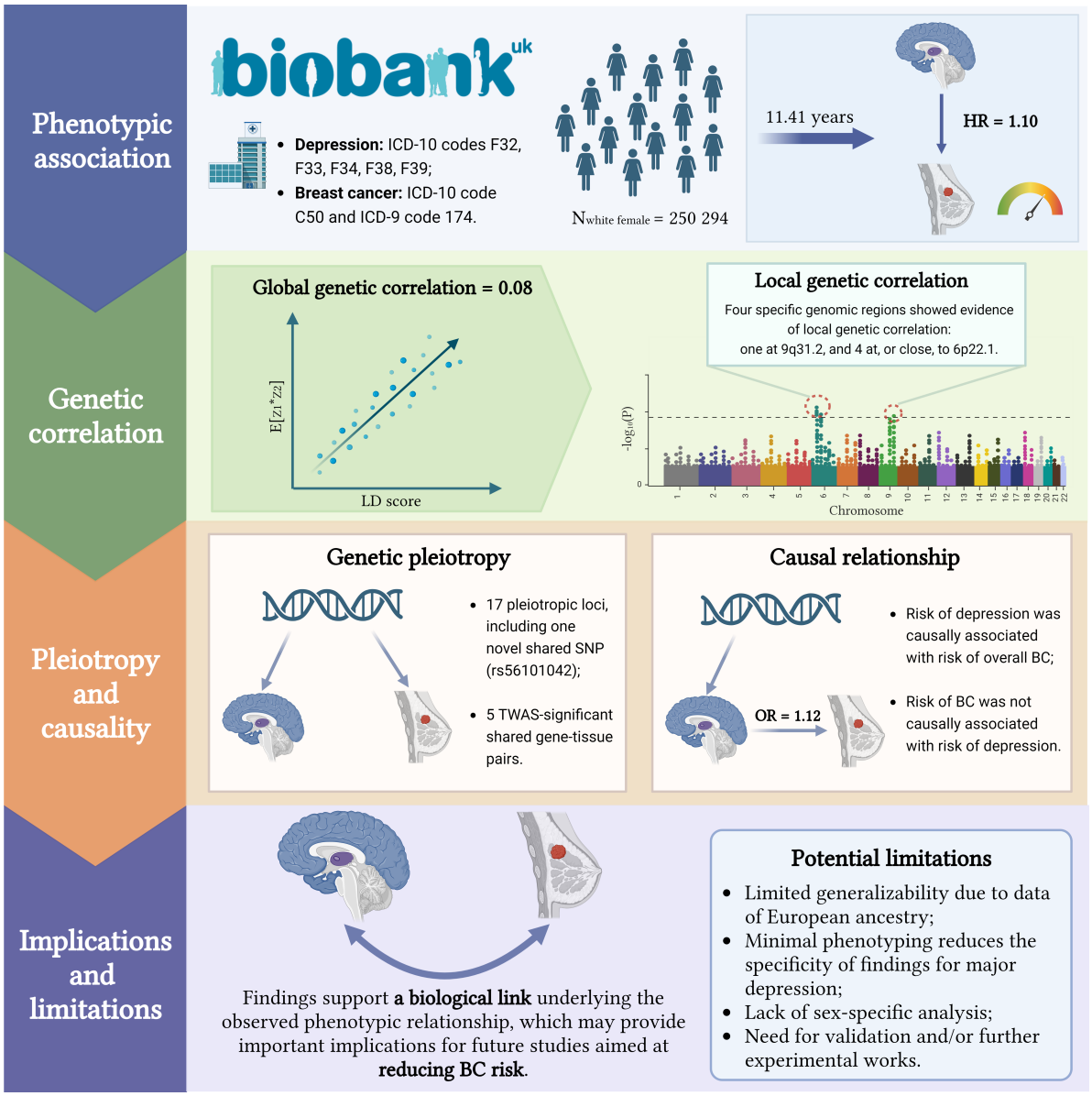


**Figure S1.** Graphical representation of findings from the present study.

ICD: international classification of diseases; LD: linkage disequilibrium; TWAS: transcriptome-wide association study; BC: breast cancer.

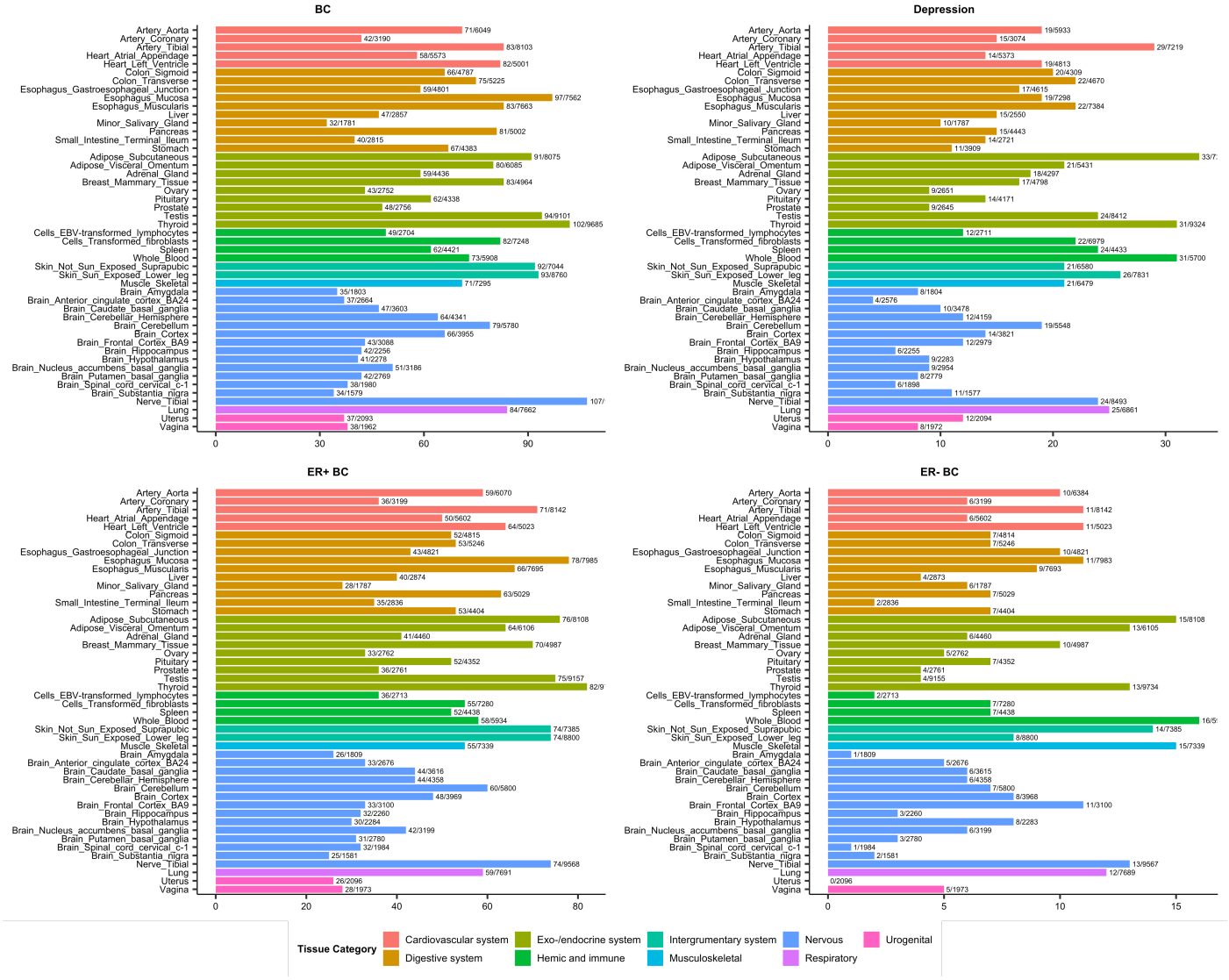


**Figure S2**. Number of TWAS significant genes for depression and breast cancer across 49 GTEx tissues (version 8). The X axis shows the count of genes from tissues in the GTEx database meeting significance thresholds for multiple testing for each trait. The Y axis lists GTEx tissues. Colors represent different tissue categories. The null hypothesis of TWAS is no expression-trait association (or genetic correlation between expression and a trait) conditional on the observed GWAS statistics at the corresponding locus. The total number of TWAS gene-tissue pairs being tested is ~290,000 across 49 GTEx tissues.

TWAS: transcriptome-wide association study; BC: breast cancer; ER: estrogen receptor.

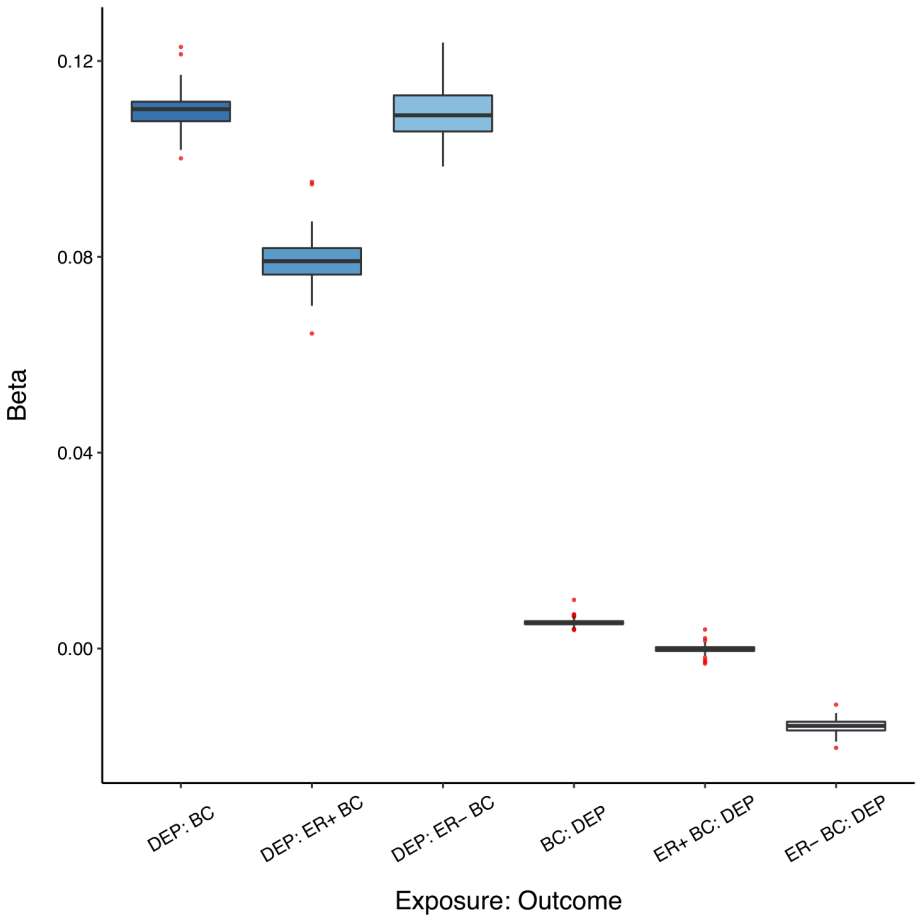


**Figure S3.** Box plot of betas in leave-one-out analysis where one SNP was removed at a time and inverse-variance weighted analysis was conducted based on the remaining SNPs.

Beta: effect allele beta coefficient; BC: breast cancer; DEP: depression; ER: estrogen receptor.

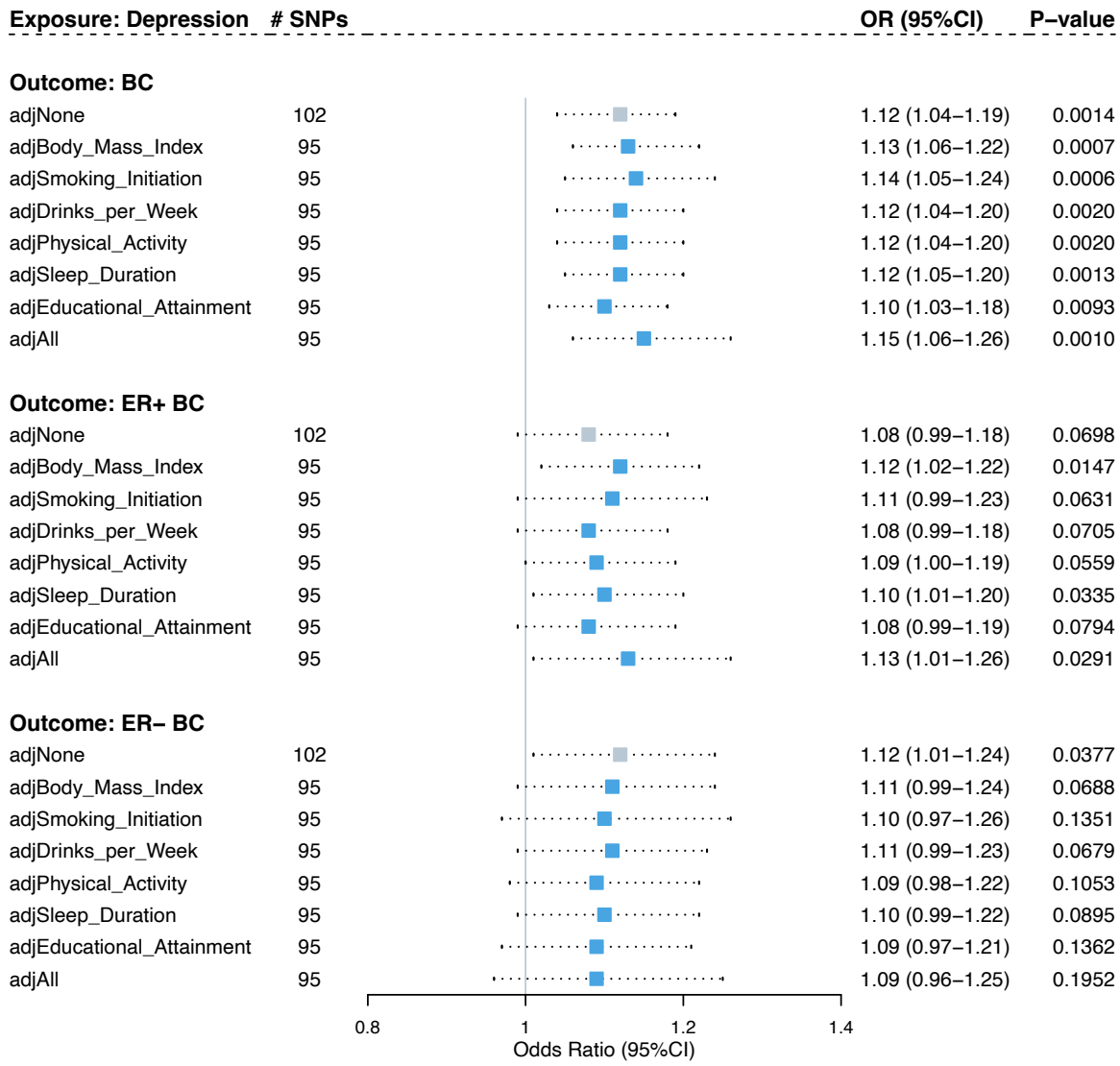


**Figure S4.** Independent effects of genetically predicted depression on overall breast cancer, ER+ breast cancer, and ER– breast cancer after adjusting for each potential confounder separately and together using multi-variable Mendelian randomization. The y-axis details the genetically predicted confounder for which adjustment was made. Boxes represent the point estimates of the causal effects of genetically predicted depression on breast cancer, and error bars represent 95% confidence intervals.

adjNone: the point estimates of the causal effects of genetically predicted depression on breast cancer using univariable Mendelian randomization; BC: breast cancer; ER: estrogen receptor.