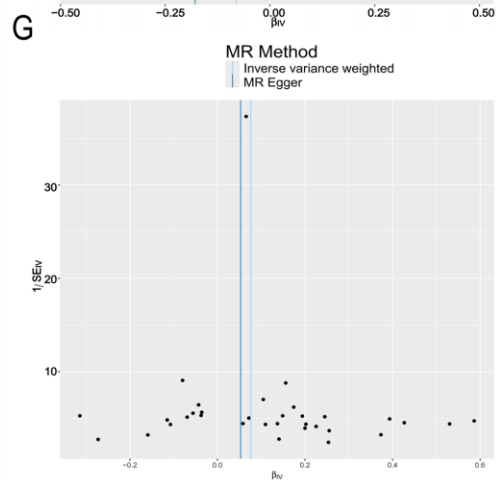
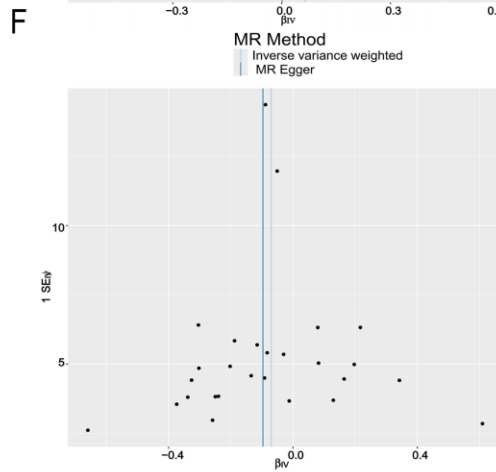
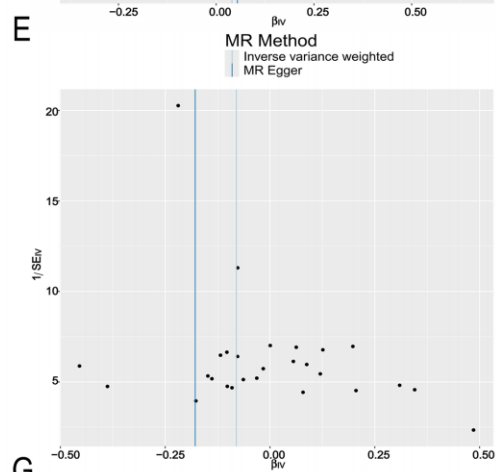
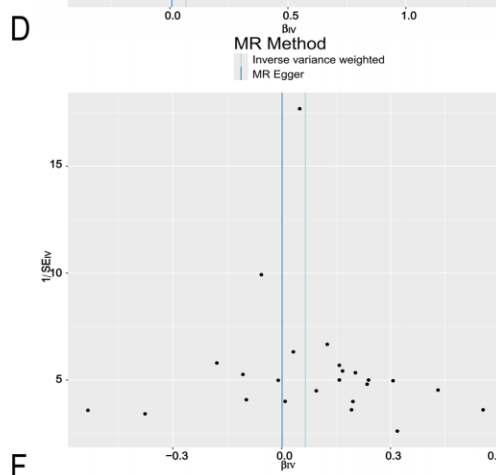
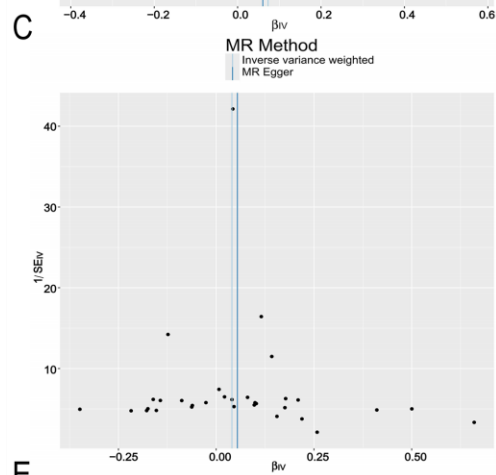
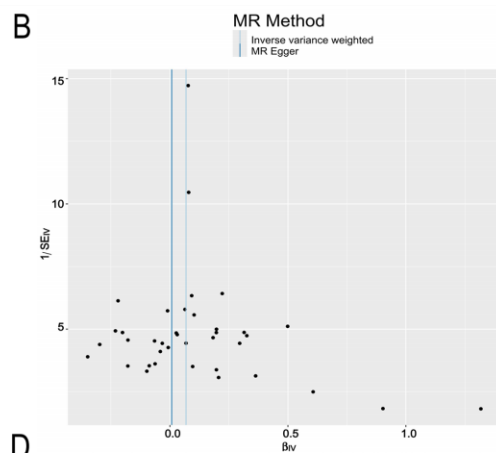
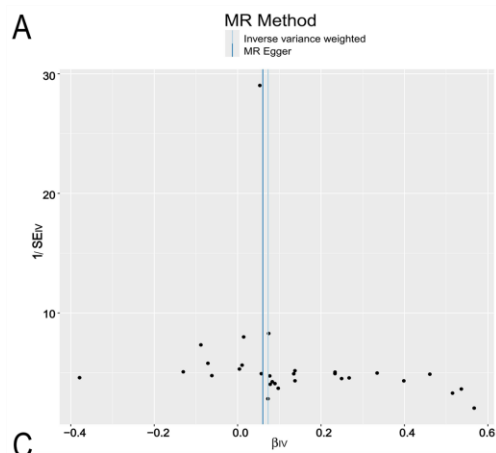
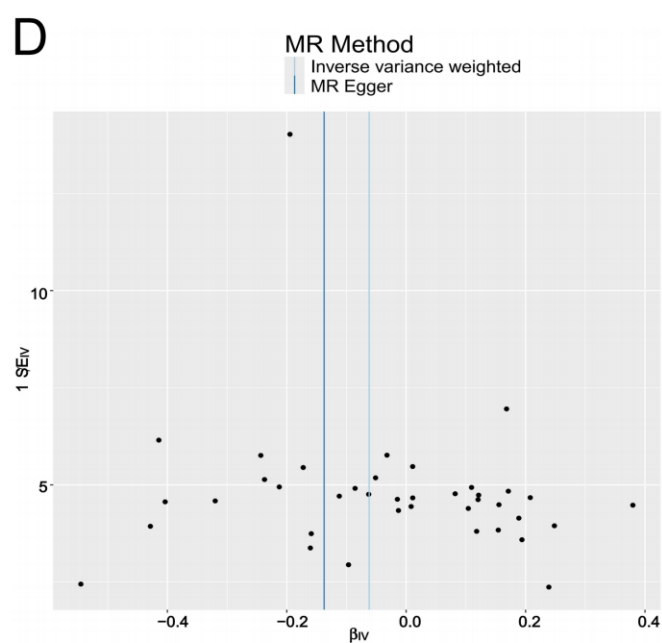
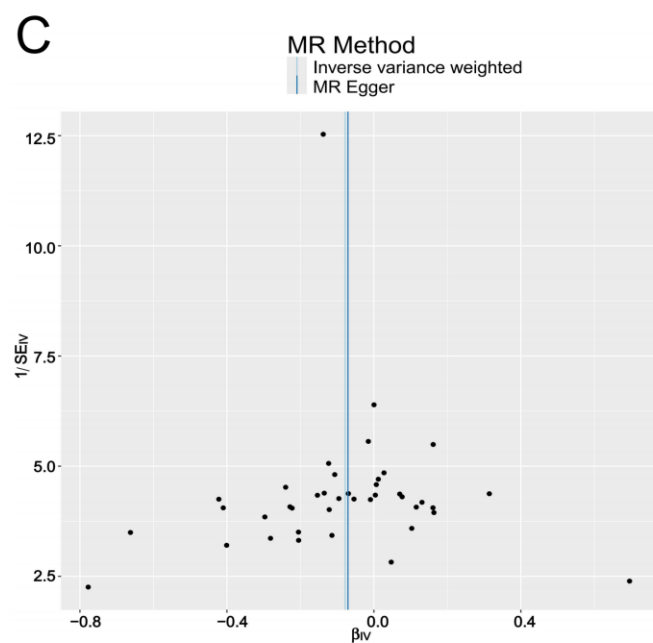
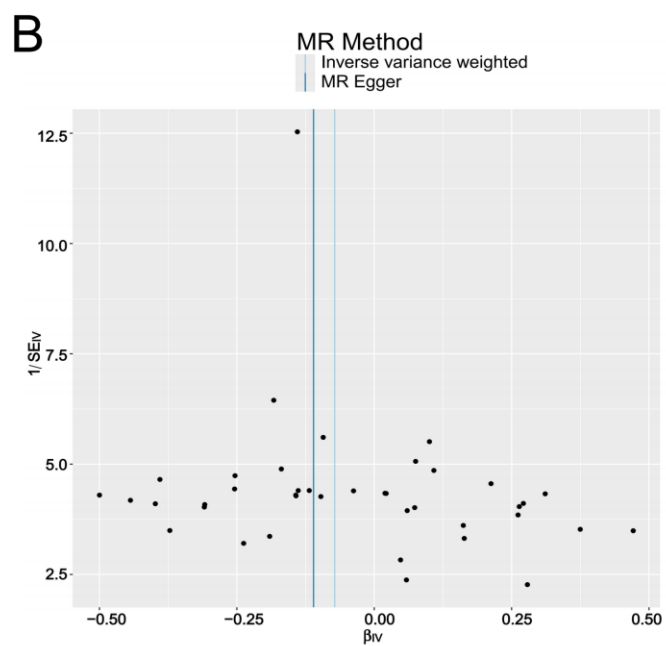
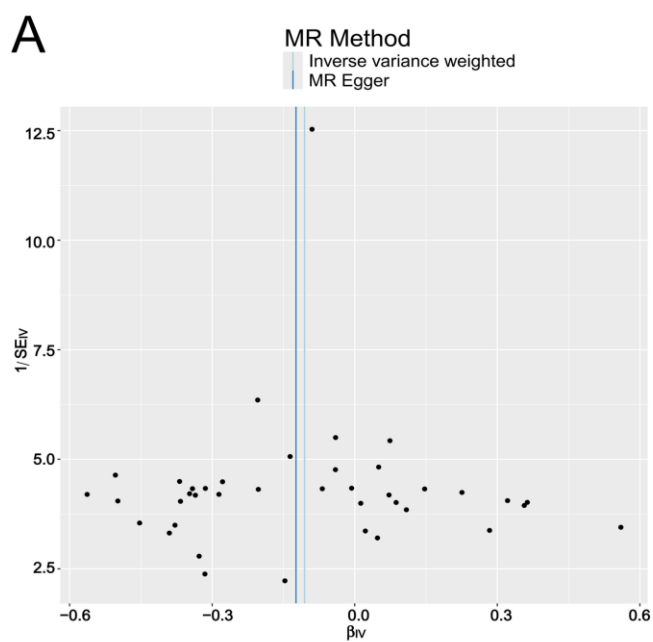


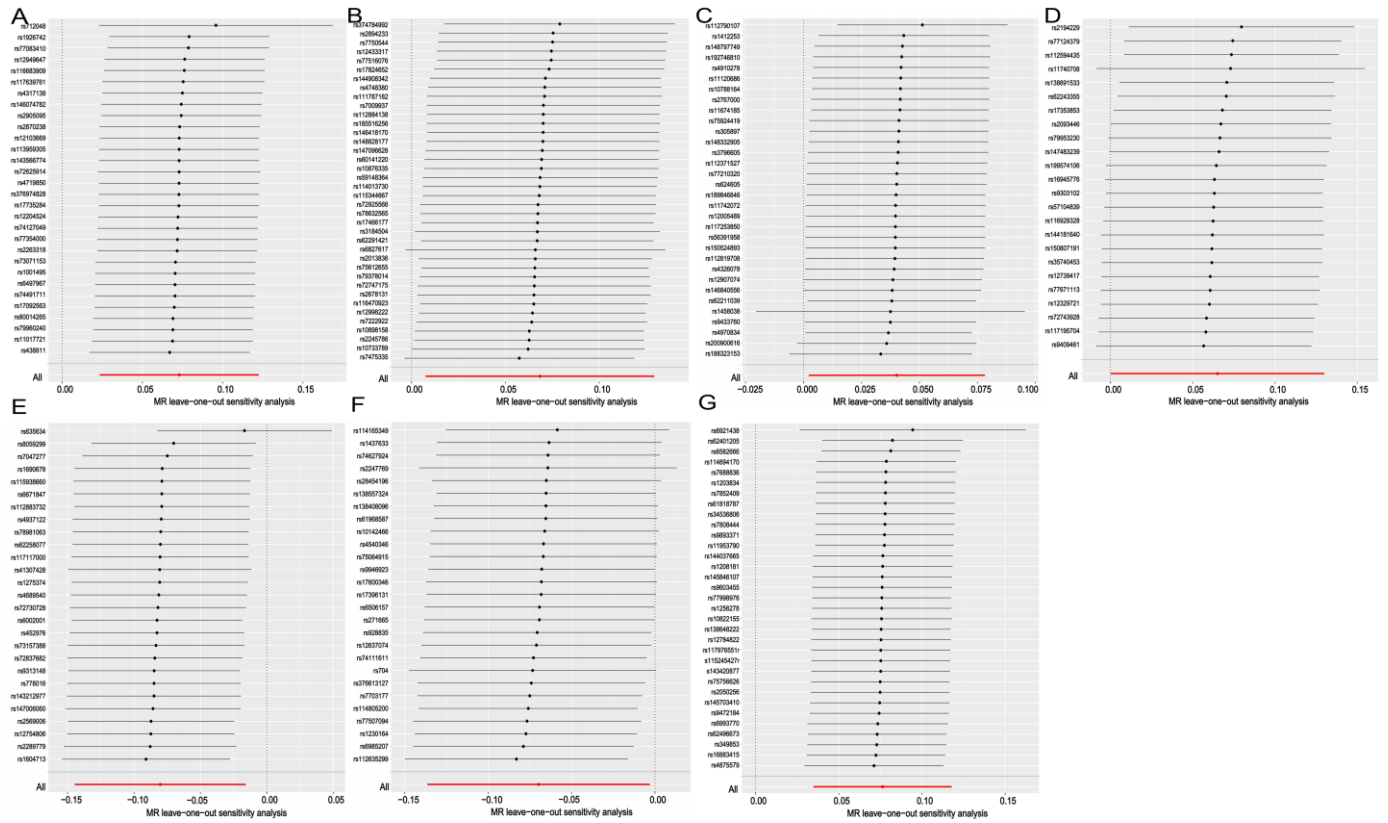
Supplementary Figure S1. Mendelian randomization (MR) scatter plots for the associations between genetically predicted circulating inflammatory factors and epilepsy. The *x*-axis shows the SNP–exposure association (effect estimate for each genetic instrument on the inflammatory factor), and the *y*-axis shows the SNP–outcome association (effect estimate on epilepsy, on the log-odds scale). Each point represents an instrumental SNP. The fitted lines indicate MR causal estimates using the inverse-variance weighted (IVW) and MR-Egger methods. Panels show MR results for (A) CCL23, (B) CXCL11, (C) FGF5, (D) GDNF, (E) LIFR, (F) OPG, and (G) VEGFA in relation to epilepsy



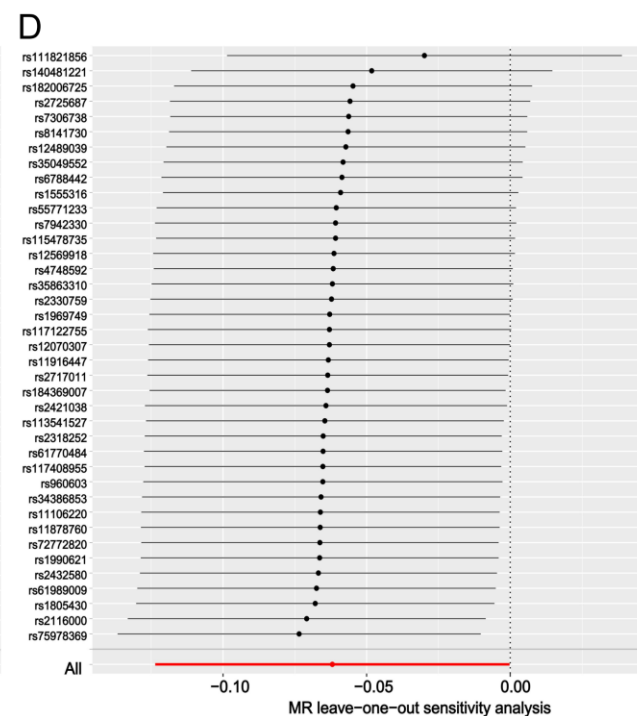
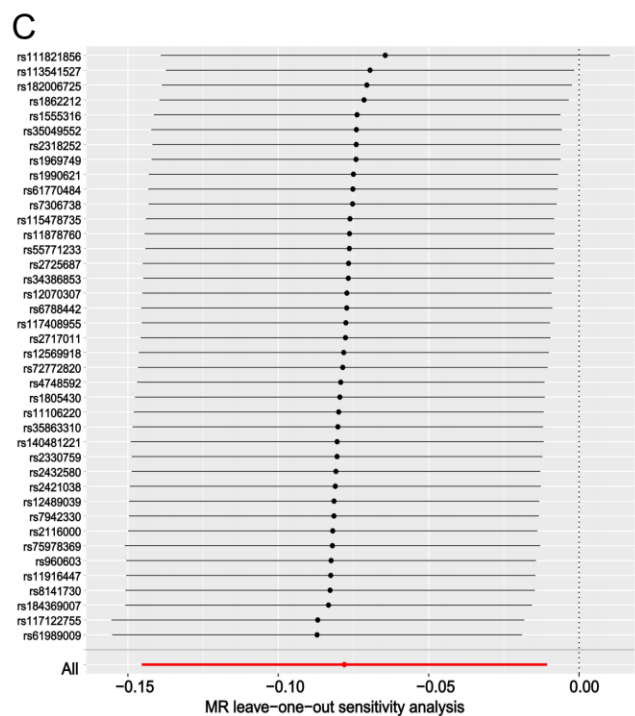
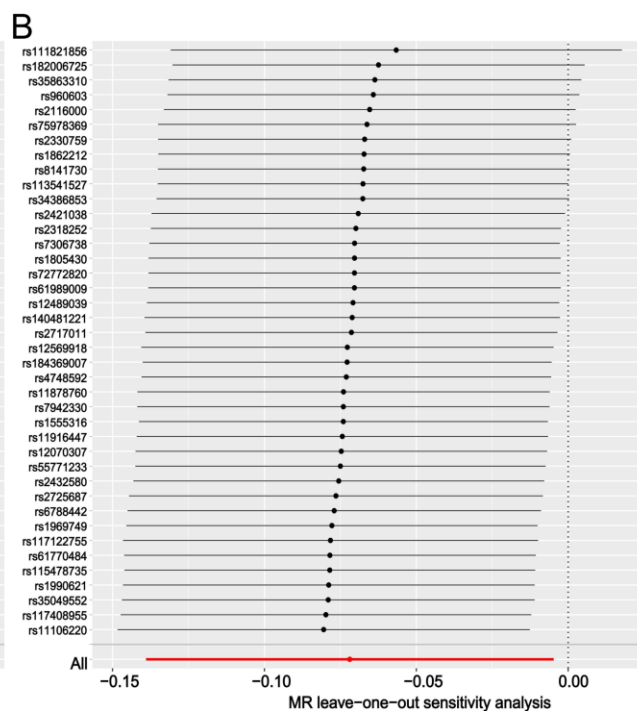
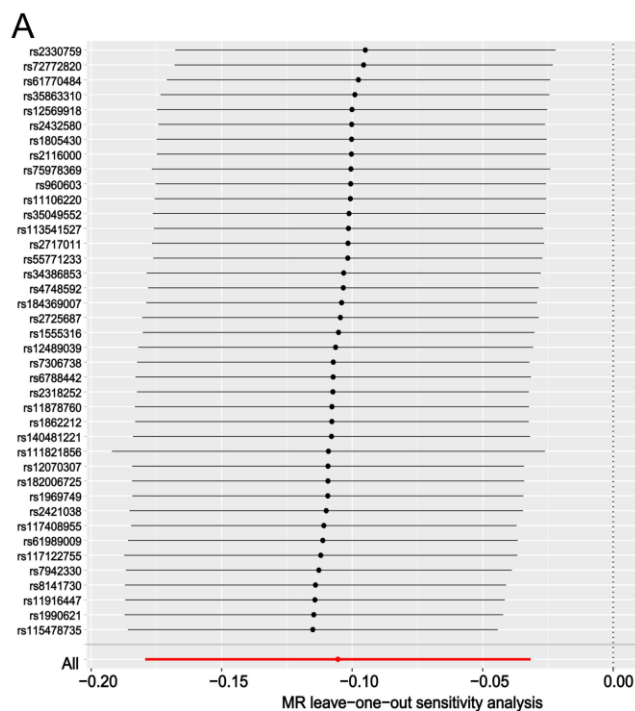
Supplementary Figure S2. Mendelian randomization (MR) scatter plots for the associations between genetic liability to epilepsy and circulating inflammatory factors. The *x*-axis shows the SNP–exposure association (effect estimate of each instrumental SNP on epilepsy, on the log-odds scale), and the *y*-axis shows the SNP–outcome association (effect estimate on the circulating protein level). Each point represents an instrumental SNP. The fitted lines denote MR causal estimates derived from the inverse-variance weighted (IVW) and MR-Egger methods. Panels show MR results for epilepsy in relation to (A) IL-10RA, (B) IL-20, (C) NRTN, and (D) SIRT2



Supplementary Figure S3. Leave-one-out sensitivity analyses for the Mendelian randomization (MR) estimates of circulating inflammatory factors on epilepsy. Each panel shows the IVW MR estimate recalculated after sequentially excluding one instrumental SNP at a time. Points indicate the leave-one-out causal estimate, and horizontal lines represent the corresponding 95% confidence intervals. Consistency of the estimates across exclusions suggests that the overall MR results are not driven by any single SNP. Panels correspond to (A) CCL23, (B) CXCL11, (C) FGF5, (D) GDNF, (E) LIFR, (F) OPG, and (G) VEGFA in relation to epilepsy



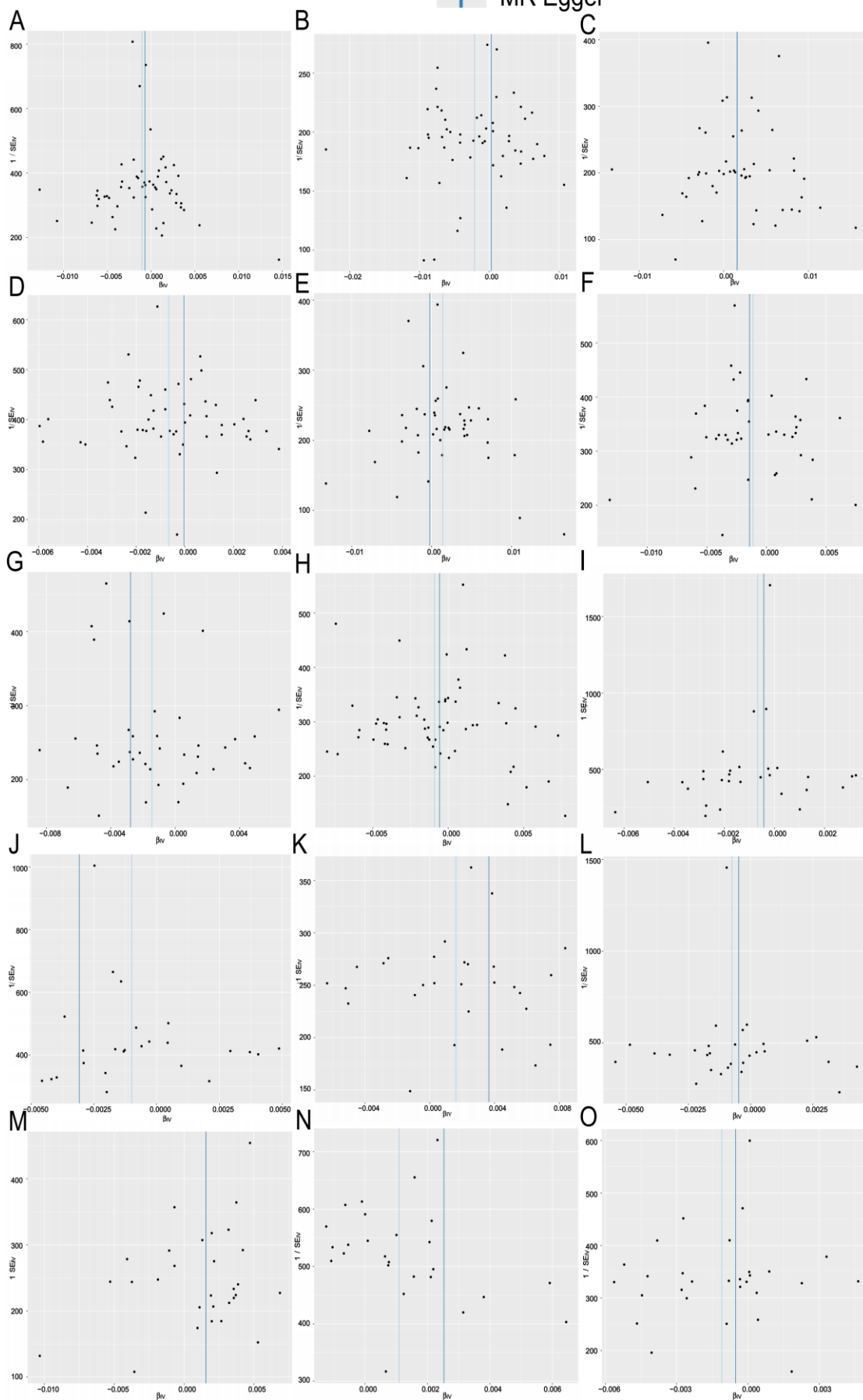
Supplementary Figure S4. Leave-one-out sensitivity analyses for the Mendelian randomization (MR) estimates of genetic liability to epilepsy on circulating inflammatory factors. Each panel shows the IVW MR estimate recalculated after iteratively removing one instrumental SNP at a time. Points represent the leave-one-out causal estimates, and horizontal bars indicate 95% confidence intervals. Stable estimates across exclusions suggest that the overall results are not driven by a single SNP. Panels correspond to the effects of genetic liability to epilepsy on **(A)** IL-10RA, **(B)** IL-20, **(C)** NRTN, and **(D)** SIRT2



Supplementary Figure S5. Mendelian randomization (MR) scatter plots for the associations between T1-weighted UDIP dimensions and epilepsy. The x-axis shows the SNP–exposure association (effect estimate of each instrumental SNP on the UDIP dimension), and the y-axis shows the SNP–outcome association (effect estimate on epilepsy, on the log-odds scale). Each point represents an instrumental SNP. The fitted lines indicate MR causal estimates using the inverse-variance weighted (IVW) and MR-Egger methods. Panels correspond to T1-weighted UDIP dimensions: (A) 7, (B) 14, (C) 18, (D) 46, (E) 49, (F) 56, (G) 104, (H) 120, (I) 16, (J) 38, (K) 50, (L) 67, (M) 76, and (N) 125

MR Method

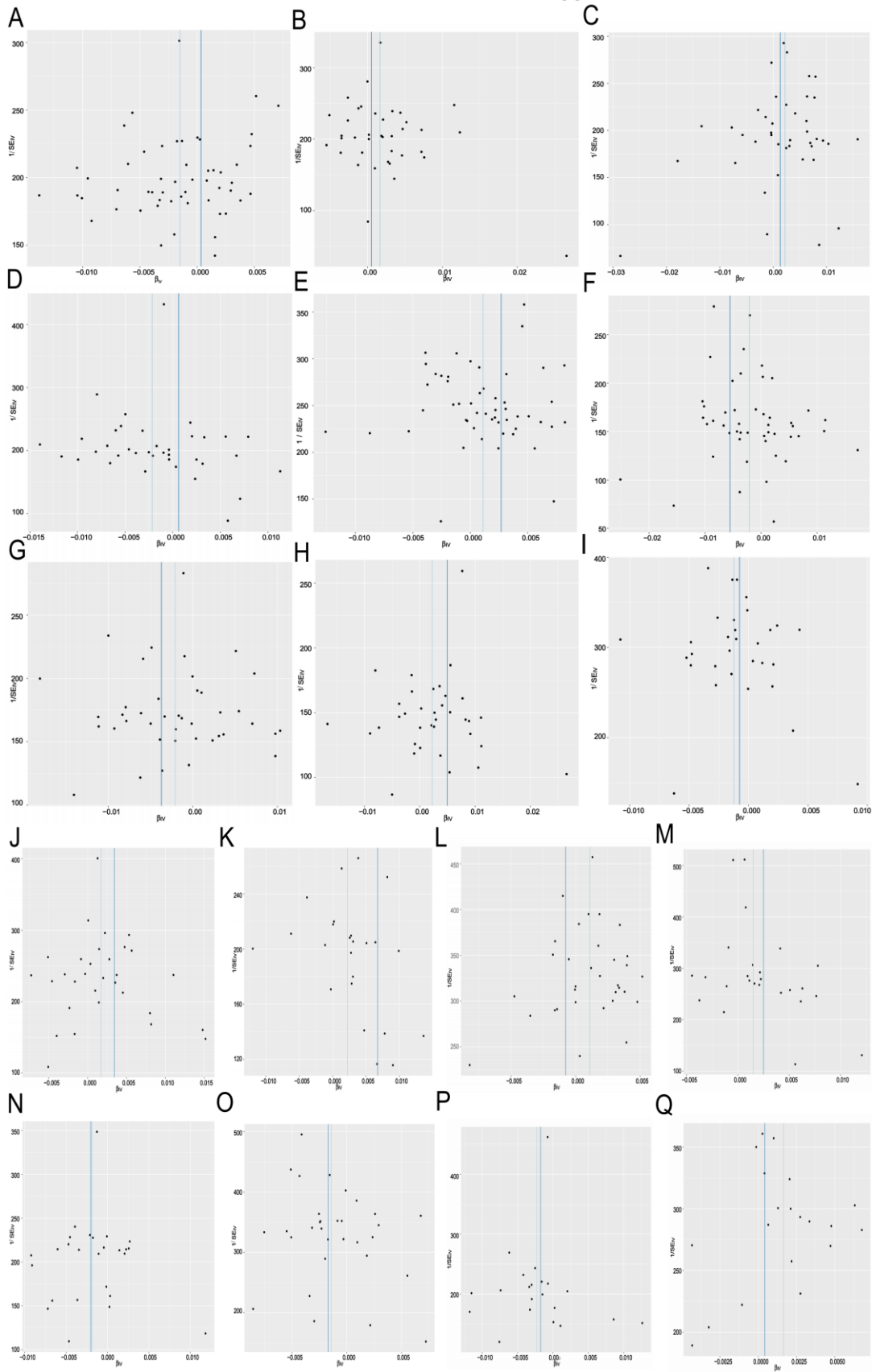
Inverse variance weighted
MR Egger



Supplementary Figure S6. Mendelian randomization (MR) scatter plots for the associations between T2-weighted UDIP dimensions and epilepsy. The x -axis shows the SNP–exposure association (effect estimate of each instrumental SNP on the UDIP dimension), and the y -axis shows the SNP–outcome association (effect estimate on epilepsy, on the log-odds scale). Each point represents an instrumental SNP. The fitted lines indicate MR causal estimates using the inverse-variance weighted (IVW) and MR-Egger methods. Panels correspond to T2-weighted UDIP dimensions: (A) 13, (B) 15, (C) 49, (D) 55, (E) 72, (F) 91, (G) 96, (H) 99, (I) 12, (J) 35, (K) 41, (L) 42, (M) 58, (N) 81, and (O) 105

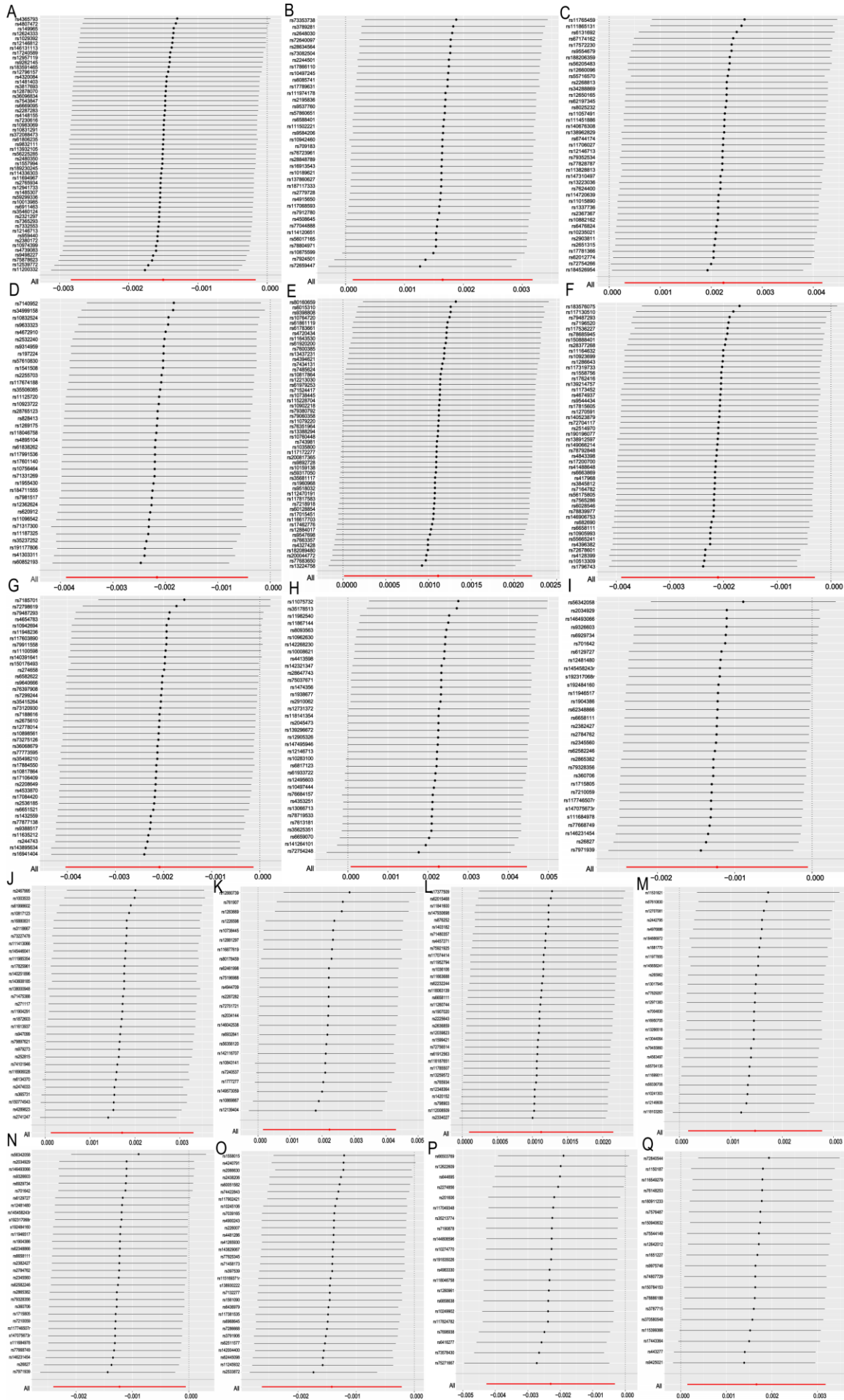
MR Method

Inverse variance weighted
MR Egger



Supplementary Figure S7. Leave-one-out sensitivity analyses for the Mendelian randomization (MR) estimates of T1-weighted UDIP dimensions on epilepsy. For each panel, the IVW MR estimate was recalculated after sequentially removing one instrumental SNP at a time. Points represent the leave-one-out causal estimates and horizontal lines denote the corresponding 95% confidence intervals. Consistent estimates across exclusions indicate that the overall MR results are not driven by any single SNP. Panels correspond to T1-weighted UDIP dimensions: (A) 7, (B) 14, (C) 18, (D) 46, (E) 49, (F) 56, (G) 104, (H) 120, (I) 16, (J) 38, (K) 50, (L) 67, (M) 76, and (N) 125

Supplementary Figure S8. Leave-one-out sensitivity analyses for the Mendelian randomization (MR) estimates of T2-weighted UDIP dimensions on epilepsy. In each panel, the IVW MR estimate was recalculated after iteratively excluding one instrumental SNP at a time. Points represent the leave-one-out causal estimates and horizontal lines indicate the corresponding 95% confidence intervals. Consistency of the estimates across exclusions suggests that the overall MR results are not driven by any single SNP. Panels correspond to T2-weighted UDIP dimensions: (A) 13, (B) 15, (C) 49, (D) 55, (E) 72, (F) 91, (G) 96, (H) 99, (I) 12, (J) 35, (K) 41, (L) 42, (M) 58, (N) 81, and (O) 105



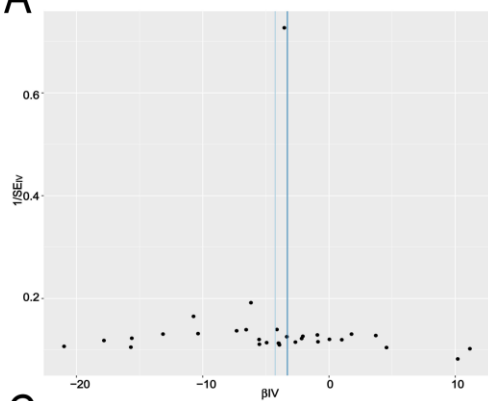
Supplementary Figure S9. Mendelian randomization (MR) scatter plots for the associations between genetically predicted circulating inflammatory factors and selected UDIP dimensions identified in the mediation analysis. The x-axis shows the SNP–exposure association (effect estimate of each instrumental SNP on the inflammatory factor), and the y-axis shows the SNP–outcome association (effect estimate on the UDIP dimension). Each point represents an instrumental SNP. The fitted lines indicate MR causal estimates derived from the inverse-variance weighted (IVW) and MR-Egger methods. Panels show MR results for the effect of (A) CCL23 on T1-weighted UDIP dimension 14, (B) CCL23 on T2-weighted UDIP dimension 96, (C) CXCL11 on T2-weighted UDIP dimension 13, (D) FGF5 on T1-weighted UDIP dimension 7, (E) FGF5 on T2-weighted UDIP dimension 15, (F) GDNF on T2-weighted UDIP dimension 35, (G) OPG on T1-weighted UDIP dimension 46, and (H) OPG on T2-weighted UDIP dimension 96

MR Method

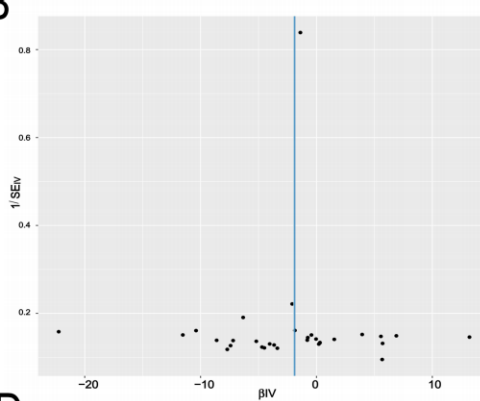


Inverse variance weighted MR Egger

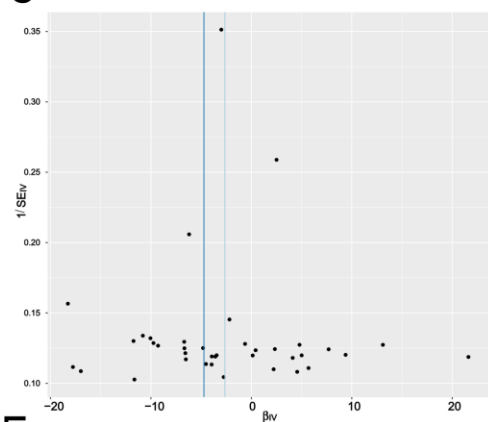
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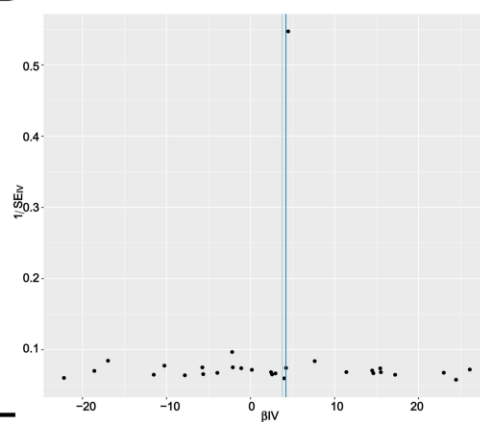
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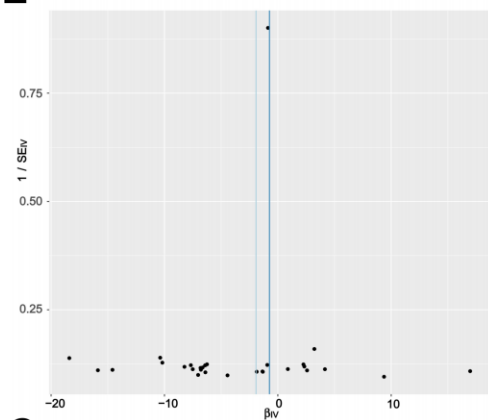
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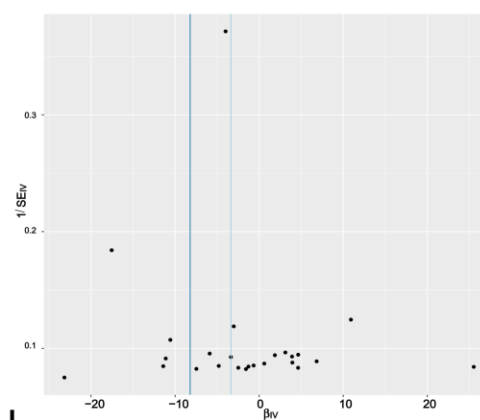
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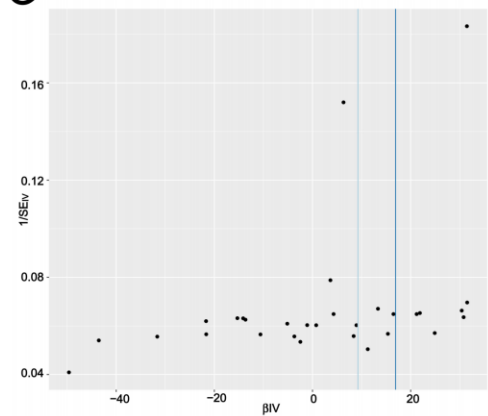
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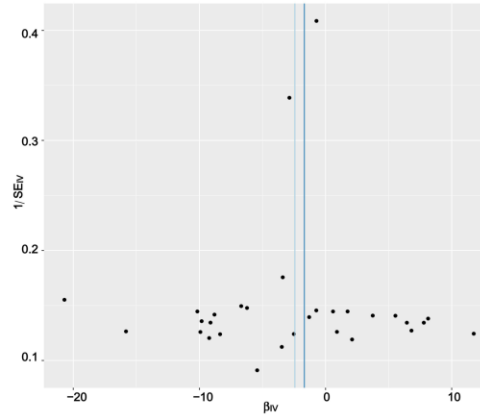
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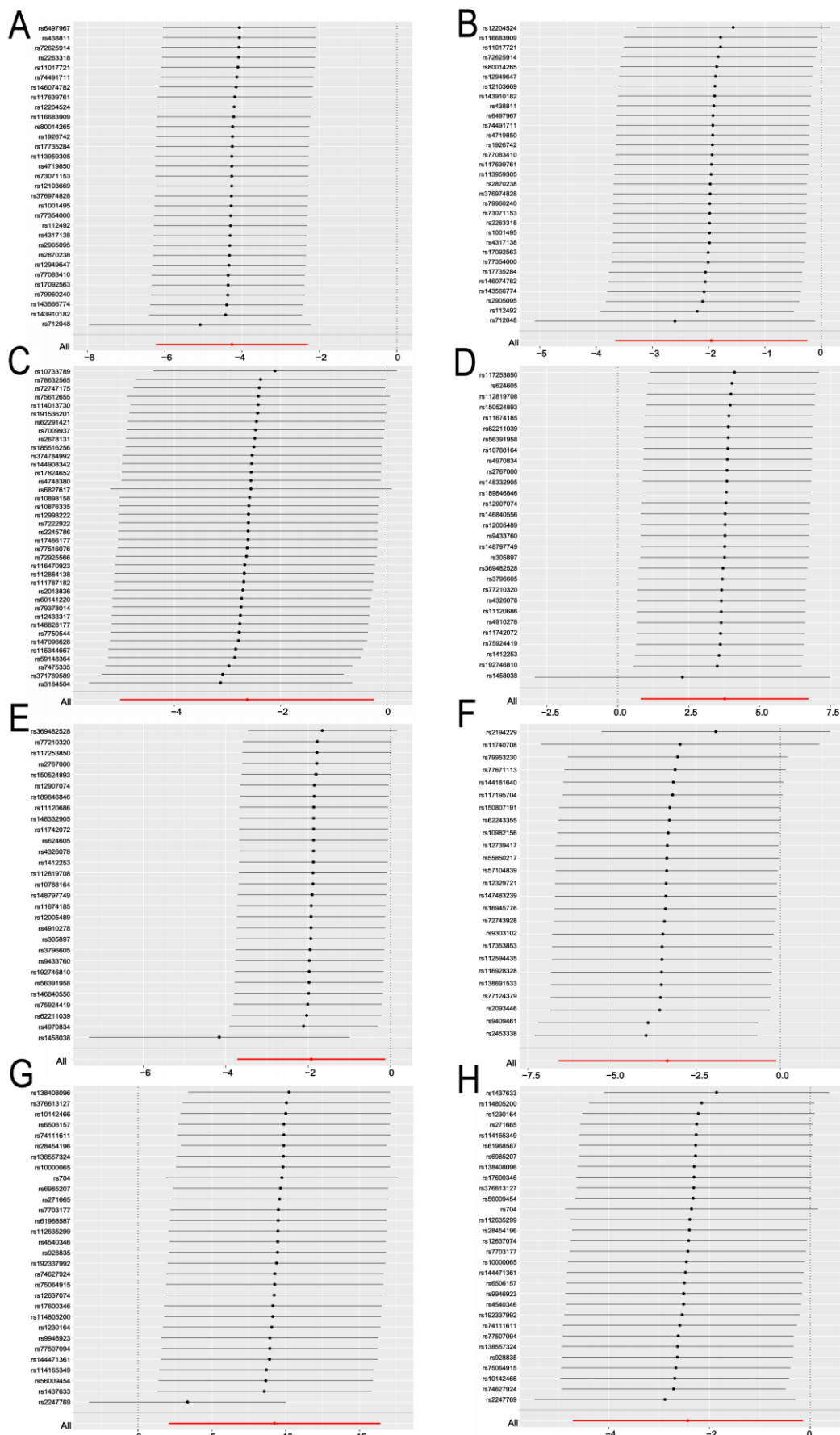
G



H



Supplementary Figure S10. Leave-one-out sensitivity analyses for the Mendelian randomization (MR) estimates of circulating inflammatory factors on selected UDIP dimensions included in the mediation analysis. In each panel, the IVW MR estimate was recalculated after sequentially excluding one instrumental SNP at a time. Points represent the leave-one-out causal estimates and horizontal lines indicate the corresponding 95% confidence intervals. Stable estimates across exclusions suggest that the overall MR results are not driven by any single SNP. Panels show MR results for the effect of (A) CCL23 on T1-weighted UDIP dimension 14, (B) CCL23 on T2-weighted UDIP dimension 96, (C) CXCL11 on T2-weighted UDIP dimension 13, (D) FGF5 on T1-weighted UDIP dimension 7, (E) FGF5 on T2-weighted UDIP dimension 15, (F) GDNF on T2-weighted UDIP dimension 35, (G) OPG on T1-weighted UDIP dimension 46, and (H) OPG on T2-weighted UDIP dimension 96



MR leave-one-out sensitivity analysis