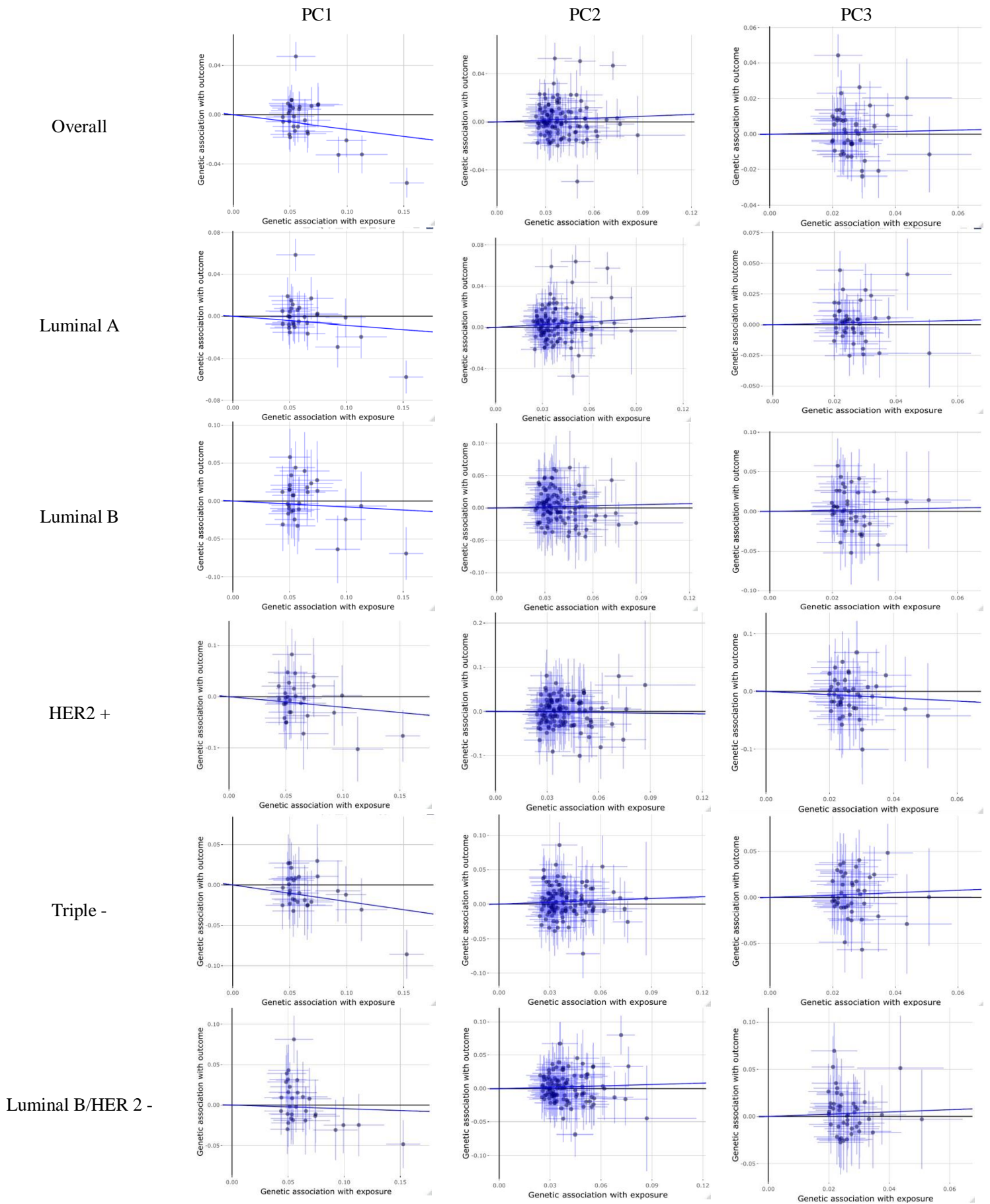


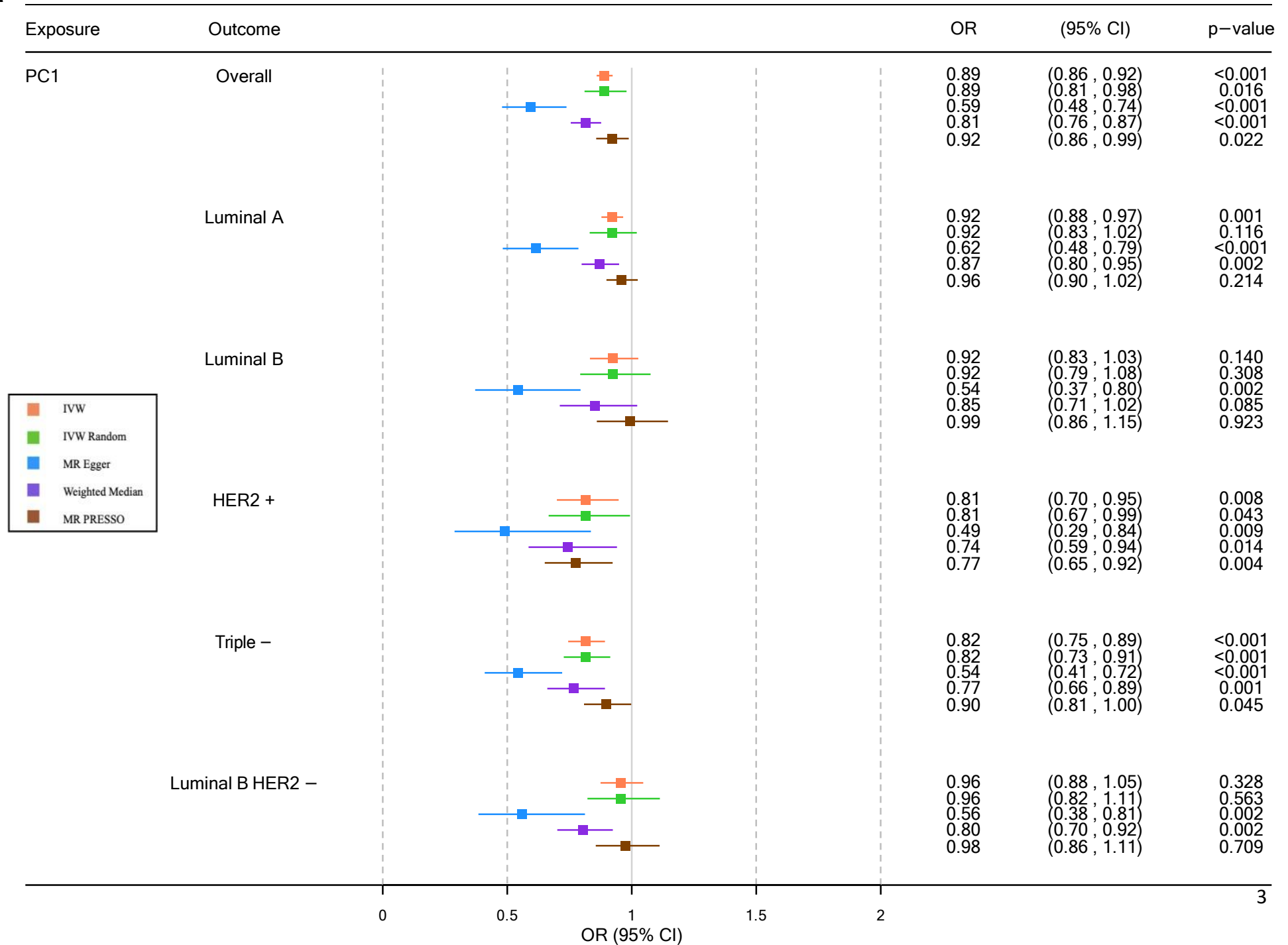
Supplementary Figures and Tables

Supplementary Figure S1	2
Supplementary Figure S2	3
Supplementary Figure S3	6
Supplementary Figure S4	7
Supplementary Table S1	8
Supplementary Table S2	9
Supplementary Table S3	10
Supplementary Table S4	11
References	12

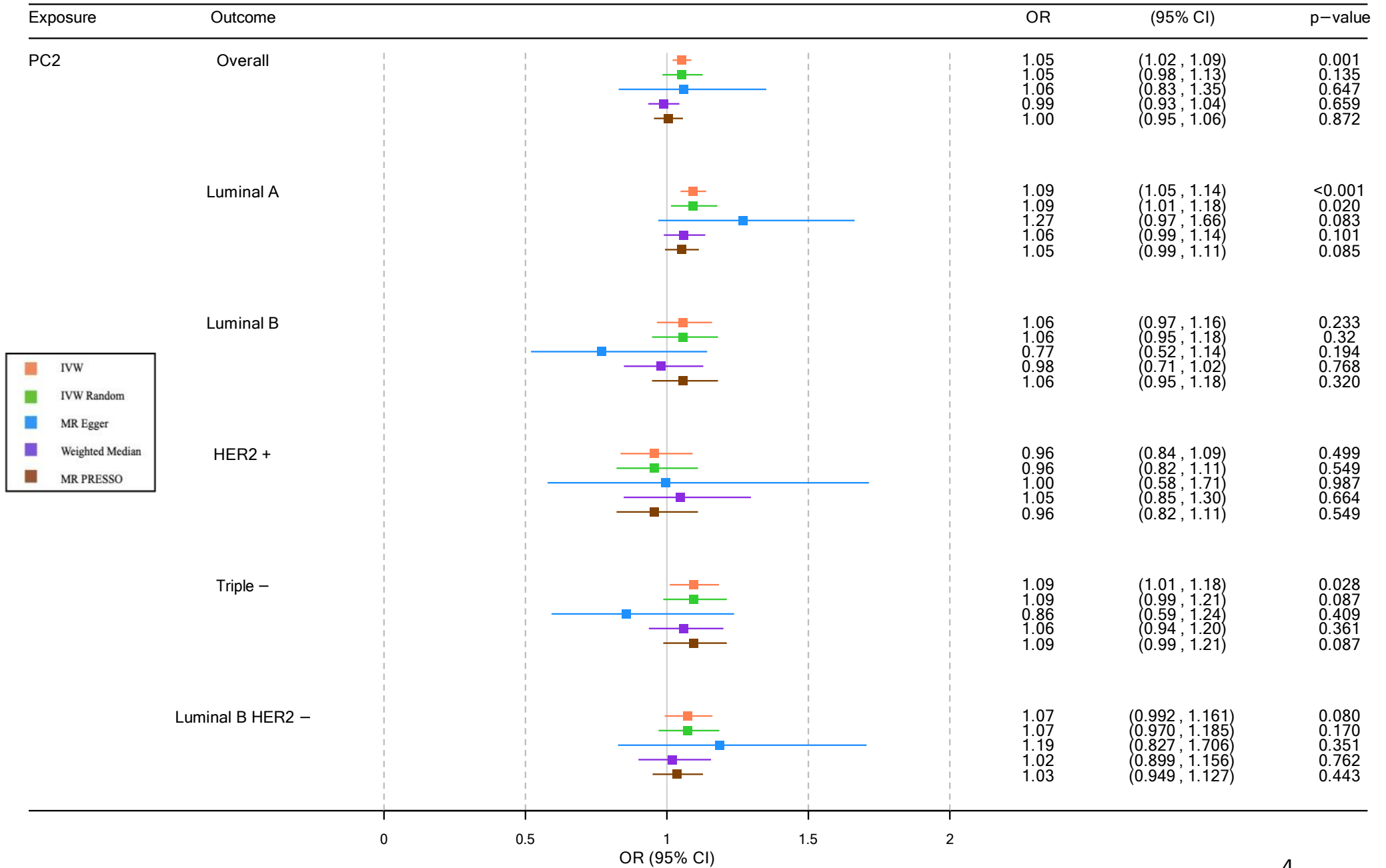


Supplementary Figure S1. Scatter plots of associations between body shapes and overall breast cancer and sub-types.

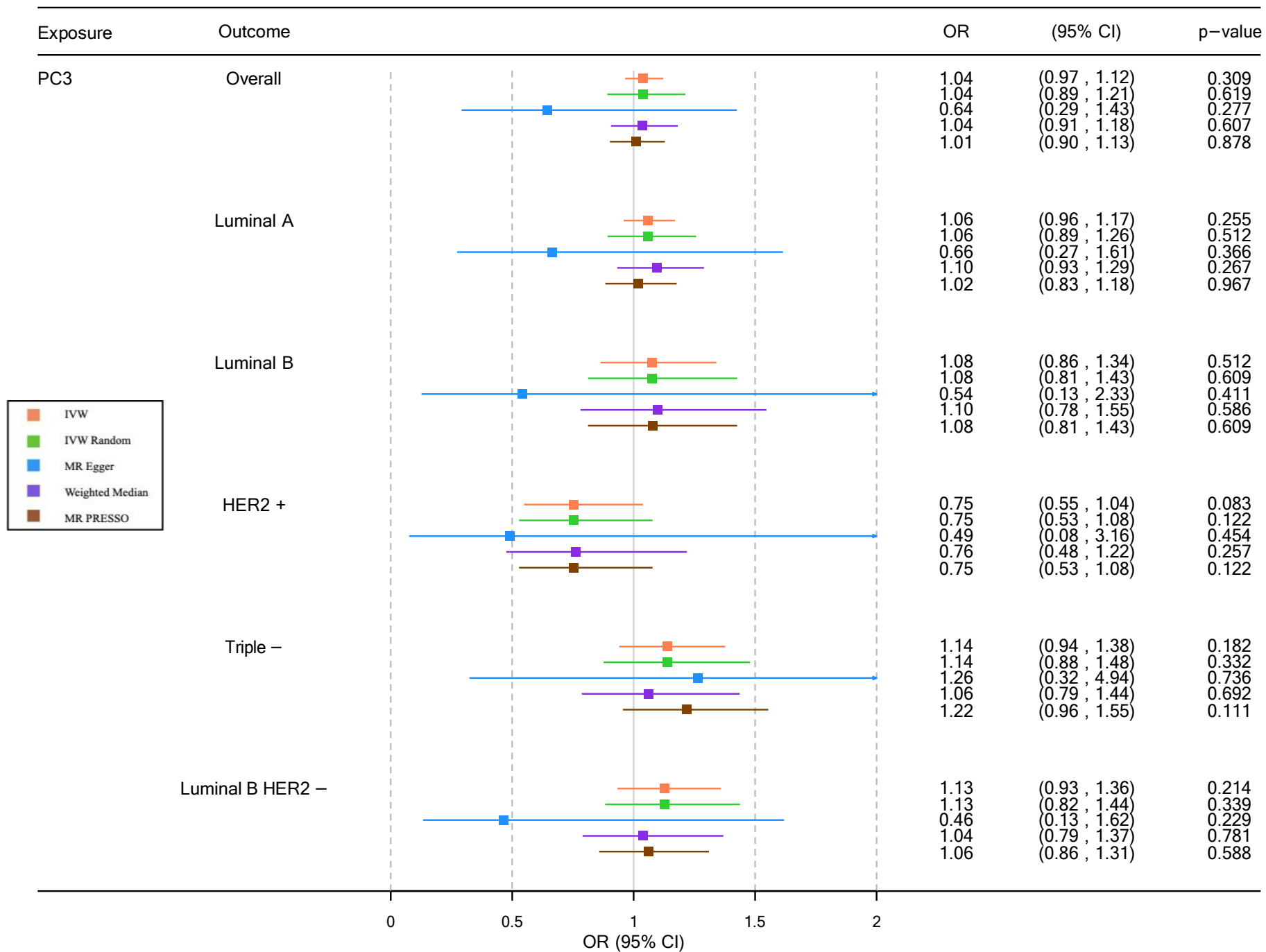
A



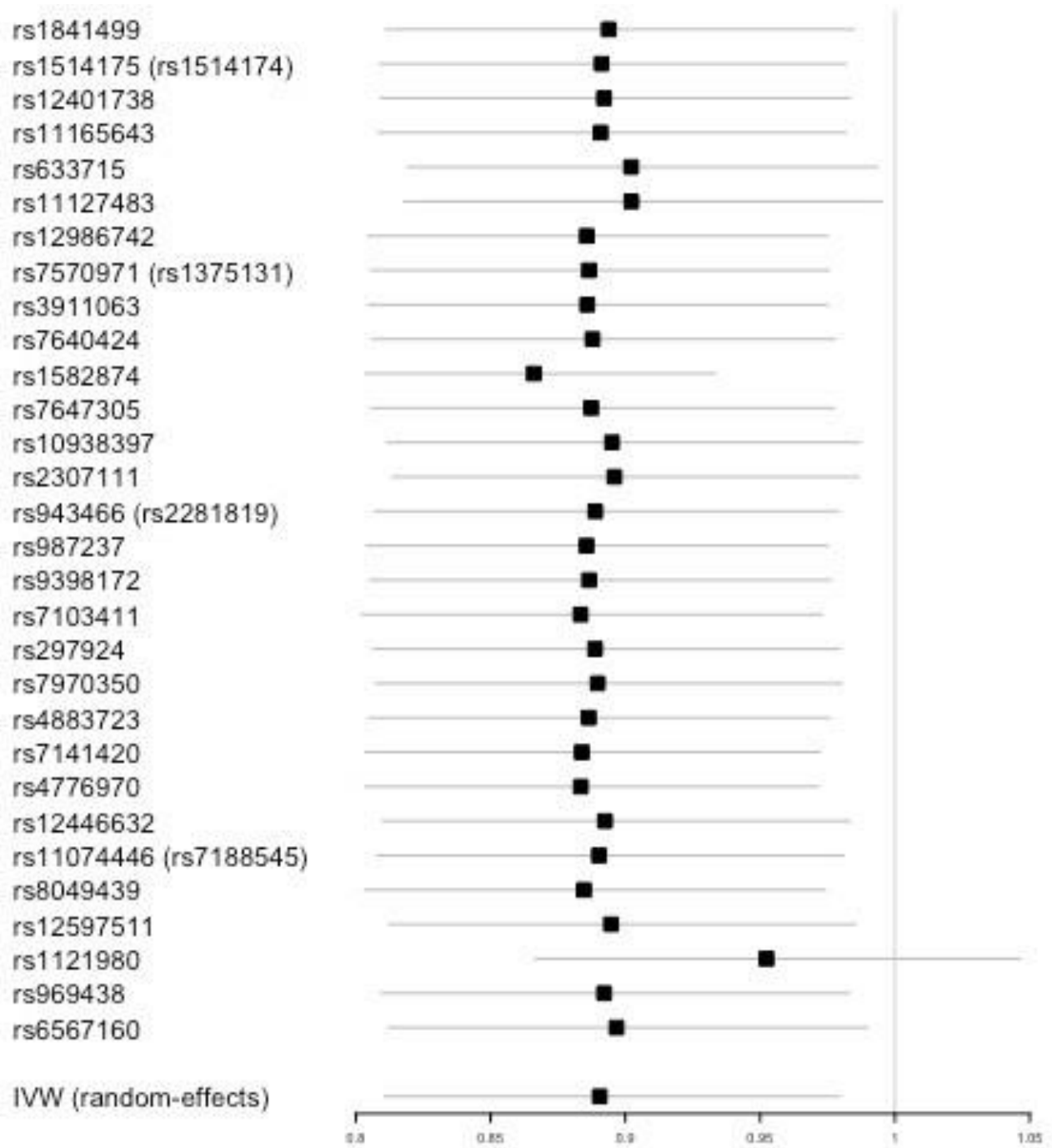
B



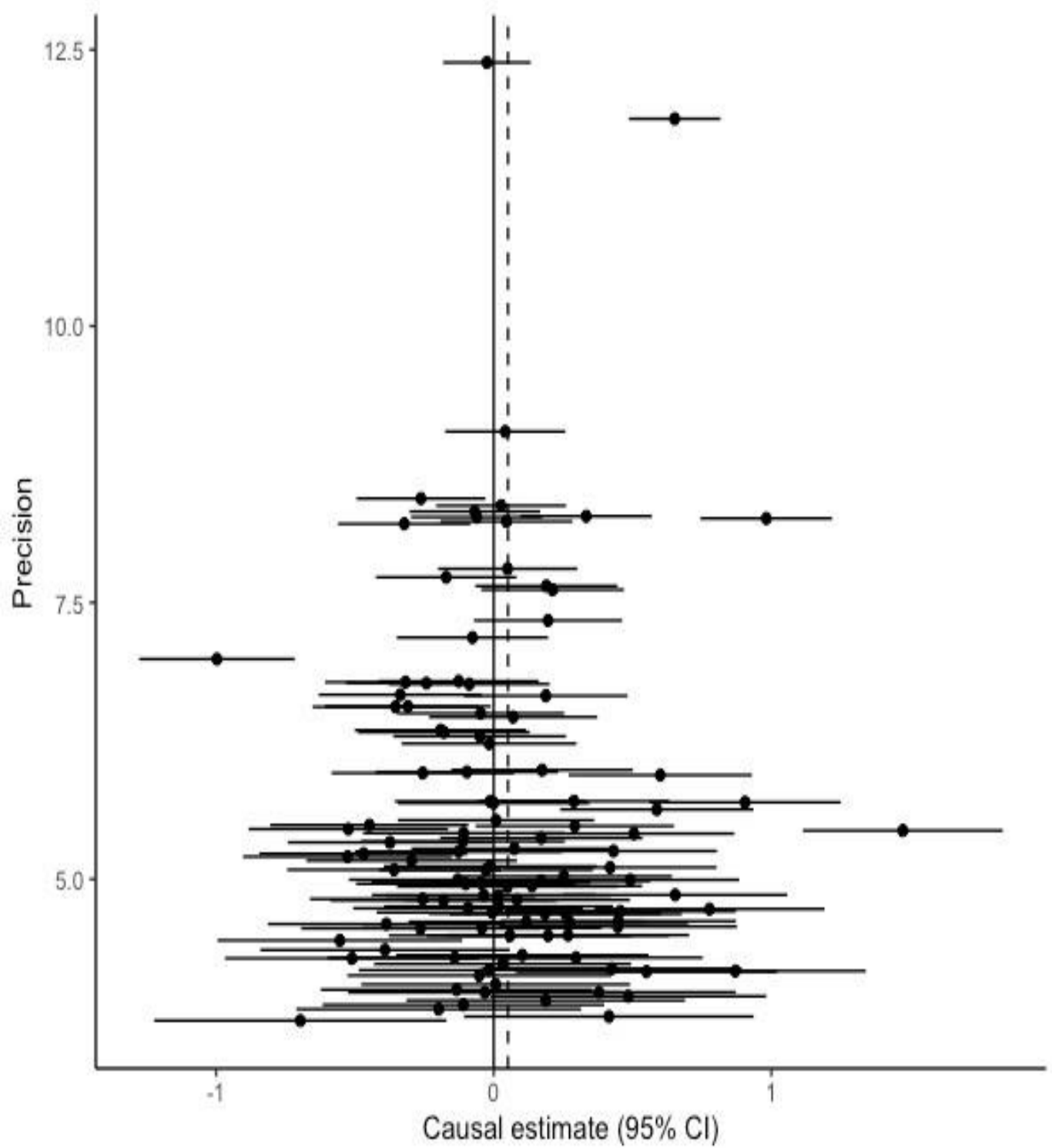
C



Supplementary Figure S2. Mendelian randomization estimates between body shape phenotype PC1 (A), PC2 (B) and PC3 (C) and overall and subtypes breast cancer risk using IVW (orange), IVW Random (green), MR Egger (blue), Weighted Median (violet) and MR PRESSO (brown) MR approaches. CI, confidence interval; OR, odds ratio.



Supplementary Figure S3. Leave-one SNP-out plot for PC1 and overall breast cancer risk.



Supplementary Figure S4. Funnel plot for PC2 and overall breast cancer risk.

	PC1	PC2	PC3
BMI	0.473	-0.128	-0.284
Height	0.131	0.803	0.513
Hip	0.444	0.197	-0.399
Waist	0.488	-0.159	0.138
Weight	0.486	0.186	-0.056
WHR	0.297	-0.490	0.689
Explained variance	64.37%	18.46%	13.79%

Supplementary Table S1. Loadings and explained variance of the three PCs.¹

Breast cancer GWAS sample size		
Breast cancer	Overall	Sub-types
Cases	133,384	106,278 (invasive cases)
Controls	113,789	91,477
Tumor marker sub-types GWAS sample size		
Estrogen Receptor status	Negative	16883
	Positive	69963
	Unknown	19432
Progesterone Receptor status	Negative	24260
	Positive	51546
	Unknown	30472
HER2 status	Negative	47645
	Positive	9502
	Unknown	49131
Grade	1	15566
	2	37532
	3	24360
	Unknown	28820
Breast cancer sub-types description		
Luminal A	ER+ and/or PR+, HER2-, grade 1 and 2	
Luminal B	ER+ and/or PR+, HER2+	
HER2 +	ER-, PR-, HER2+	
Triple -	ER-, PR-, HER2 -	
Luminal B/HER 2 -	ER+ and/or PR+, HER2-, grade 3	

Supplementary Table S2. Sample size for overall breast cancer and sub-types GWAS as well as according to tumor marker (Estrogen Receptor (negative, positive and unknown), Progesterone Receptor (negative, positive and unknown), HER2 (negative, positive and unknown), and grade (1, 2, 3 and unknown)). Finally, sub-types studied description regarding tumor markers.²

Outcome	Exposure	Heterogeneity			Egger intercept		
		Cochran's Q	df	p-value	Estimate	95% CI	p-value
Overall	PC1	199.5858	29	<0.001	0.029	0.014 , 0.043	<0.001
	PC2	515.5738	113	<0.001	0	-0.010 , 0.009	0.961
	PC3	180.1254	43	<0.001	0.013	-0.008 , 0.033	0.228
Luminal A	PC1	136.8719	29	<0.001	0.029	0.012 , 0.045	0.001
	PC2	368.3768	113	<0.001	-0.006	-0.017 , 0.004	0.256
	PC3	129.4055	43	<0.001	0.012	-0.011 , 0.036	0.293
Luminal B	PC1	60.9838	29	0.0005	0.038	0.012 , 0.063	0.003
	PC2	162.6251	113	0.0016	0.013	-0.003 , 0.028	0.1
	PC3	70.7185	43	0.0049	0.018	-0.02 , 0.056	0.348
HER2 +	PC1	49.9252	29	0.0092	0.036	0.001 , 0.071	0.046
	PC2	143.6335	113	0.0273	-0.002	-0.023 , 0.02	0.876
	PC3	54.0215	43	0.1209	0.011	-0.037 , 0.06	0.644
Triple -	PC1	45.7765	29	0.0247	0.029	0.01 , 0.048	0.003
	PC2	187.1135	113	<0.001	0.01	-0.004 , 0.025	0.175
	PC3	81.4148	43	0.0004	-0.003	-0.038 , 0.033	0.878
Luminal B/ HER2 -	PC1	82.7505	29	<0.001	0.038	0.013 , 0.063	0.003
	PC2	183.9729	113	<0.001	-0.004	-0.018 , 0.01	0.565
	PC3	72.6526	43	0.0031	0.023	-0.009 , 0.056	0.156

Supplementary Table S3. Heterogeneity test and Egger intercept results for body shape phenotypes and overall breast cancer risk and sub-types.

Breast Cancer	PC1	PC2	PC3
Overall	rs1582874 rs1121980	rs11205303 rs724016 rs6569648 rs11049611 rs3764419	rs9425301 rs6726261 rs9838625 rs272885 rs1936809
	$\rho = 0.130$	$\rho = 0.013$	$\rho = 0.123$
Luminal A	rs1582874 rs1121980	rs11205303 rs724016 rs6569648 rs11049611 rs1182199	rs9838625 rs272885 rs1516883
	$\rho = 0.053$	$\rho = 0.020$	$\rho = 0.038$
Luminal B	rs3911063 rs1121980	-	-
	$\rho = 0.039$		
HER2 +	rs1582874	-	-
	$\rho = 0.692$		
Triple -	rs1121980	rs6569648 rs11049611	rs9425301
	$\rho = 0.007$	$\rho = 0.769$	$\rho = 0.545$
Luminal B/HER2 -	rs1582874 rs1121980	rs1415288 rs724016 rs11049611	rs9838625
	$\rho = 0.334$	$\rho = 0.204$	$\rho = 0.266$

Supplementary Table S4. Genetic variants considered as outliers for overall and subtypes breast cancer and each body shape phenotype. We also provide P-distortion (ρ) for each test performed.

References

1. Ried JS, Jeff JM, Chu AY, Bragg-Gresham JL, Van Dongen J, Huffman JE, et al. A principal component meta-analysis on multiple anthropometric traits identifies novel loci for body shape. *Nat Commun.* 2016;7.
2. Zhang H, Ahearn TU, Lecarpentier J, Barnes D, Beesley J, Qi G, et al. Genome-wide association study identifies 32 novel breast cancer susceptibility loci from overall and subtype-specific analyses. *Nat Genet.* 2020;52(6).