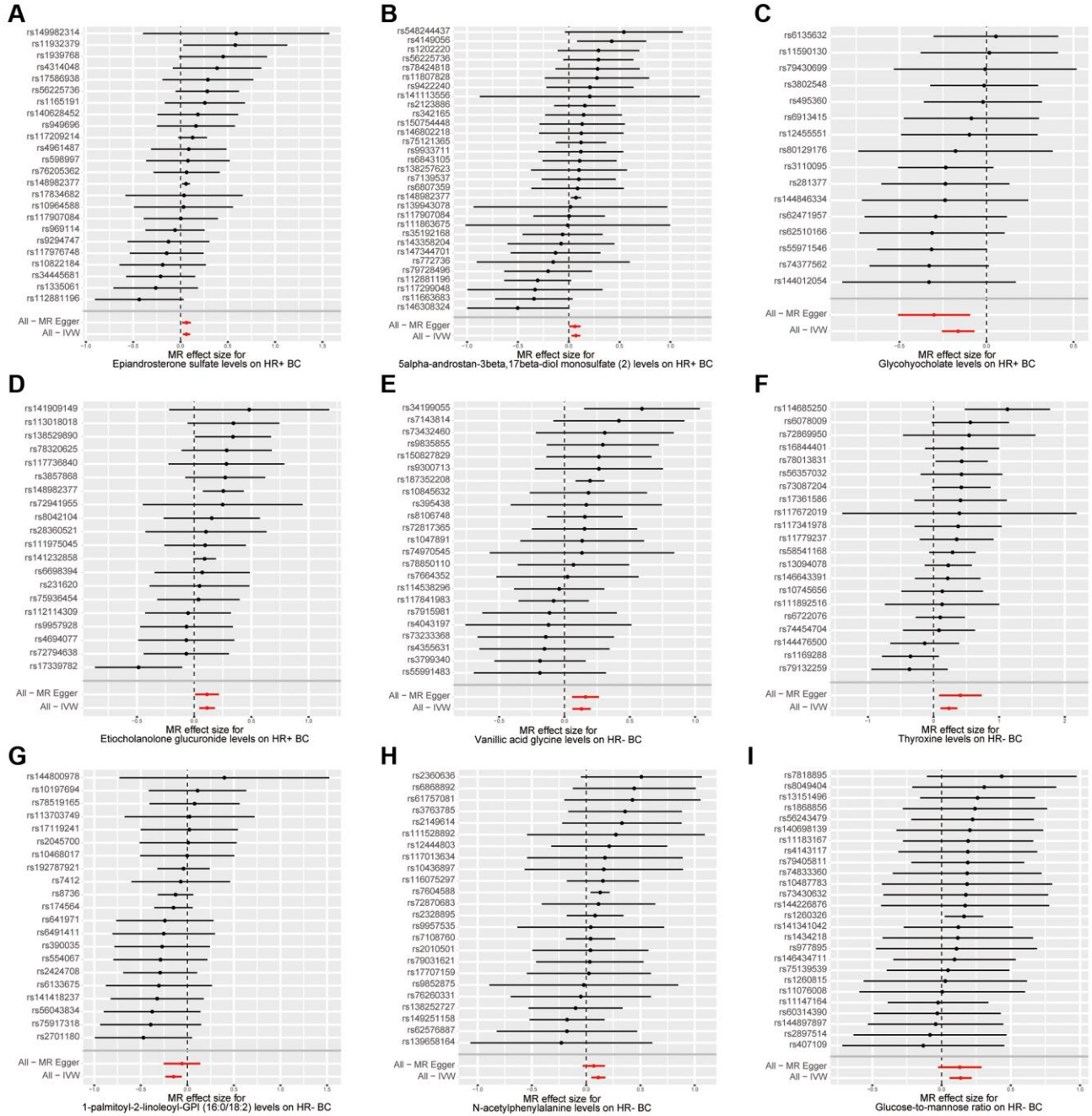
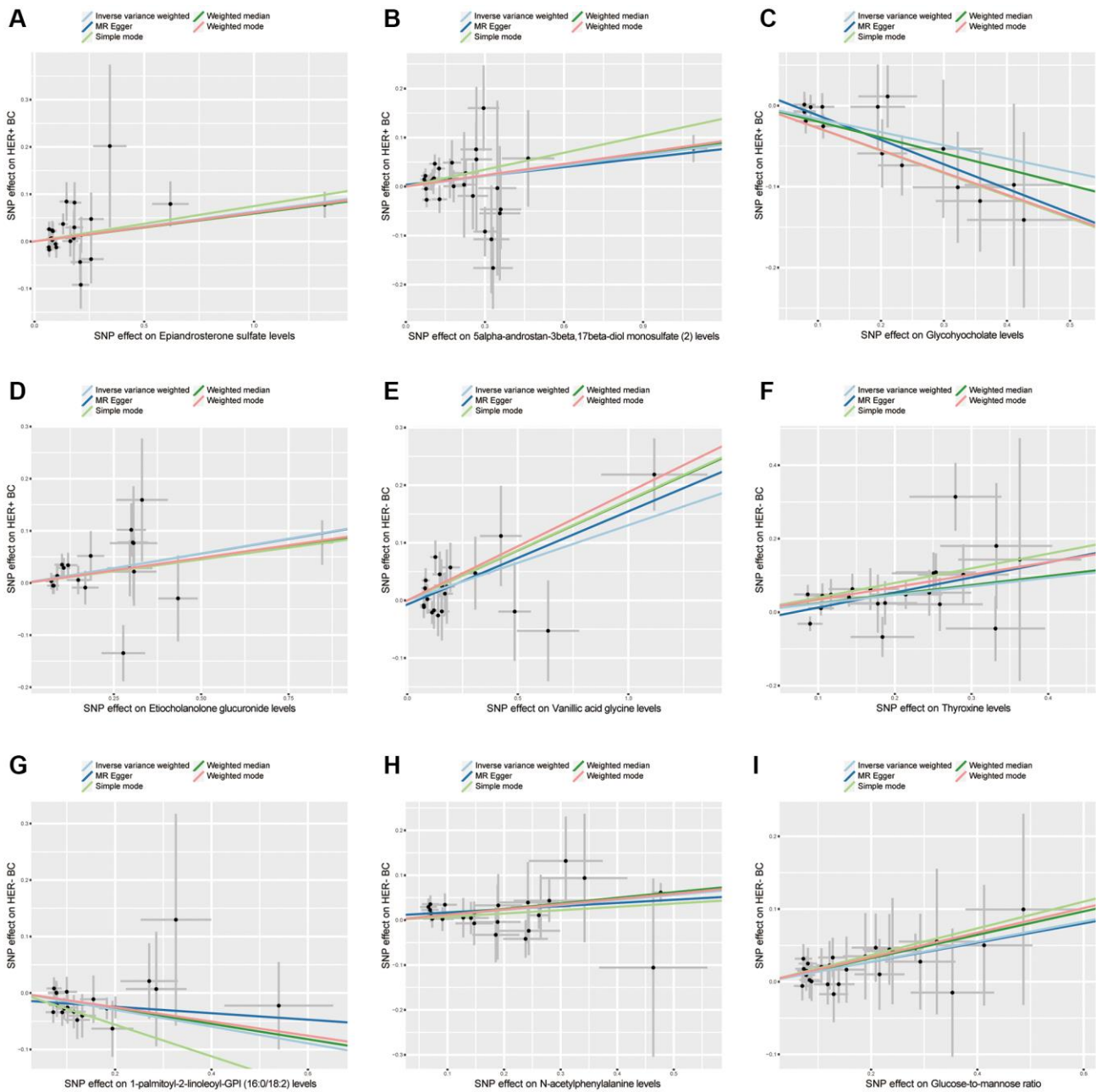


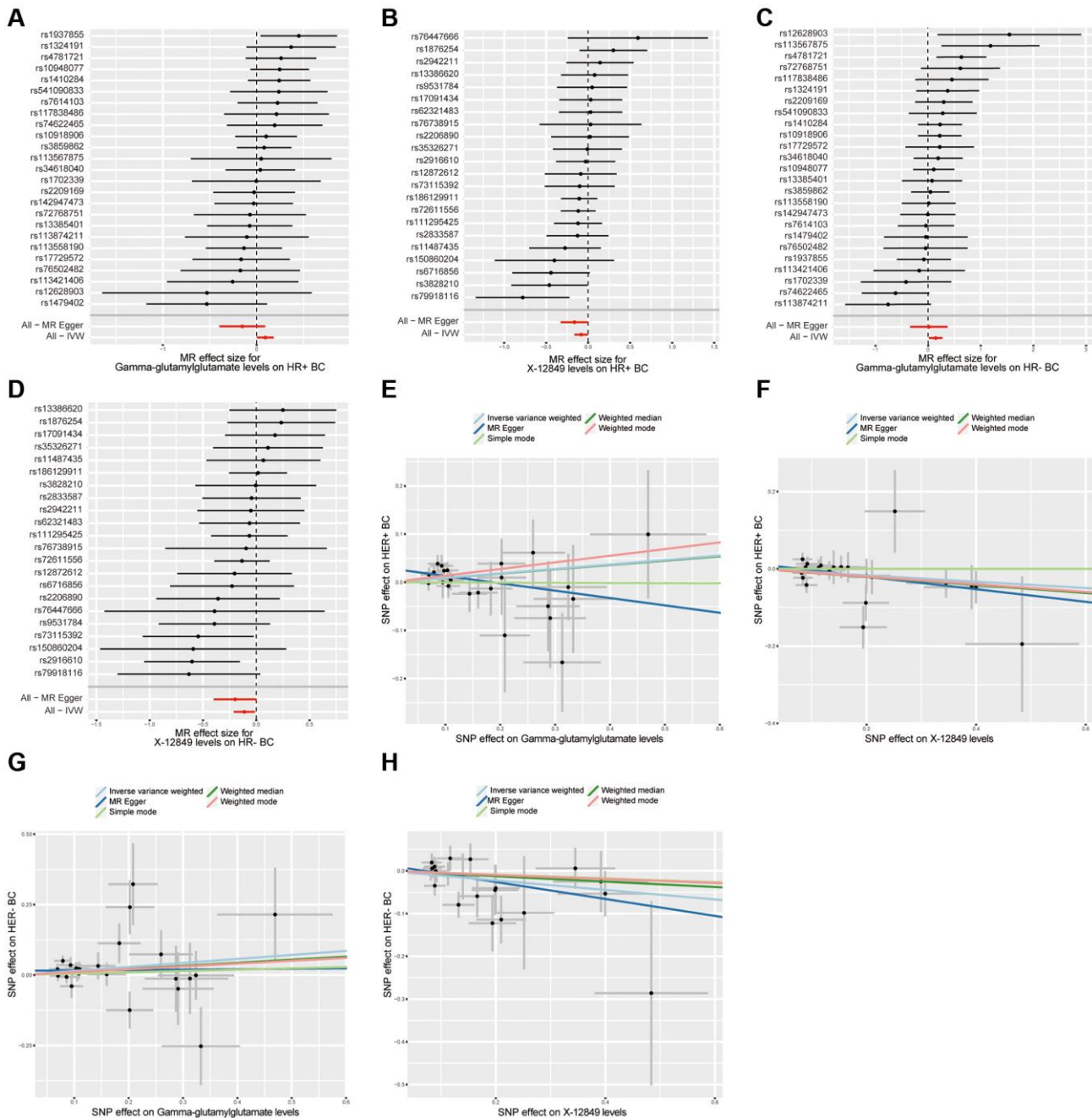
SUPPLEMENTARY FIGURES



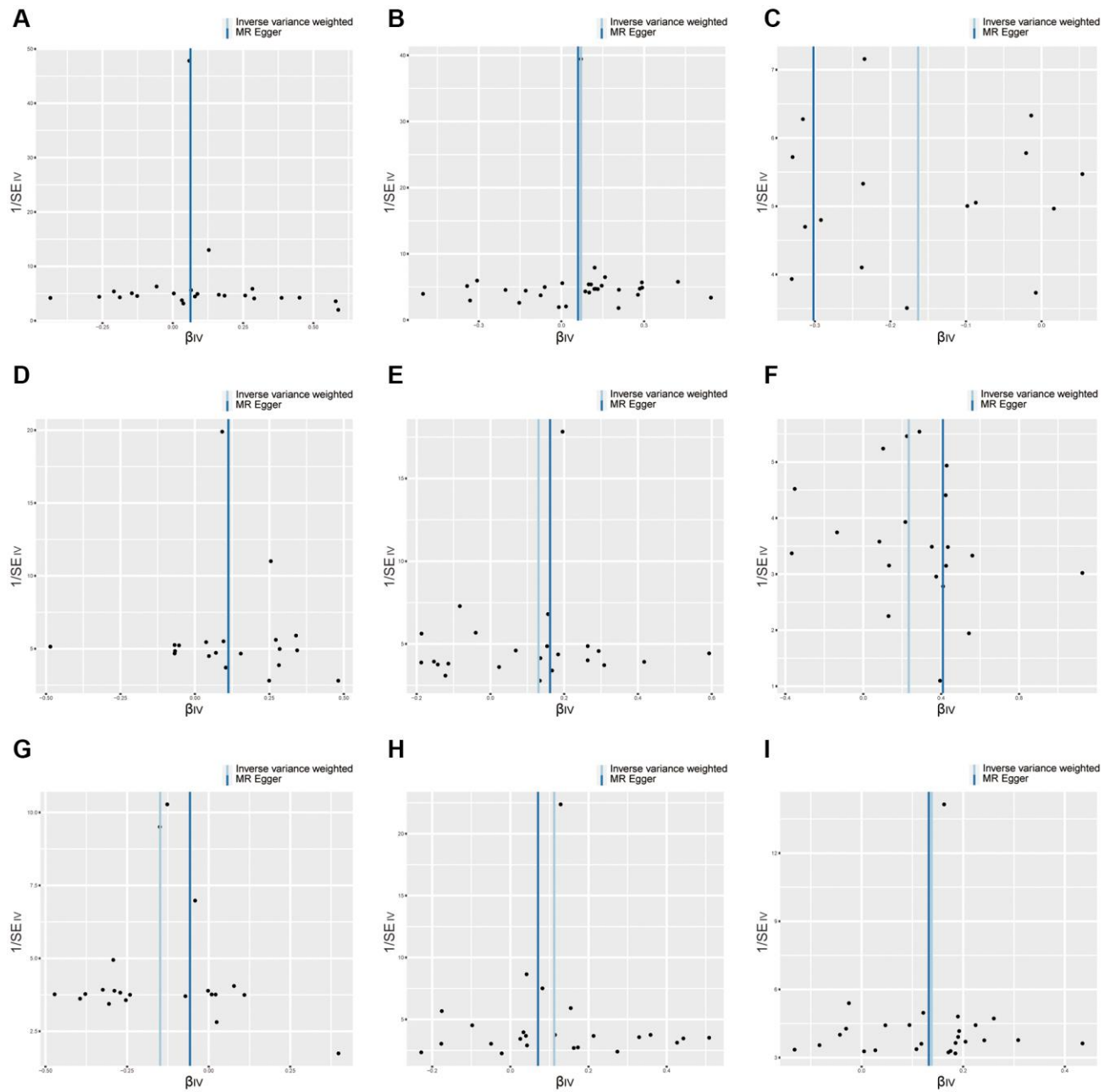
Supplementary Figure 1. Forest plots of SNPs associated with metabolic factors and the risk of HER+/HER- BC. (A) Epiandrosterone sulfate levels on HER+ BC. **(B)** 5alpha-androstan-3beta,17beta-diol monosulfate (2) levels on HER+ BC. **(C)** Glycocholelate levels on HER+ BC. **(D)** Etiocholanolone glucuronide levels on HER+ BC. **(E)** Vanillic acid glycine levels on HER- BC. **(F)** Thyroxine levels on HER- BC. **(G)** 1-palmitoyl-2-linoleoyl-GPI (16:0/18:2) levels on HER-BC. **(H)** N-acetylphenylalanine levels on HER- BC. **(I)** Glucose-to-mannose ratio on HER- BC. Abbreviations: SNP: single nucleotide polymorphisms; HER: human epidermal growth factor receptor; BC: breast cancer; IVW: inverse-variance weighted.



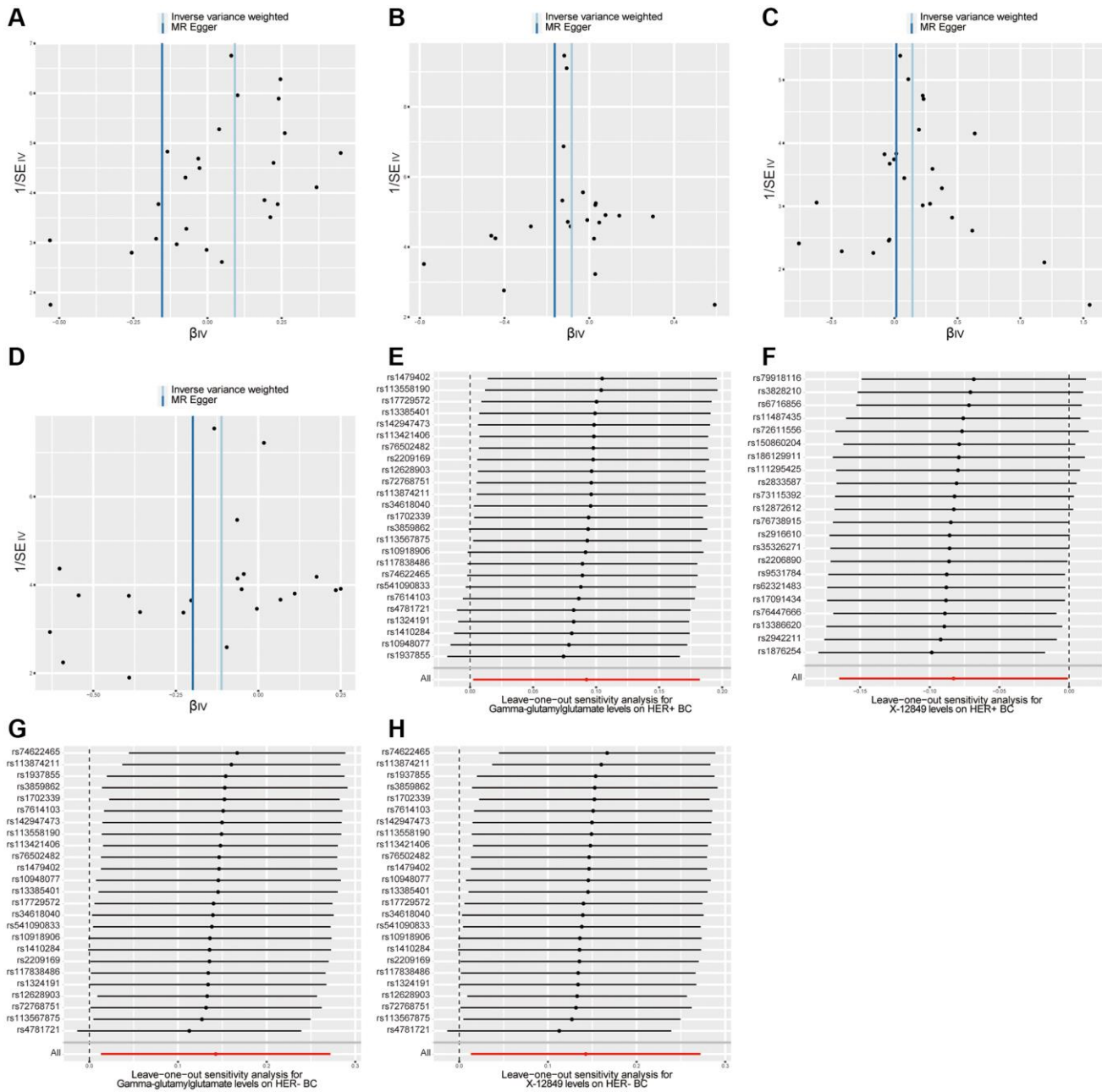
Supplementary Figure 2. Scatter plots showed the genetic associations of metabolic factors and HER+/HER- BC. (A) Epiandrosterone sulfate levels on HER+ BC. **(B)** 5alpha-androstan-3beta,17beta-diol monosulfate (2) levels on HER+ BC. **(C)** Glycoyochoolate levels on HER+ BC. **(D)** Etiocholanolone glucuronide levels on HER+ BC. **(E)** Vanillic acid glycine levels on HER- BC. **(F)** Thyroxine levels on HER- BC. **(G)** 1-palmitoyl-2-linoleoyl-GPI (16:0/18:2) levels on HER-BC. **(H)** N-acetylphenylalanine levels on HER- BC. **(I)** Glucose-to-mannose ratio on HER- BC. Abbreviations: SNP: single nucleotide polymorphisms; HER: human epidermal growth factor receptor; BC: breast cancer.



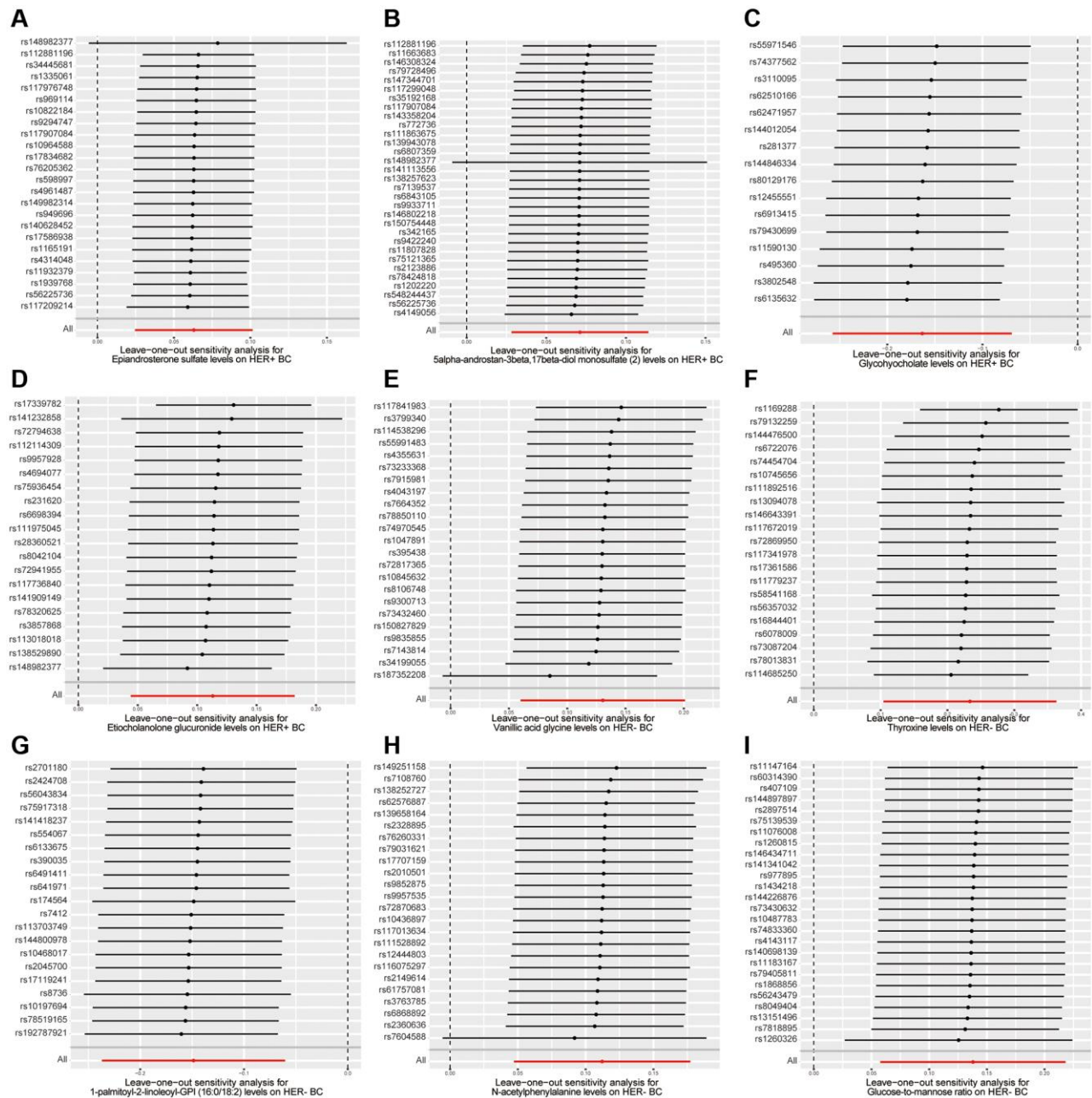
Supplementary Figure 3. Forest plots and scatter plots of metabolic factors on HER+/HER- BC. (A) Forest plot of Gamma-glutamylglutamate levels on HER+ BC. (B) Forest plot of X-12849 levels on HER+ BC. (C) Forest plot of Gamma-glutamylglutamate levels on HER- BC. (D) Forest plot of X-12849 levels on HER- BC. (E) Scatter plot of Gamma-glutamylglutamate levels on HER+ BC. (F) Scatter plot of X-12849 levels on HER+ BC. (G) Scatter plot of Gamma-glutamylglutamate levels on HER- BC. (H) Scatter plot of X-12849 levels on HER- BC. Abbreviations: SNP: single nucleotide polymorphisms; HER: human epidermal growth factor receptor; BC: breast cancer.



Supplementary Figure 4. Funnel plots showed the heterogeneity between metabolic factors and HER+/HER- BC. (A) Epiandrosterone sulfate levels on HER+ BC. **(B)** 5alpha-androstan-3beta,17beta-diol monosulfate (2) levels on HER+ BC. **(C)** Glycoyochoolate levels on HER+ BC. **(D)** Etiocholanolone glucuronide levels on HER+ BC. **(E)** Vanillic acid glycine levels on HER- BC. **(F)** Thyroxine levels on HER- BC. **(G)** 1-palmitoyl-2-linoleoyl-GPI (16:0/18:2) levels on HER-BC. **(H)** N-acetylphenylalanine levels on HER- BC. **(I)** Glucose-to-mannose ratio on HER- BC. Abbreviations: Beta: risk index; Se: standard error.



Supplementary Figure 5. Funnel plots and leave-one-out plots of metabolic factors on HER+/HER- BC. (A) Funnel plot of Gamma-glutamylglutamate levels on HER+ BC. (B) Funnel plot of X-12849 levels on HER+ BC. (C) Funnel plot of Gamma-glutamylglutamate levels on HER-BC. (D) Funnel plot of X-12849 levels on HER- BC. (E) Leave-one-out plot of Gamma-glutamylglutamate levels on HER+ BC. (F) Leave-one-out plot of X-12849 levels on HER+ BC. (G) Leave-one-out plot of Gamma-glutamylglutamate levels on HER- BC. (H) Leave-one-out plot of X-12849 levels on HER- BC. Abbreviations: SNP: single nucleotide polymorphisms; HER: human epidermal growth factor receptor; BC: breast cancer.



Supplementary Figure 6. Leave-one-out plots for the causal effects of metabolic factors on HER+/HER- BC. (A) Epiandrosterone sulfate levels on HER+ BC. **(B)** 5alpha-androstan-3beta,17beta-diol monosulfate (2) levels on HER+ BC. **(C)** Glycohyocholate levels on HER+ BC. **(D)** Etiocholanolone glucuronide levels on HER+ BC. **(E)** Vanillic acid glycine levels on HER- BC. **(F)** Thyroxine levels on HER- BC. **(G)** 1-palmitoyl-2-linoleoyl-GPI (16:0/18:2) levels on HER-BC. **(H)** N-acetylphenylalanine levels on HER- BC. **(I)** Glucose-to-mannose ratio on HER- BC. Abbreviations: HER: human epidermal growth factor receptor; BC: breast cancer.