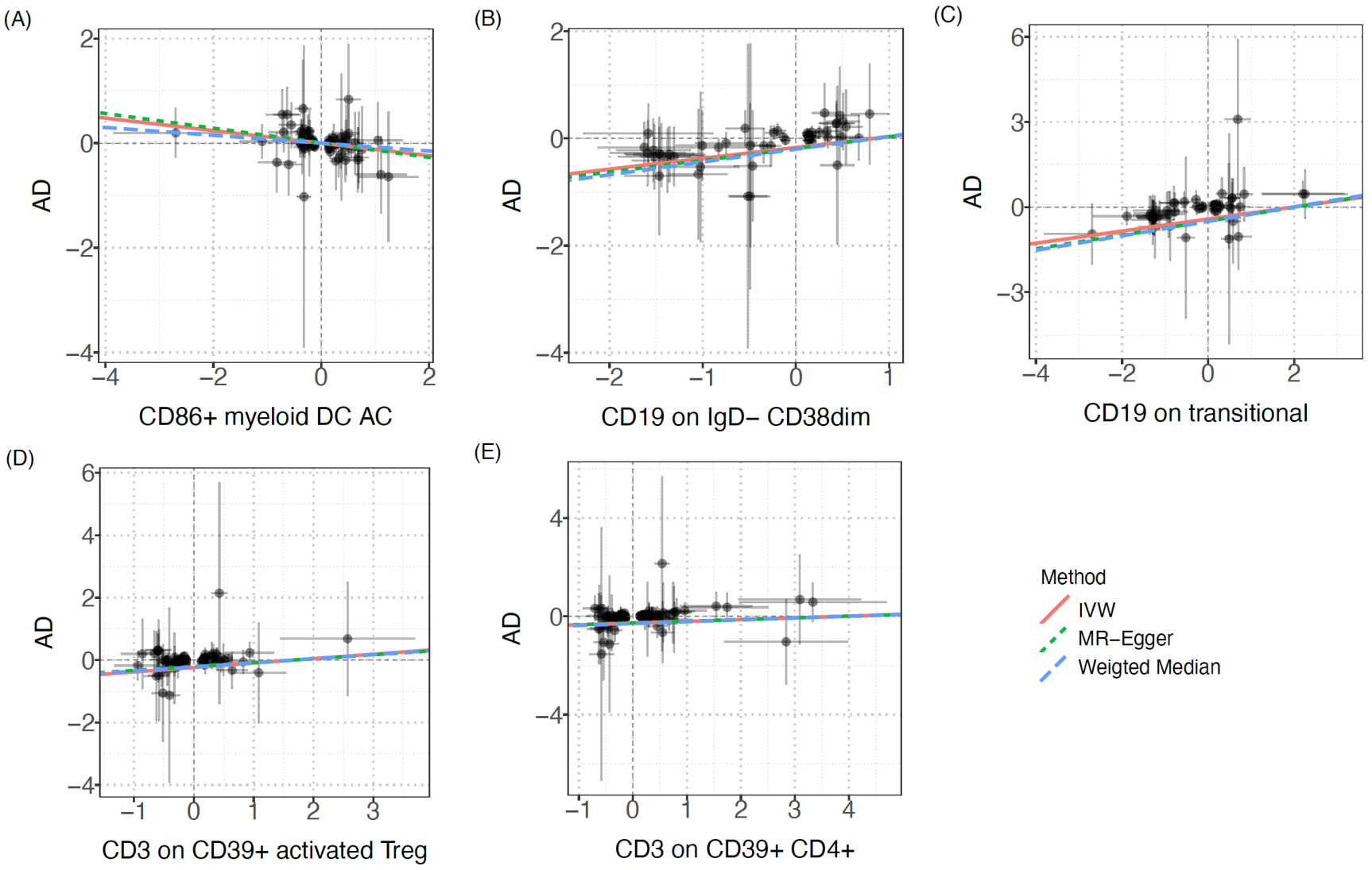
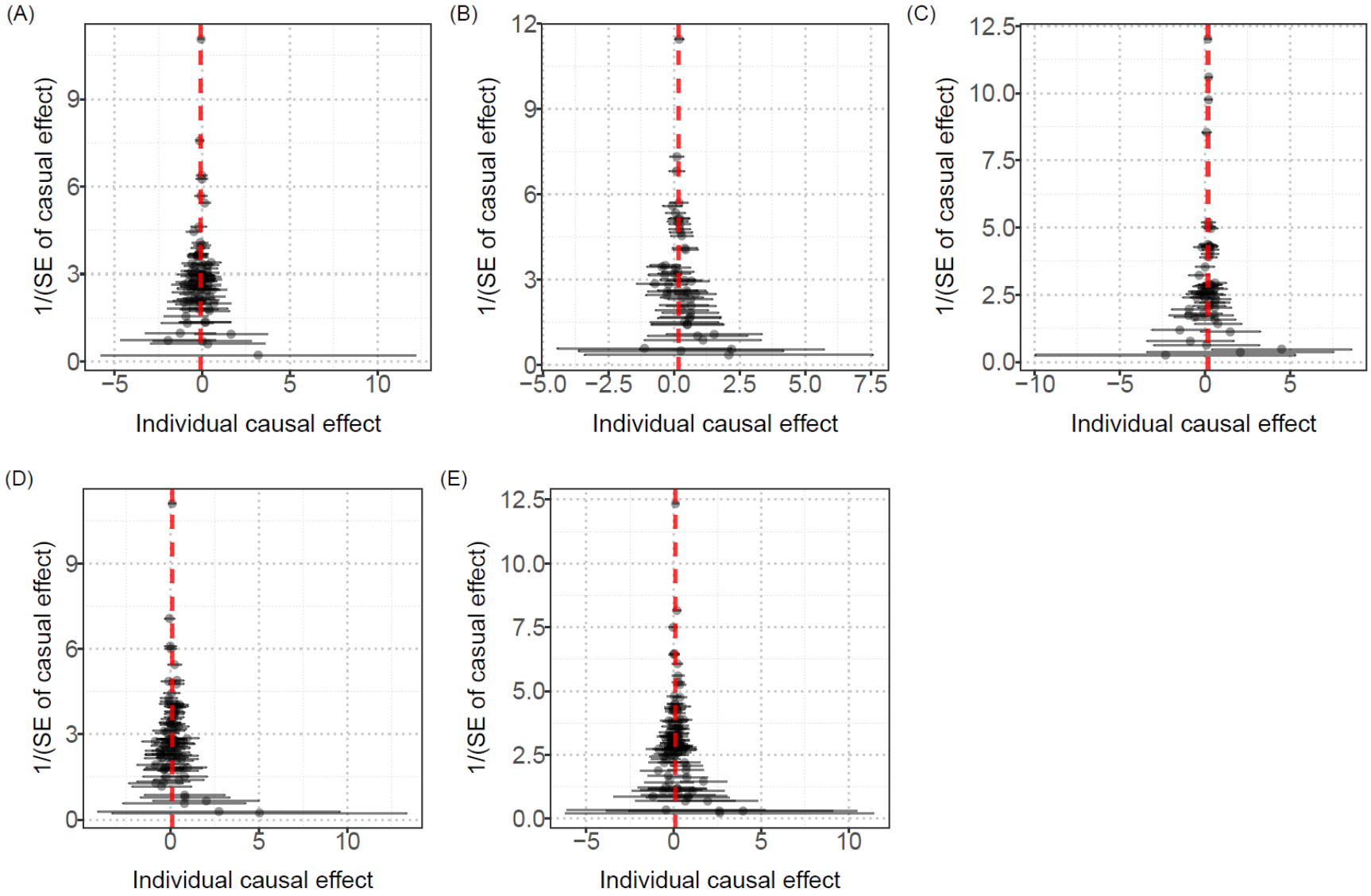
Supplementary Material

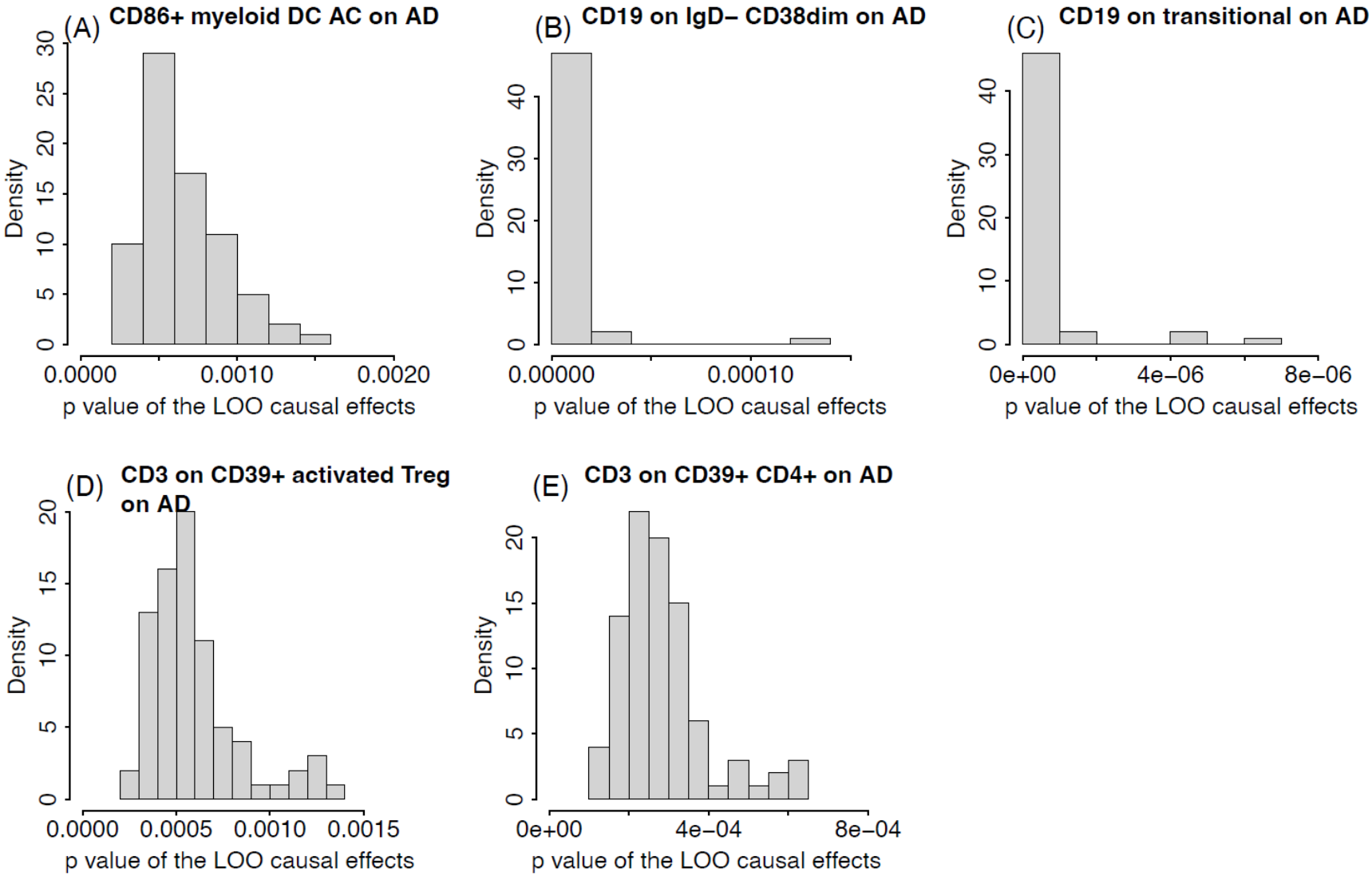
Supplementary Figure 1: Scatter plot analysis based on inverse-variance weighted Mendelian randomisation for causal inference. The red solid line represents the inverse-variance weighted method, and the green dashed line represents the weighted median method.



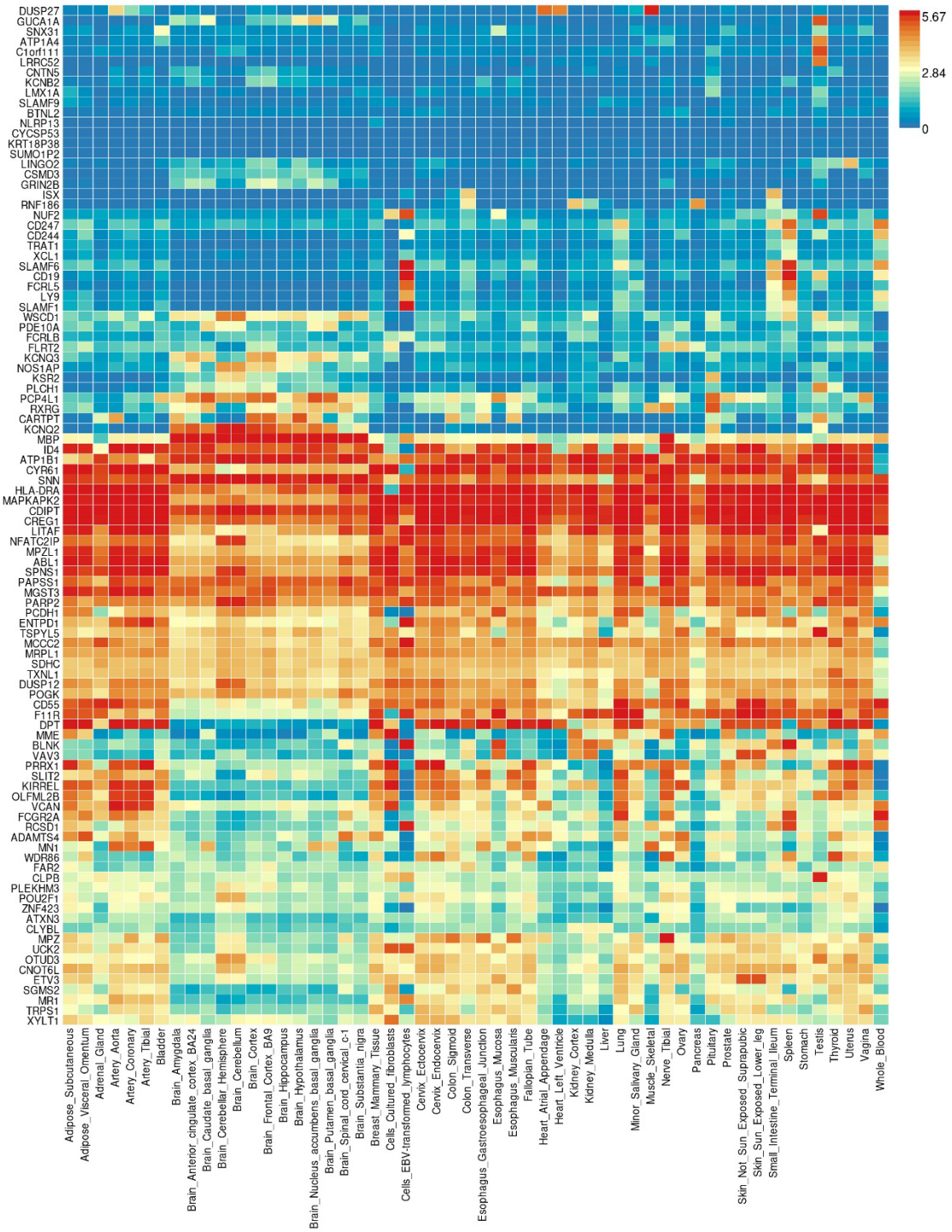
Supplementary Figure 2: Funnel plot analysis based on inverse-variance weighted Mendelian randomisation for causal inference.



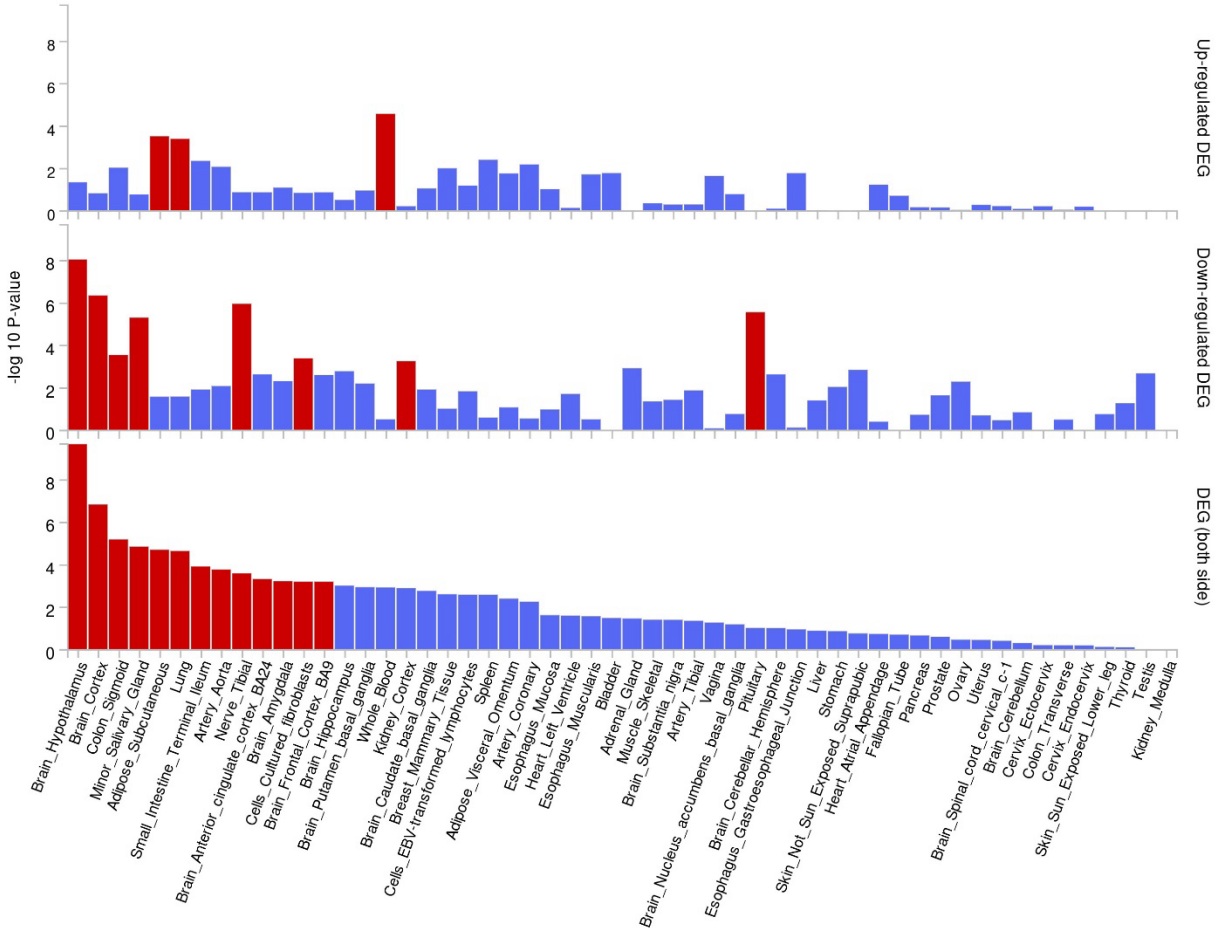
Supplementary Figure 3: Leave-One-Out Cross-Validation (LOOCV) analysis based on inverse-variance weighted Mendelian randomisation for causal inference.



Supplementary Figure 4: Expression analysis of risk SNP-mapping genes in different tissues at the transcription level. The mapped genes were derived from the 10bp vicinity of the risk SNP loci of the causally associated immune cells. The scale was converted from transcription values using log2(RPKM+1). The colour scale on the right represents gene expression levels, with blue indicating low expression, green indicating moderate expression, and red indicating high expression. The x-axis represents various tissues, while the y-axis represents differentially expressed genes.



Supplementary Figure 5: Enrichment analysis of risk SNP-mapping genes across different tissues. The figure illustrates the expression profiles of differentially expressed genes (DEGs) in various tissues. The top row represents up-regulated DEGs, the middle row shows down-regulated DEGs, and the bottom row displays the overall expression profiles of DEGs. Red bars indicate statistical significance, while purple bars indicate no statistical significance. The height of each bar represents the -log10 P-value, indicating the level of statistical significance. This analysis identifies which tissues exhibit significant gene expression changes associated with risk SNPs, providing insights into the potential biological impact of these genetic variations.



Supplementary Table 1. Differential Causal Effects of Immunophenotypes on Aortic Dissection Identified through IVW-MR Analysis.

ID	Trait type	Panel	Trait	BETA	Standard Error	P	FDR
90001742	MFI	B cell	CD19 on transitional	0.175873	0.03489178	4.64E-07	0.000339
90001735	MFI	B cell	CD19 on IgD- CD38dim	0.166584	0.037353214	8.21E-06	0.003
90001860	MFI	Treg	CD3 on CD39+ CD4+	0.107383	0.029288251	0.000246	0.059936
90001854	MFI	Treg	CD3 on CD39+ activated Treg	0.116962	0.033665096	0.000512	0.081799
90001464	Absolute count	cDC	CD86+ myeloid DC AC	-0.11953	0.034641681	0.000559	0.081799

Supplementary Table 2. Validation of Immunophenotype Causal Associations Using Alternative MR Methods.

ID	Trait type	Panel	Trait	Proportion of Variance Explained	Minimum F-statistic	Number of SNPs
90001735	MFI	B cell	CD19 on IgD- CD38dim	0.415852778	19.57617846	50
90001742	MFI	B cell	CD19 on transitional	0.384216413	19.72894711	51
90001860	MFI	Treg	CD3 on CD39+ CD4+	0.92195337	19.66315082	91
90001464	Absolute count	cDC	CD86+ myeloid DC AC	0.921316644	19.62339737	77
90001854	MFI	Treg	CD3 on CD39+ activated Treg	0.759768759	19.62660908	81

ID	IVW_fix	standard error	odd ratio	lower limit of the 95% confidence interval	Upper limit of the 95% confidence interval	P value
90001735	0.166584385	0.037353	1.181263213	1.097871637	1.270989003	8.21E-06
90001742	0.175872699	0.034892	1.19228627	1.113475347	1.276675369	4.64E-07
90001860	0.107382905	0.029288	1.113360484	1.051249006	1.179141726	0.000245974
90001464	0.013832182	0.025542	1.013928289	0.964419443	1.065978692	0.588129091
90001854	-0.018321068	0.025321	0.981845742	0.934306984	1.031803334	0.46934869

ID	IVW_random	standard error	odd ratio	lower limit of the 95% confidence interval	Upper limit of the 95% confidence interval	P value
90001735	0.166584385	0.037353	1.181263213	1.097871637	1.270989003	8.21E-06
90001742	0.175872699	0.034892	1.19228627	1.113475347	1.276675369	4.64E-07
90001860	0.107382905	0.029288	1.113360484	1.051249006	1.179141726	0.000245974
90001464	0.013832182	0.026187	1.013928289	0.96320008	1.067328167	0.597360188
90001854	-0.018321068	0.025321	0.981845742	0.934306984	1.031803334	0.46934869

ID	weighted_Mode	standard error	odd ratio	lower limit of the 95% confidence interval	Upper limit of the 95% confidence interval	P value
90001735	0.174522685	0.060273	1.190677753	1.058010363	1.339980742	0.003785003
90001742	0.201296615	0.057568	1.222987474	1.092496244	1.369064993	0.000471105
90001860	0.110377857	0.051704	1.116699944	1.009081077	1.235796402	0.032776734
90001464	-0.005342995	0.04118	0.994671254	0.91754471	1.078280865	0.896765909

90001854	-0.040336613	0.046299	0.960466079	0.877146701	1.05169989	0.383634263
ID	**weighted_Median**	**standard error**	**odd ratio**	**lower limit of the 95% confidence interval**	**Upper limit of the 95% confidence interval**	**P value**
90001735	0.19695652	0.057991	1.217691094	1.086862838	1.364267457	0.000683024
90001742	0.210835742	0.053637	1.234709527	1.111499268	1.371577706	8.47E-05
90001860	0.115783894	0.047981	1.122753212	1.021980084	1.233463152	0.015817582
90001464	-0.003957438	0.04106	0.996050383	0.919033583	1.07952134	0.92321643
90001854	-0.036445985	0.038877	0.964210174	0.893468521	1.0405529	0.348521579
ID	**DIVW**	**standard error**	**odd ratio**	**lower limit of the 95% confidence interval**	**Upper limit of the 95% confidence interval**	**P value**
90001735	0.172261926	0.039457	1.187988958	1.099579624	1.283506654	1.27E-05
90001742	0.183316187	0.038148	1.20119415	1.114658582	1.294447833	1.54E-06
90001860	0.110721263	0.030329	1.117083491	1.052615246	1.185500144	0.000261538
90001464	0.014208658	0.026879	1.01431008	0.962256541	1.069179471	0.597078953
90001854	-0.018940951	0.026184	0.981237301	0.932150419	1.032909091	0.469450942
ID	**MR-RAPS**	**standard error**	**odd ratio**	**lower limit of the 95% confidence interval**	**Upper limit of the 95% confidence interval**	**P value**
90001735	0.170922681	0.039575	1.186399014	1.097853052	1.282086539	1.57E-05
90001742	0.178292279	0.03812	1.195174595	1.10913137	1.287892806	2.91E-06
90001860	0.109578867	0.030362	1.115808068	1.051344198	1.184224583	0.000307272
90001464	0.014170089	0.026273	1.014270961	0.963363238	1.067868839	0.589650247
90001854	-0.01865973	0.026391	0.981513285	0.932034137	1.033619145	0.479533878
ID	**Egger_slope**	**standard error**	**odd ratio**	**lower limit of the 95% confidence interval**	**Upper limit of the 95% confidence interval**	**P value**
90001735	0.180408758	0.052136	1.197706835	1.081364817	1.326565873	0.0006837
90001742	0.201000033	0.044474	1.222624812	1.120564676	1.333980504	1.60E-05
90001860	0.105553932	0.052434	1.111326038	1.002788545	1.23161116	0.044107085
90001464	-0.005443164	0.048826	0.994571623	0.902389678	1.096170244	0.91153222
90001854	-0.065675905	0.049017	0.936434309	0.850655473	1.030862954	0.180293766
ID	**Egger_intercept**	**standard error**	**odd ratio**	**lower limit of the 95% confidence interval**	**Upper limit of the 95% confidence interval**	**P value**

90001735	-0.006782465	0.017845	-0.006782465	-0.04175722	0.02819229	0.703882171
90001742	-0.01713519	0.018806	-0.01713519	-0.053993766	0.019723385	0.362206837
90001860	0.000653272	0.015534	0.000653272	-0.029793683	0.031100227	0.966456335
90001464	0.006048827	0.012905	0.006048827	-0.019658623	0.031756278	0.640621426
90001854	0.014668568	0.013001	0.014668568	-0.010812368	0.040149503	0.259197809

ID	Heterogeneity Estimate	Heterogeneity P value
90001735	43.72874868	0.686104
90001742	44.49213183	0.693241
90001860	77.51486764	0.823078
90001464	79.88989288	0.357867
90001854	56.64133589	0.977831

Supplementary Table 3. Exclusion of Horizontal Pleiotropy Among Immunophenotypes via MR-PRESSO Global Test.

Exposure (ID)	Global Residual Sum of Squares observed	Global P value	mrpresso	standard error	lower limit of the 95% confidence interval	Upper limit of the 95% confidence interval	P value
90001464	82.10388821	0.3158	-0.119531962	0.036111142	-0.190309801	-0.048754124	1.44E-03
90001735	44.97392577	0.7272	0.166584385	0.035286897	0.097422067	0.235746703	2.00E-05
90001742	45.29729189	0.7558	0.175872699	0.032913929	0.111361398	0.240384	2.25E-06
90001854	73.75006032	0.6816	0.11696243	0.032386172	0.053485532	0.180439327	0.000536
90001860	78.88322738	0.8406	0.107382905	0.027180954	0.054108235	0.160657575	0.000155

Supplementary Table 4. Eliminating Reverse Causation in Immunophenotypes with Reverse MR Analysis.

Exposures	Outcomes	Methods	BETA	Standard Error	Odd ratio	lower limit of the 95% CI	Upper limit of the 95% CI	P value	Heterogeneity Estimate	Heterogeneity P value
I9_AORTDIS	90001464	IVW_fix	-0.0316	0.05559	0.96885	0.86883974	1.080374577	0.56918	1.823919942	0.176847383
I9_AORTDIS	90001464	IVW_random	-0.0316	0.07507	0.96885	0.83628389	1.122432683	0.67338	1.823919942	0.176847383
I9_AORTDIS	90001464	Egger_slope	NA	NA	NA	NA	NA	NA	NA	NA
I9_AORTDIS	90001464	Egger_ intercept	NA	NA	NA	NA	NA	NA	NA	NA
I9_AORTDIS	90001464	weighted_ mode	NA	NA	NA	NA	NA	NA	NA	NA
I9_AORTDIS	90001464	weighted_ Median	NA	NA	NA	NA	NA	NA	NA	NA
I9_AORTDIS	90001464	DIVW	-0.0324	0.05707	0.96811	0.86566177	1.082677124	0.57006	NA	NA
I9_AORTDIS	90001464	MR-RAPS	-0.0323	0.05731	0.96818	0.8653064	1.083283089	0.5726	NA	NA
I9_AORTDIS	90001735	IVW_fix	0.01561	0.05272	1.01573	0.91601557	1.126308074	0.76715	0.217417193	0.641014974
I9_AORTDIS	90001735	IVW_random	0.01561	0.05272	1.01573	0.91601557	1.126308074	0.76715	0.217417193	0.641014974
I9_AORTDIS	90001735	Egger_slope	NA	NA	NA	NA	NA	NA	NA	NA
I9_AORTDIS	90001735	Egger_ intercept	NA	NA	NA	NA	NA	NA	NA	NA
I9_AORTDIS	90001735	weighted_ mode	NA	NA	NA	NA	NA	NA	NA	NA
I9_AORTDIS	90001735	weighted_ Median	NA	NA	NA	NA	NA	NA	NA	NA
I9_AORTDIS	90001735	DIVW	0.01599	0.05404	1.01612	0.91400683	1.129639622	0.76728	NA	NA
I9_AORTDIS	90001735	MR-RAPS	0.01564	0.05463	1.01577	0.912628	1.130557998	0.77461	NA	NA
I9_AORTDIS	90001742	IVW_fix	-0.0392	0.05333	0.96155	0.86612519	1.067488283	0.46218	2.180871888	0.13973528
I9_AORTDIS	90001742	IVW_random	-0.0392	0.07875	0.96155	0.82402266	1.122030423	0.61857	2.180871888	0.13973528
I9_AORTDIS	90001742	Egger_slope	NA	NA	NA	NA	NA	NA	NA	NA
I9_AORTDIS	90001742	Egger_ intercept	NA	NA	NA	NA	NA	NA	NA	NA
I9_AORTDIS	90001742	weighted_ mode	NA	NA	NA	NA	NA	NA	NA	NA
I9_AORTDIS	90001742	weighted_ Median	NA	NA	NA	NA	NA	NA	NA	NA
I9_AORTDIS	90001742	DIVW	-0.0402	0.05679	0.96063	0.85944591	1.073737666	0.47945	NA	NA

I9_AORTDIS	90001742	MR-RAPS	-0.0403	0.055	0.96054	0.86238341	1.069866204	0.46414	NA	NA
I9_AORTDIS	90001854	IVW_fix	0.06802	0.05768	1.07038	0.95596227	1.198498883	0.23833	1.003627278	0.316434402
I9_AORTDIS	90001854	IVW_random	0.06802	0.05779	1.07038	0.95576646	1.198744423	0.23918	1.003627278	0.316434402
I9_AORTDIS	90001854	Egger_slope	NA	NA	NA	NA	NA	NA	NA	NA
I9_AORTDIS	90001854	Egger_ intercept	NA	NA	NA	NA	NA	NA	NA	NA
I9_AORTDIS	90001854	weighted_ mode	NA	NA	NA	NA	NA	NA	NA	NA
I9_AORTDIS	90001854	weighted_ Median	NA	NA	NA	NA	NA	NA	NA	NA
I9_AORTDIS	90001854	DIVW	0.06967	0.05965	1.07215	0.95384655	1.205132547	0.24286	NA	NA
I9_AORTDIS	90001854	MR-RAPS	0.06896	0.06021	1.07139	0.95213269	1.205592735	0.25207	NA	NA
I9_AORTDIS	90001860	IVW_fix	0.07323	0.05837	1.07598	0.95966165	1.206391349	0.20964	0.236587762	0.626681549
I9_AORTDIS	90001860	IVW_random	0.07323	0.05837	1.07598	0.95966165	1.206391349	0.20964	0.236587762	0.626681549
I9_AORTDIS	90001860	Egger_slope	NA	NA	NA	NA	NA	NA	NA	NA
I9_AORTDIS	90001860	Egger_ intercept	NA	NA	NA	NA	NA	NA	NA	NA
I9_AORTDIS	90001860	weighted_ mode	NA	NA	NA	NA	NA	NA	NA	NA
I9_AORTDIS	90001860	weighted_ Median	NA	NA	NA	NA	NA	NA	NA	NA
I9_AORTDIS	90001860	DIVW	0.07501	0.06044	1.07789	0.95747195	1.213458839	0.21462	NA	NA
I9_AORTDIS	90001860	MR-RAPS	0.0733	0.06094	1.07605	0.9548954	1.212578337	0.22909	NA	NA