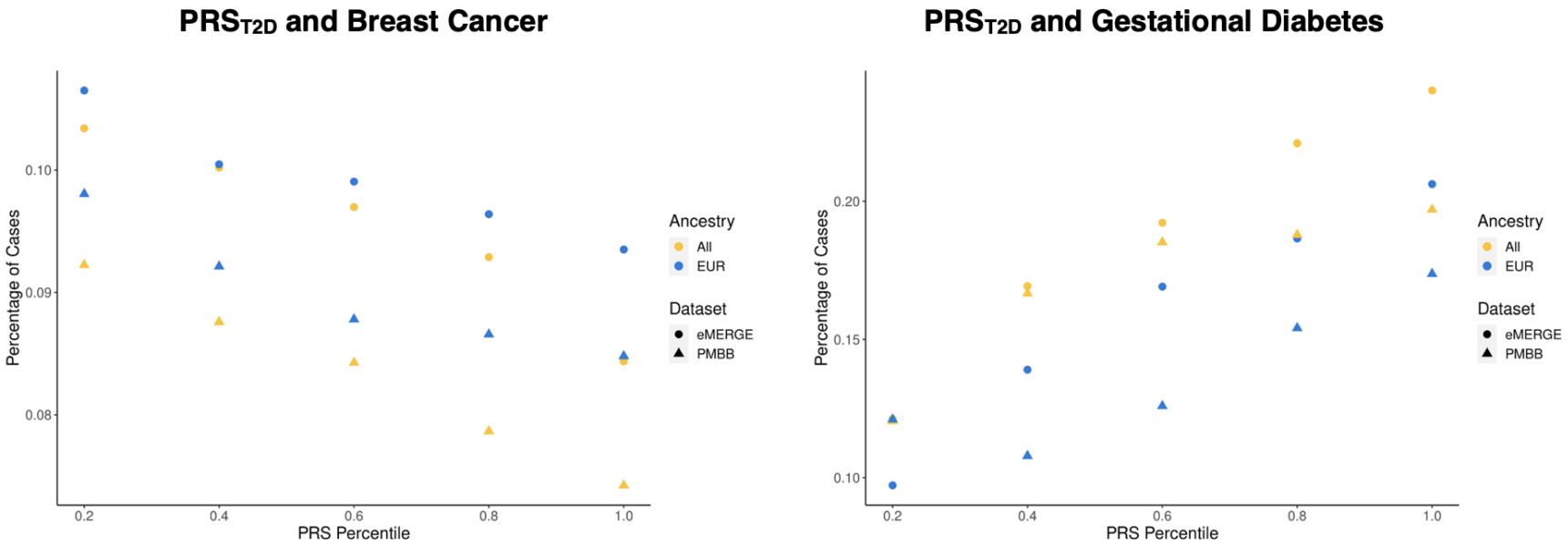


Figure S14. Prevalence by PRS quintile plot (PRS_{T2D} and gestational hypertension and PRS_{T2D} and PCOS)

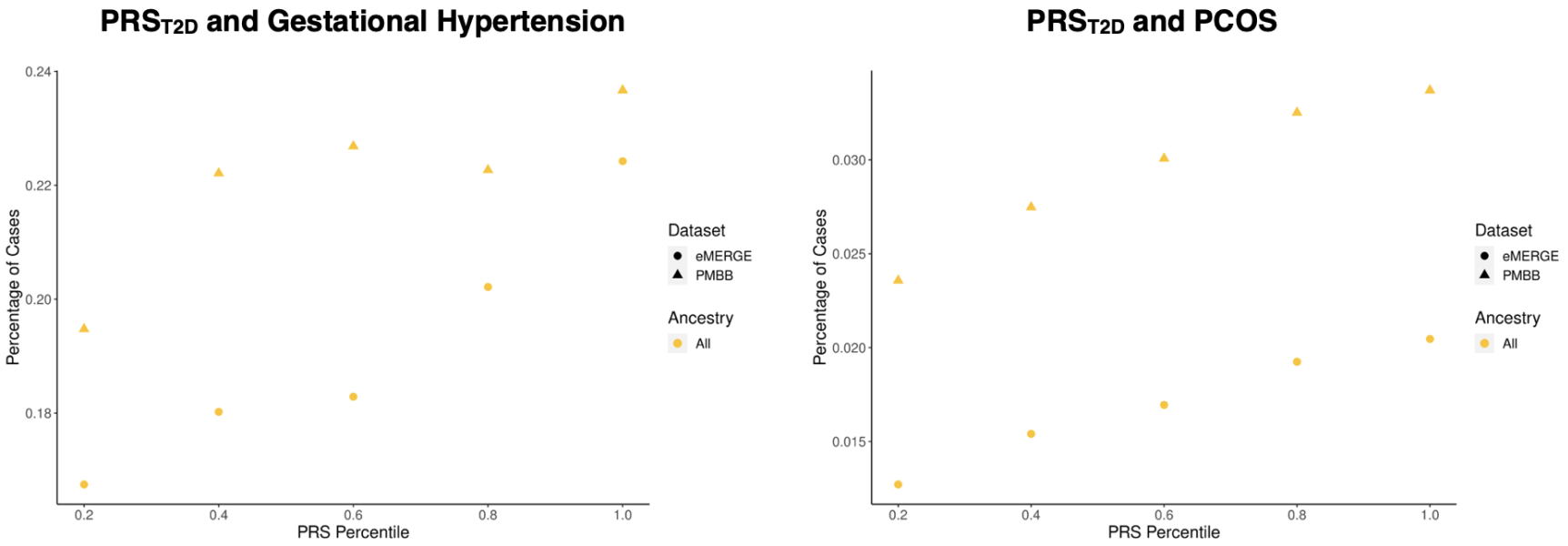
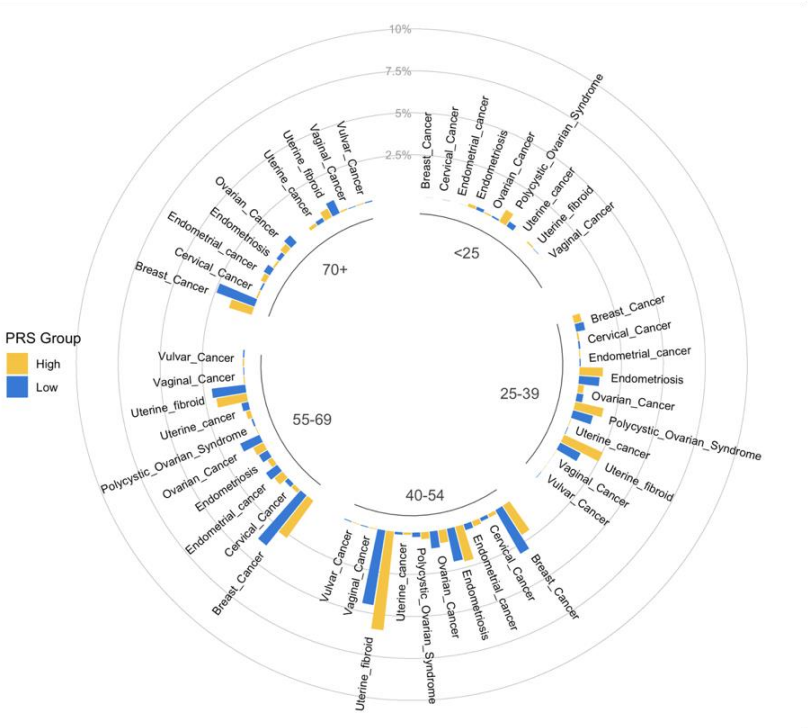


Figure S15. Chronological map for patients with high and low PRS_{CAD}



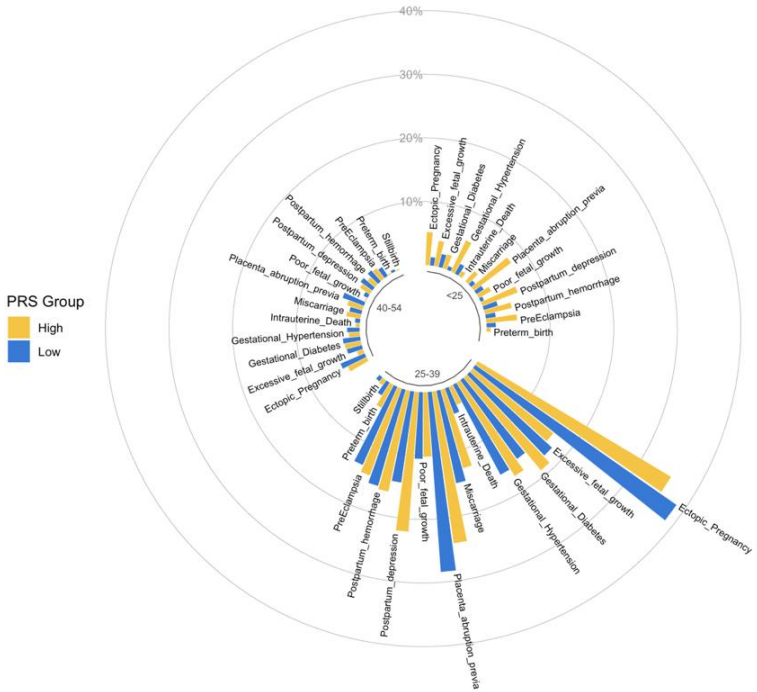


Figure S16. Chronological map for patients with high and low PRS_{DBP}

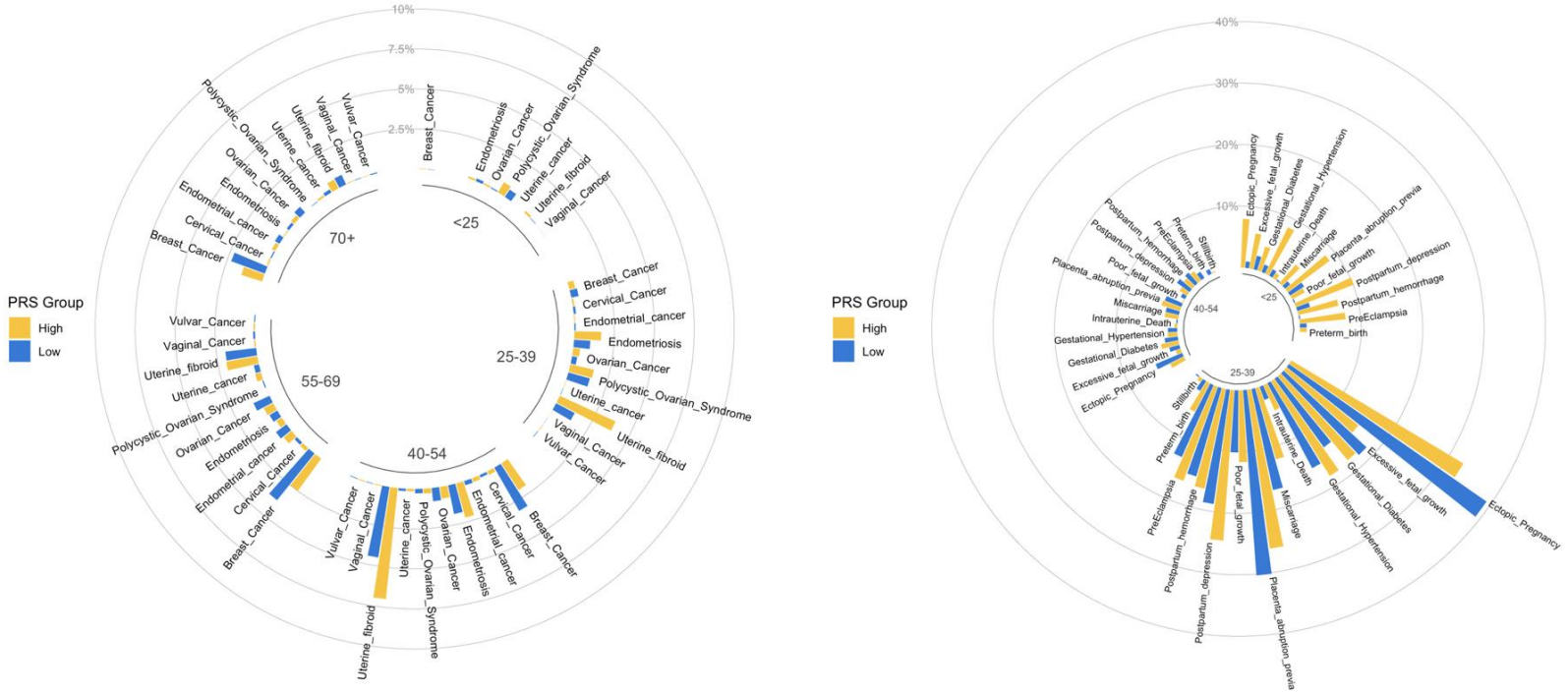


Figure S17. Chronological map for patients with high and low PRS_{PP}

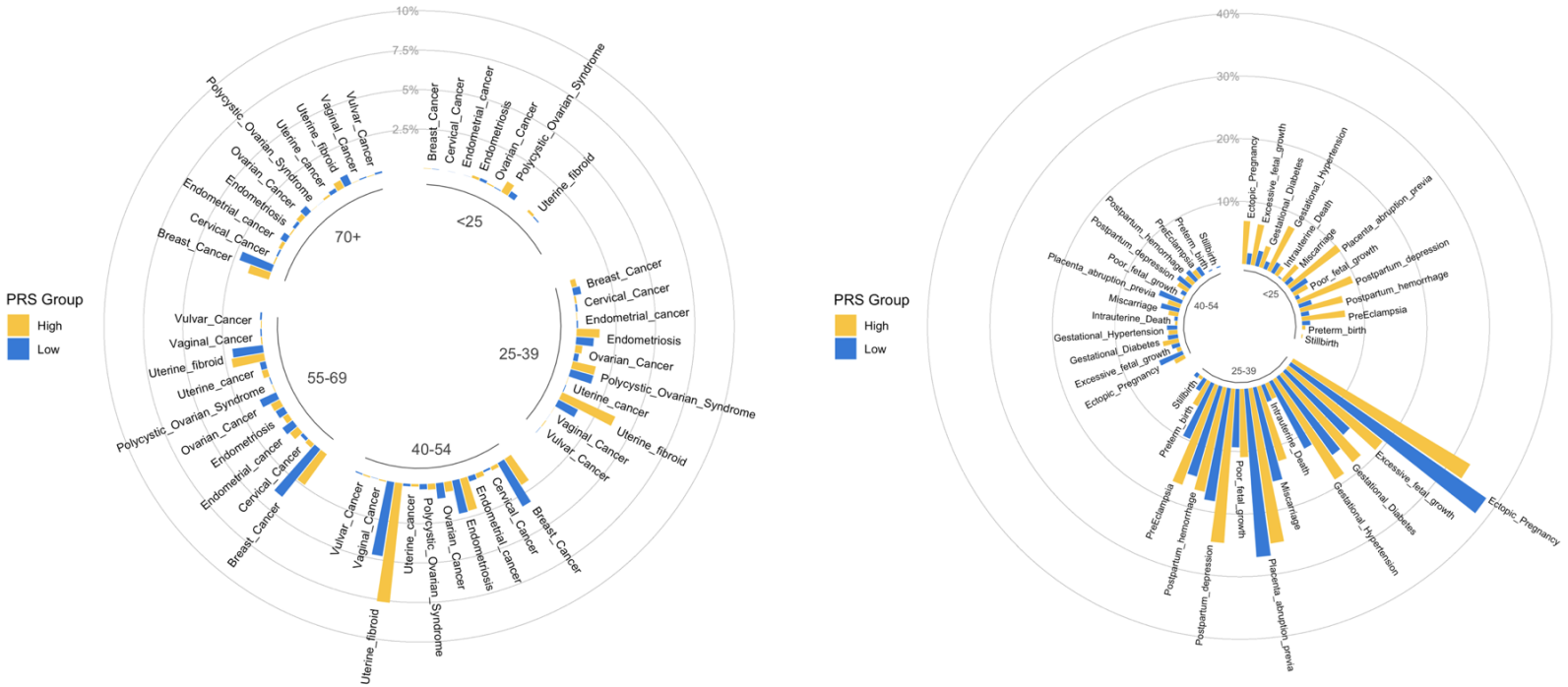


Figure S18. Chronological map for patients with high and low PRS_{SBP}

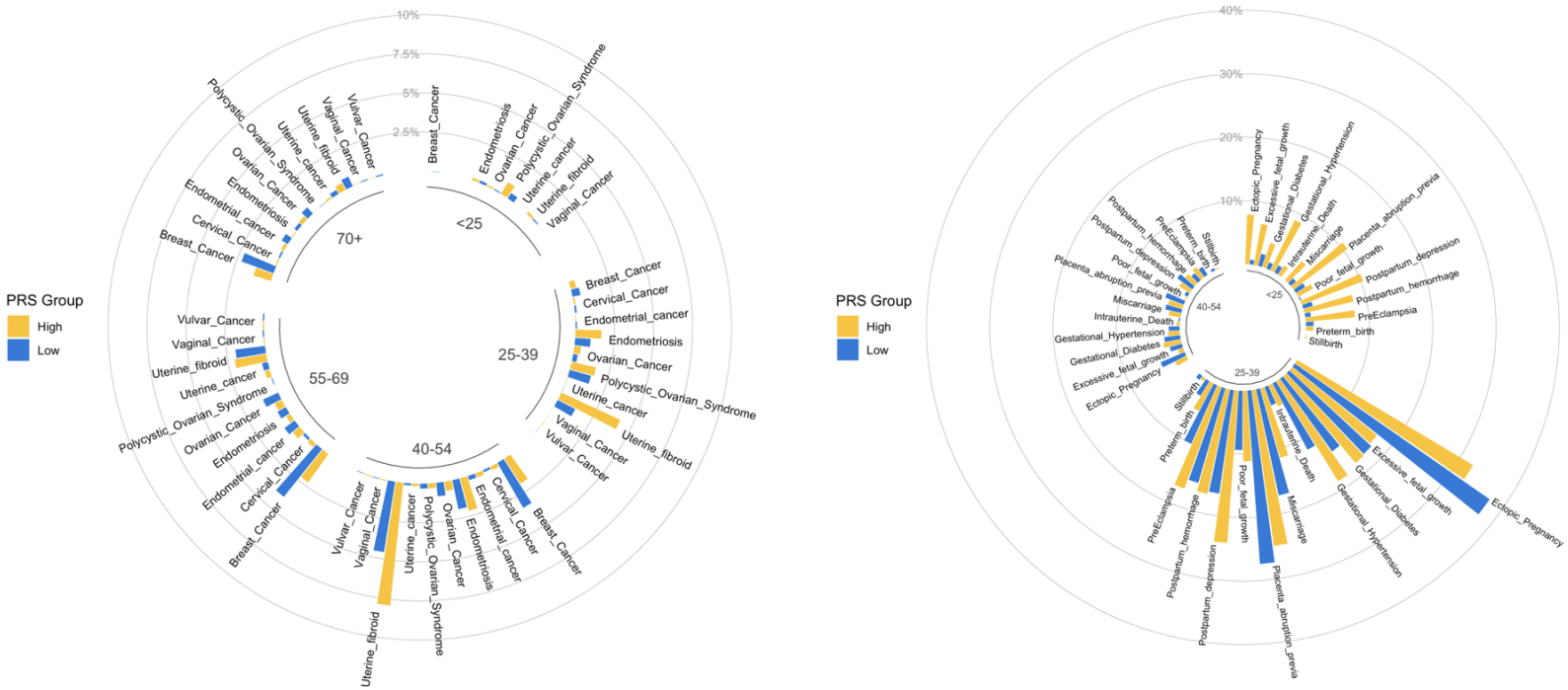


Figure S19. Chronological map for patients with high and low PRS_{T2D}