

Supplementary figures

The contribution of germline pathogenic variants in breast cancer genes to contralateral breast cancer in *BRCA1/BRCA2/PALB2*-negative women

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<i>Supp. Figure S1: Study flowchart</i>	<i>2</i>
<i>Supp. Figure S2: PCA for Group 1</i>	<i>3</i>
A: Projecting to 1KGP	3
B: Scree plot	3
<i>Supp. Figure S3: PCA for Group 2</i>	<i>4</i>
A: Projecting to 1KGP	4
B: Scree plot	4
<i>Supp. Figure S4: WECARE-Group1 + NFFE PCA Scree plot.....</i>	<i>5</i>
<i>Supp. Figure S5: Burden of PGVs stratified by latency</i>	<i>6</i>
A: Group 1	6
B: Group 2	6
<i>Supp. Figure S6: WECARE-Group1 + NFFE PGVs burden</i>	<i>7</i>

Supp. Figure S1: Study flowchart

Secondary bioinformatics

following Broad's Best Practices

- FastQC and FASTQ Trimming
- Alignment (BWA MEM, GRCh37)
- BAM files QC and processing
- Variant Calling (GATK HC)
- Joined genotyping with NFFE
- Variants QC and filtering (VQSR & hard filters)
- Variants normalization & splitting multiallelic sites
- Variants Annotation (VEP, ClinVar, CADD)

Samples check and filtering

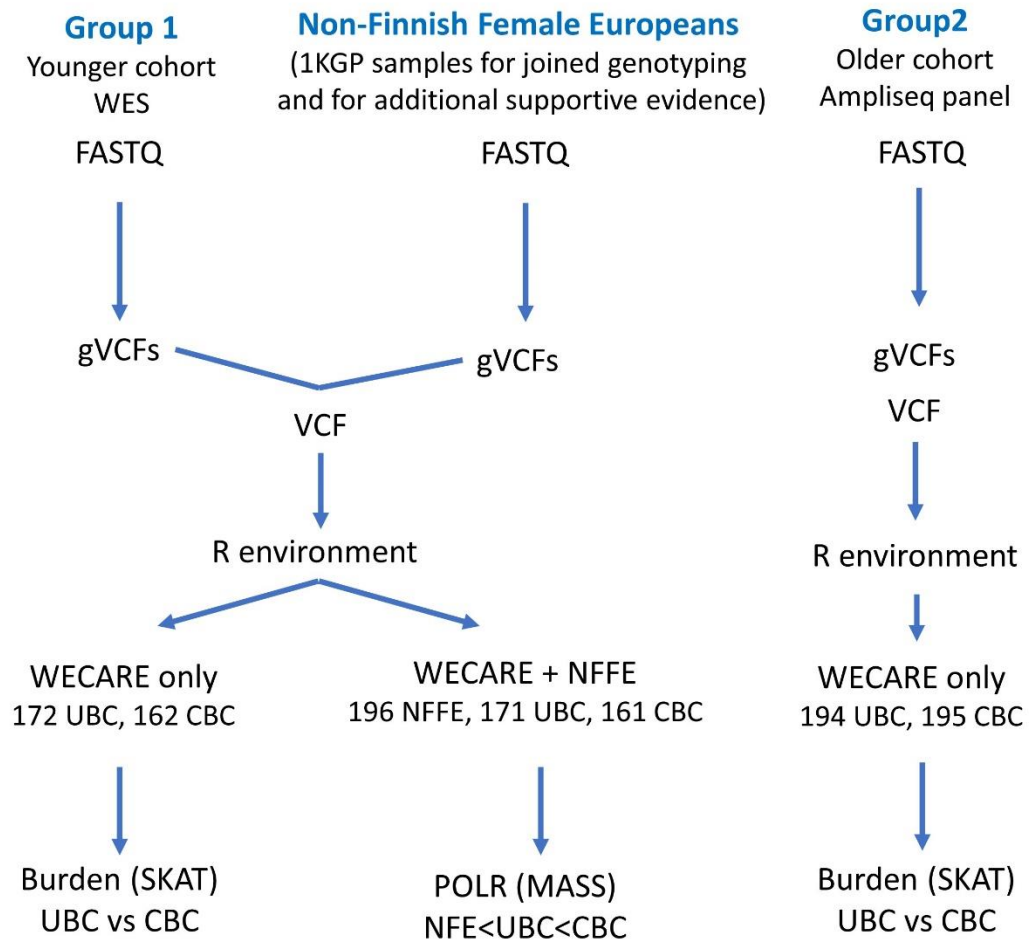
- pairwise concordance
- concordance with previous GWAS data

PCA

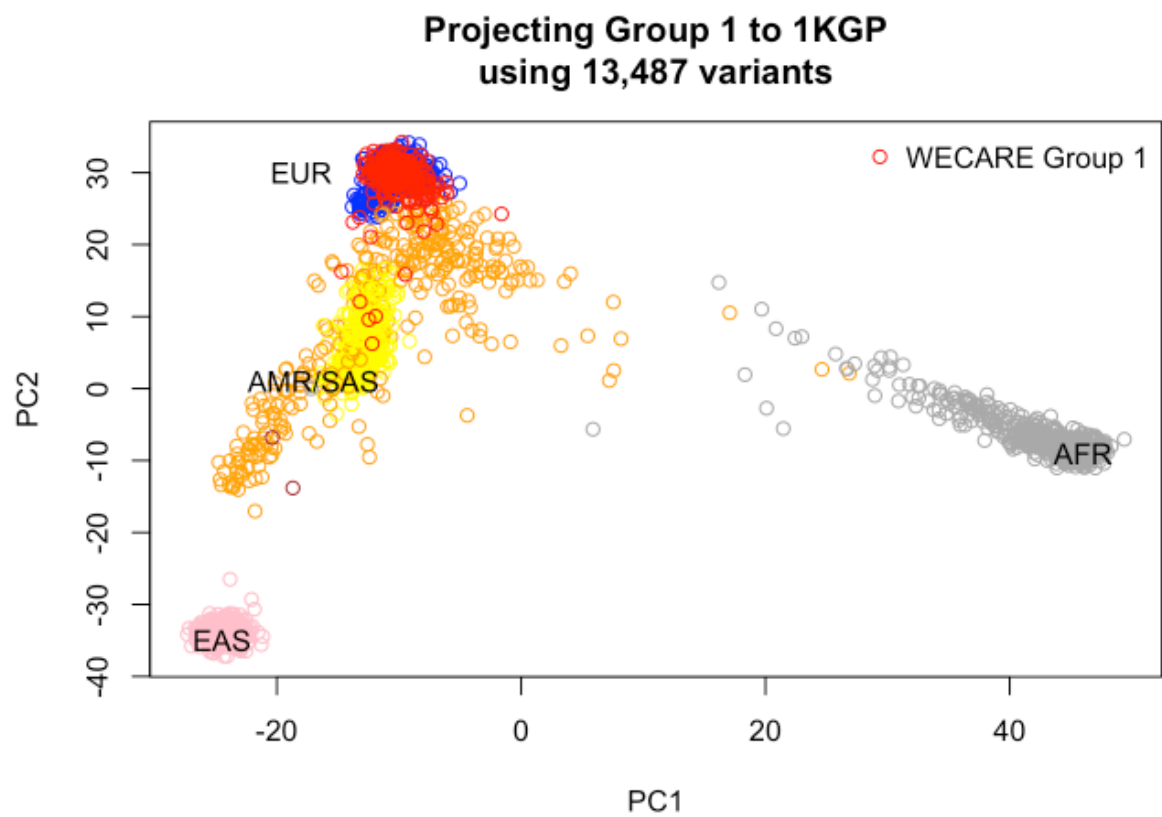
- PC-s for regression models,
- ethnicity assessment by projecting to 1KGP

Statistical analysis

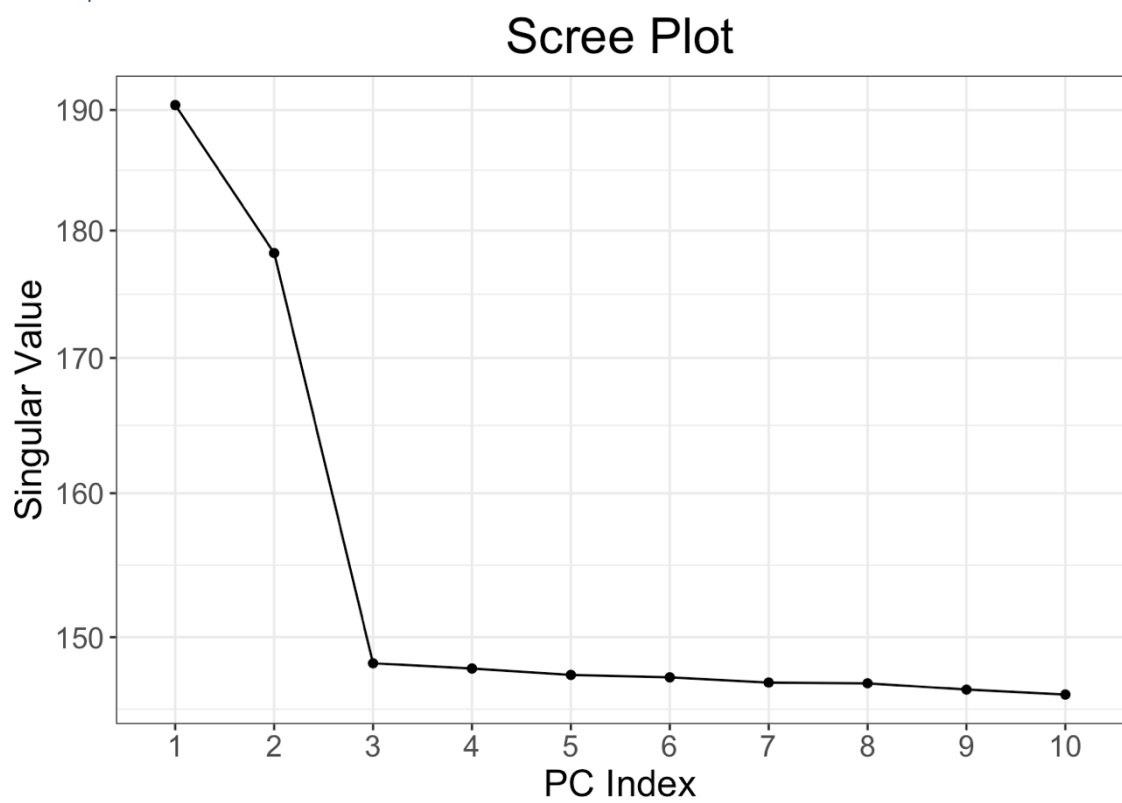
- crude counts for bar-plots
- regression models for statistical significance



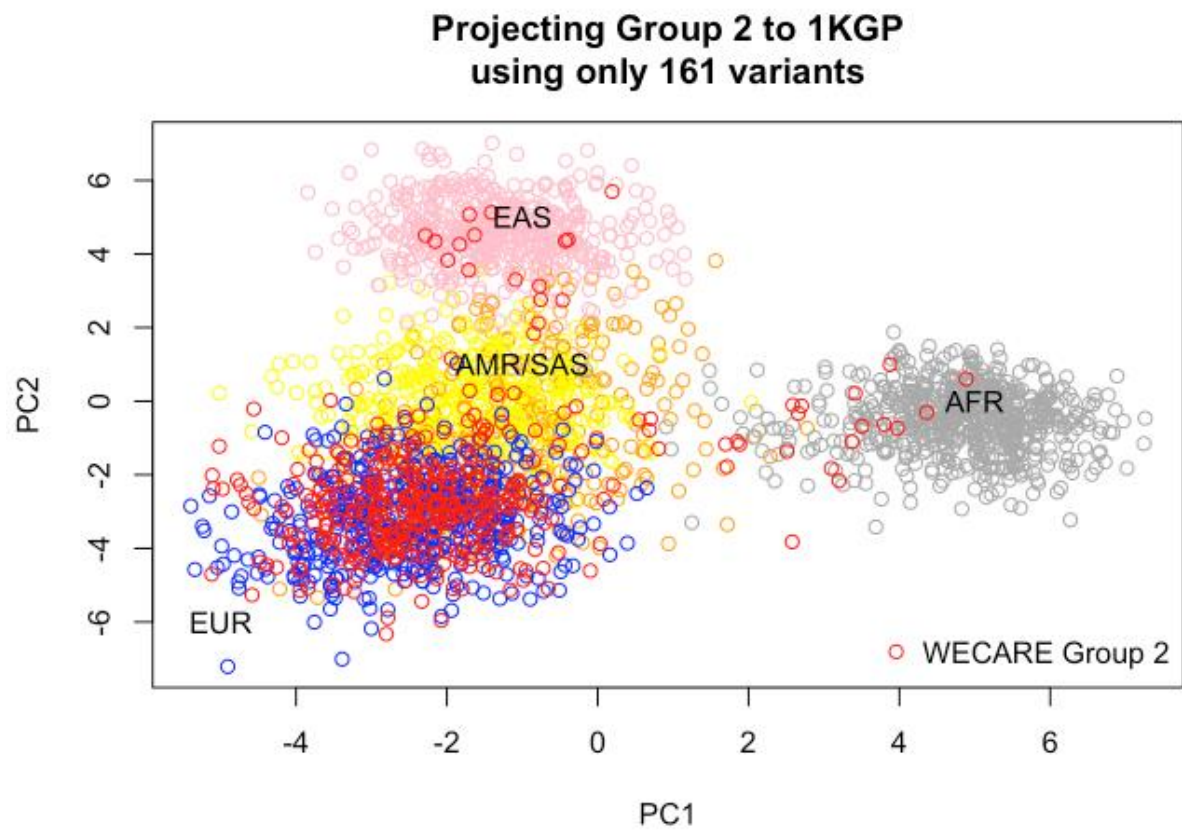
Supp. Figure S2: PCA for Group
1



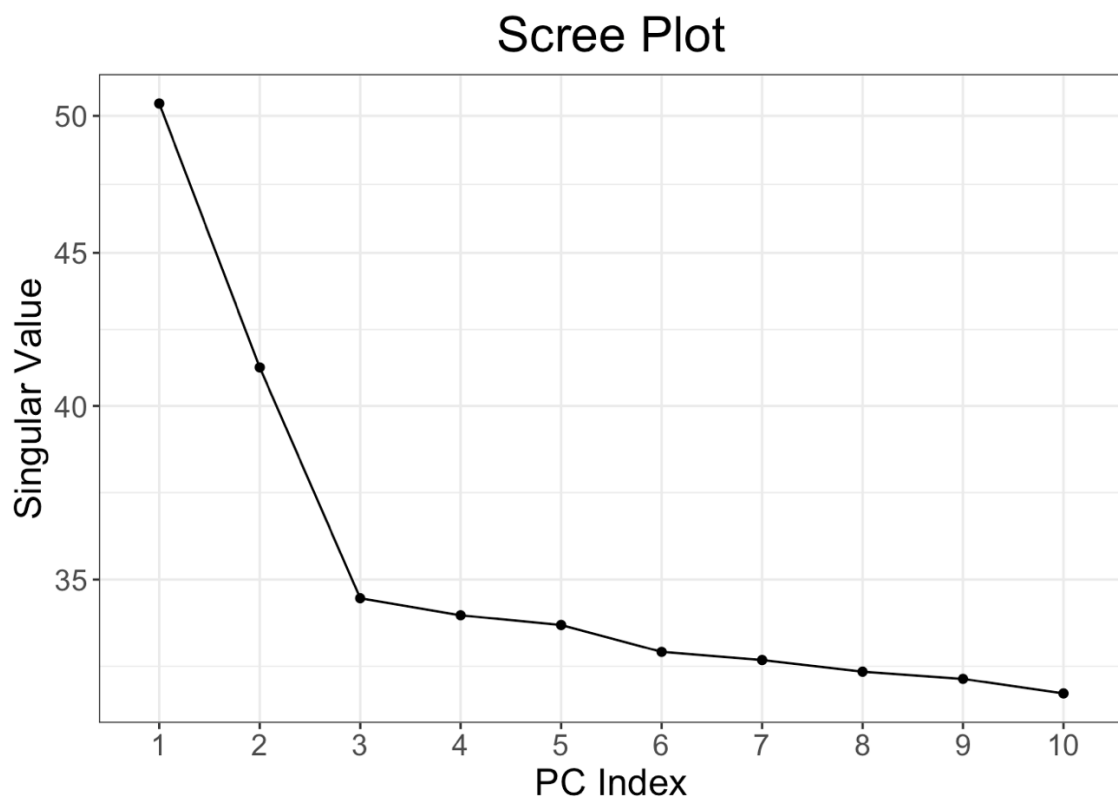
B: Scree plot



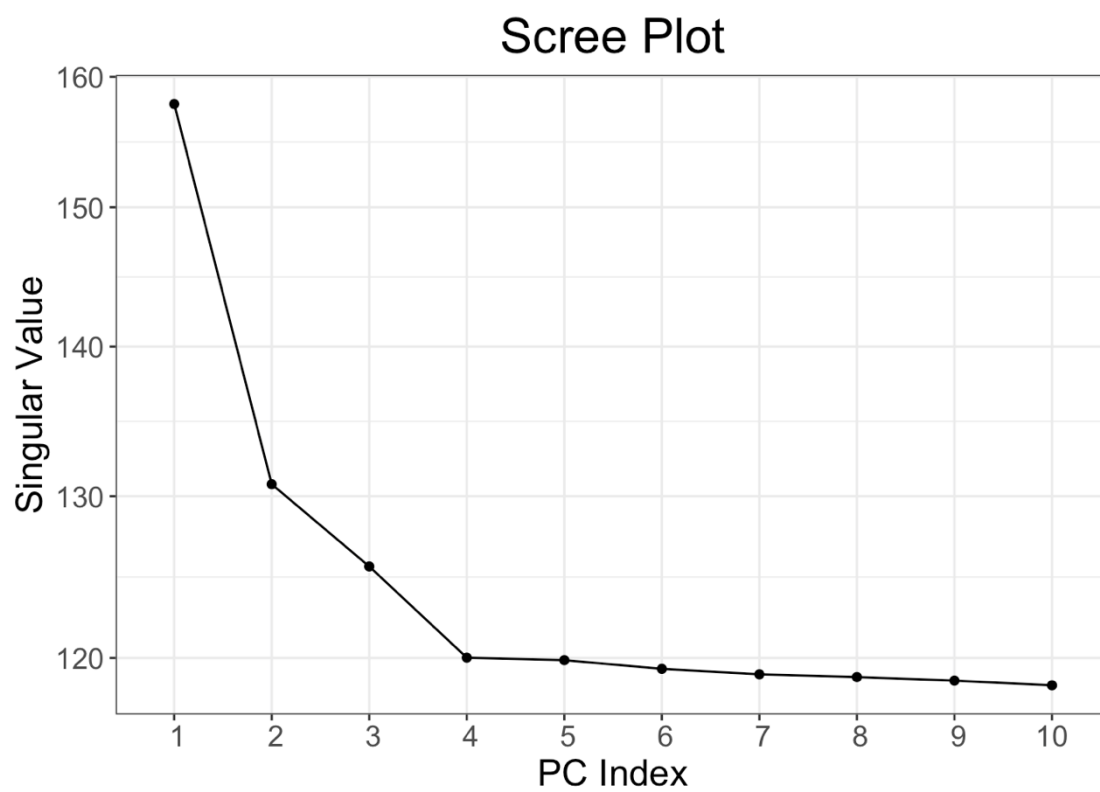
Supp. Figure S3: PCA for Group
2



B: Scree plot

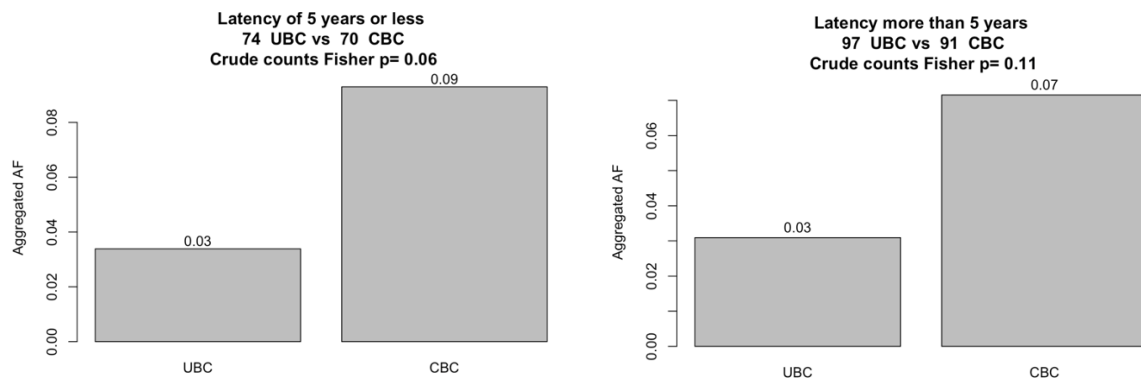


Supp. Figure S4: WECARE-Group1 + NFFE PCA Scree plot

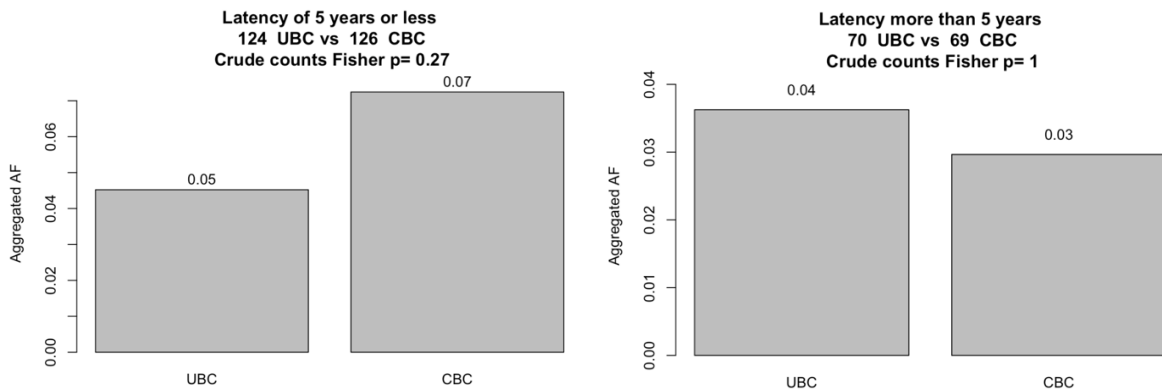


Supp. Figure S5: Burden of PGVs stratified by latency

A: Group 1

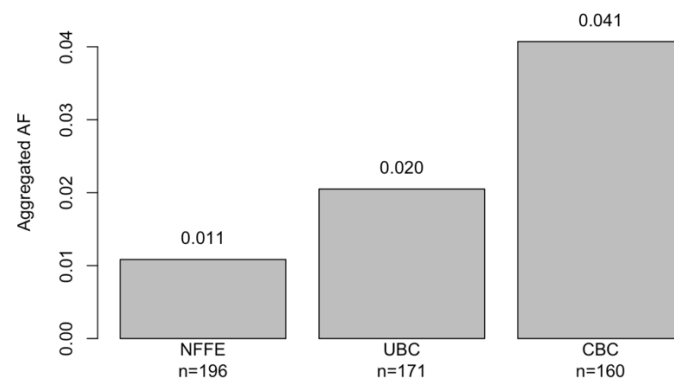


B: Group 2



Note: In CBC the latency is the time between the 1st cancer and 2nd cancer (lack of 2nd cancer in UBC)

Supp. Figure S6: WECARE-Group1 + NFFE PGVs burden



Note: The NFFE<UBC<CBC trend is statistically significant (POLR test $p = 0.02$). The absolute AF values are smaller than in WECARE-only analysis because variants with low coverage in NFFE samples were removed (see Figure 1 and Methods section in the main text).