

SUPPLEMENTAL MATERIALS

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Supplemental Table 1. Description of data sources about the MR analyses.

Trait	Consortium	Sample size (Cases/Controls)	Population
AS	FinnGen (2023)	2,860/270,964	European
RA	FinnGen (2023)	12,555/240,862	European
SS	FinnGen (2023)	2,495/365,533	European
SLE	FinnGen (2023)	1023/281,127	European
Sepsis	UK Biobank (2021)	11,643/474,841	European

MR, Mendelian Randomization; AS, ankylosing spondylitis; RA, rheumatoid arthritis; SS, sicca syndrome; SLE, Systemic Lupus Erythematosus.

Supplemental Table 2. Detailed information for the genetic variants associated with AS.

SNP	Effect allele	Other allele	Eaf	Beta	SE	pval	F-statistic
rs10456271	T	C	0.030	0.455	0.068	1.61E-11	3339.478
rs10807943	C	T	0.936	-0.374	0.049	3.77E-14	4667.009
rs114799031	T	A	0.062	1.274	0.036	8.24E-269	63723.257
rs13192159	T	C	0.160	0.534	0.032	2.50E-64	22730.997
rs140932965	T	C	0.017	0.540	0.089	1.23E-09	2694.933
rs142695953	A	C	0.187	0.215	0.033	7.38E-11	3903.577
rs17190120	T	G	0.035	1.606	0.044	3.63E-295	57774.184
rs2032890	C	T	0.269	-0.243	0.031	6.97E-15	6510.226
rs2844841	C	A	0.369	0.548	0.025	3.20E-103	44519.587
rs3130165	G	C	0.249	0.320	0.029	1.47E-28	10904.633
rs652888	G	A	0.219	0.635	0.028	3.98E-116	43814.361
rs6759003	C	T	0.662	-0.188	0.028	1.12E-11	4400.786
rs72749142	A	G	0.139	-0.235	0.041	1.04E-08	3668.175
rs78724843	A	C	0.043	0.620	0.054	9.54E-31	8946.321
rs9461388	C	T	0.028	-0.579	0.096	1.44E-09	5089.793

Supplemental Table 3. Detailed information for the genetic variants associated with RA.

SNP	Effect allele	Other allele	Eaf	Beta	SE	pval	F-statistic
rs10821948	A	C	0.426	0.076	0.013	1.34E-08	717.860
rs114335056	G	A	0.154	0.623	0.016	0	28512.450
rs114889222	T	C	0.038	-0.218	0.036	1.65E-09	883.579
rs11513729	T	C	0.381	0.098	0.014	4.36E-13	1153.193
rs117292830	A	G	0.037	0.714	0.029	5.87E-138	9553.401
rs16903065	A	C	0.116	-0.143	0.021	2.09E-11	1067.259
rs188302747	G	C	0.015	-0.578	0.064	1.44E-19	2526.703
rs192741093	A	G	0.024	-0.282	0.046	9.43E-10	947.638
rs2476601	G	A	0.852	-0.349	0.017	4.83E-92	8030.896
rs3087243	A	G	0.330	-0.106	0.014	7.01E-14	1265.395
rs34536443	C	G	0.030	-0.308	0.042	3.53E-13	1406.893
rs3757387	C	T	0.425	0.091	0.013	6.23E-12	1029.824
rs4274624	T	C	0.769	-0.111	0.015	4.84E-13	1114.171
rs548877	G	A	0.176	0.096	0.017	1.46E-08	679.215
rs6065926	G	A	0.729	0.085	0.015	1.56E-08	725.502
rs6456160	C	T	0.557	-0.079	0.013	2.34E-09	782.916
rs75431337	T	C	0.073	0.273	0.024	4.75E-31	2582.219
rs7731626	A	G	0.279	-0.108	0.015	4.81E-13	1194.791
rs78248443	T	C	0.075	-0.179	0.026	9.69E-12	1131.635
rs78782944	T	C	0.095	0.125	0.022	1.13E-08	682.689
rs8002731	C	A	0.363	-0.090	0.014	7.18E-11	952.847
rs9332735	A	G	0.036	-0.425	0.040	7.17E-27	3217.354
rs9368699	C	T	0.032	0.398	0.034	2.33E-32	2511.521

Supplemental Table 4. Detailed information for the genetic variants associated with SS.

SNP	Effect allele	Other allele	Eaf	Beta	SE	p-value	F-statistic
rs10174238	A	G	0.764	-0.205	0.032	2.56E-10	5663.090
rs113858286	G	C	0.029	0.426	0.075	1.41E-08	3800.200
rs150724213	A	G	0.029	0.451	0.075	1.99E-09	4264.640
rs16869677	T	C	0.078	0.369	0.048	1.03E-14	7351.509
rs3117581	G	A	0.091	0.733	0.040	5.77E-76	35904.589

Supplemental Table 5. Detailed information for the genetic variants associated with SLE.

SNP	Effect allele	Other allele	Eaf	Beta	SE	pval	F-statistic
rs1270942	G	A	0.086	0.803	0.061	2.34E-39	31827.416
rs150724213	A	G	0.028	0.748	0.104	7.95E-13	8862.708
rs35000415	T	C	0.149	0.410	0.055	1.33E-13	12563.499
rs4853458	G	A	0.772	-0.339	0.036	5.13E-12	11895.797
rs998683	A	G	0.261	0.271	0.048	1.80E-08	8226.439

Supplemental Table 6. Detailed information for the genetic variants associated with sepsis.

SNP	Effect allele	Other allele	Eaf	Beta	SE	pval	F-statistic
rs11068069	T	C	0.176	0.083	0.018	3.60E-06	974.006
rs112431283	A	T	0.025	-0.233	0.046	4.49E-07	1290.934
rs11980516	T	G	0.824	0.089	0.018	9.50E-07	1120.252
rs12544445	T	C	0.183	-0.085	0.018	2.95E-06	1053.288
rs139409755	T	C	0.041	-0.167	0.035	1.55E-06	1069.266
rs147734876	T	G	0.011	-0.315	0.068	3.30E-06	1052.557
rs147793338	A	G	0.030	0.193	0.042	4.80E-06	1056.932
rs150753765	G	A	0.016	-0.272	0.056	1.09E-06	1135.959
rs2226602	T	A	0.232	0.076	0.016	3.00E-06	1003.386
rs3851566	G	A	0.444	0.063	0.014	4.63E-06	955.1850
rs4841254	A	G	0.653	-0.068	0.014	1.85E-06	1021.570
rs72820148	T	A	0.076	0.122	0.026	4.09E-06	1019.086
rs80054869	C	T	0.012	-0.300	0.064	2.27E-06	1040.412

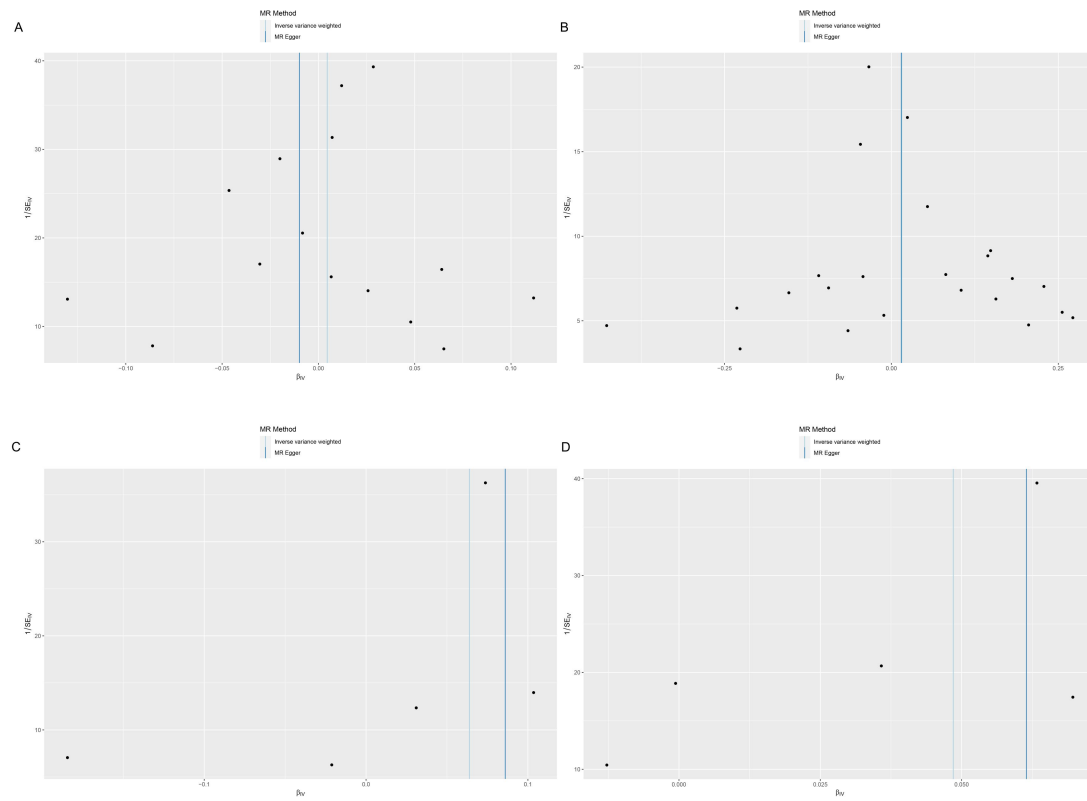
Supplemental Table 7. Mendelian randomization estimates for the causal effect of autoimmune diseases on sepsis risk.

Exposure	Methods	SNP	OR(95CI)	se	P-value	Cochran's Q statistic (p-value)	Egger intercept (pvalue)
AS	MR-egger	15	0.99(0.95-1.04)	0.02	0.68	10.15(0.68)	0.01(0.49)
	Weighted median	15	1.01(0.98-1.04)	0.02	0.54		
	Inverse variance Weighted	15	1.00(0.98-1.03)	0.01	0.70	10.65(0.71)	
	Simple mode	15	1.01(0.97-1.06)	0.02	0.63		
	Weighted mode	15	1.01(0.98-1.04)	0.02	0.60		
RA	MR-egger	23	1.01(0.94-1.09)	0.04	0.71	24.55(0.27)	0.00(0.98)
	Weighted median	23	0.99(0.92-1.05)	0.03	0.71		
	Inverse variance Weighted	23	1.02(0.97-1.07)	0.02	0.52	24.55(0.32)	
	Simple mode	23	0.99(0.88-1.12)	0.06	0.93		
	Weighted mode	23	0.99(0.93-1.06)	0.03	0.78		
SS	MR-egger	5	1.09(0.98-1.21)	0.05	0.21	3.69(0.30)	-0.01(0.68)
	Weighted median	5	1.07(1.02-1.13)	0.03	0.00		
	Inverse variance Weighted	5	1.07(1.02-1.12)	0.02	0.01	3.96(0.41)	
	Simple mode	5	1.06(0.97-1.15)	0.04	0.25		
	Weighted mode	5	1.08(1.02-1.13)	0.03	0.05		
SLE	MR-egger	5	1.06(0.97-1.16)	0.05	0.27	1.72(0.63)	-0.01(0.77)
	Weighted median	5	1.06(1.01-1.10)	0.02	0.01		
	Inverse variance Weighted	5	1.05(1.01-1.09)	0.02	0.01	1.82(0.77)	
	Simple mode	5	1.06(0.99-1.13)	0.03	0.17		
	Weighted mode	5	1.06(1.01-1.11)	0.02	0.07		

Supplemental Table 8. Mendelian randomization estimates for the causal effect of sepsis on autoimmune diseases risk.

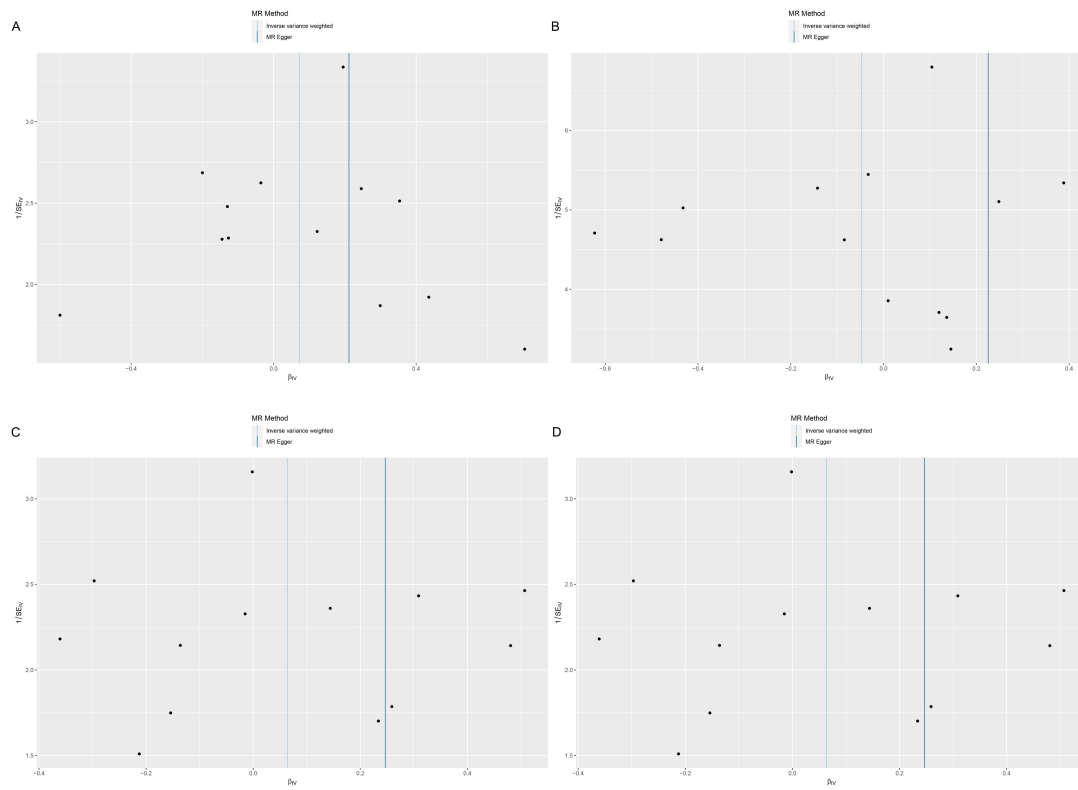
Outcome	Methods	SNP	OR(95CI)	se	P-value	Cochran's Q statistic (p-value)	Egger intercept (pvalue)
AS	MR-egger	13	1.24(0.77-1.98)	0.24	0.40	4.95(0.93)	-0.02(0.53)
	Weighted median	13	1.12(0.82-1.53)	0.16	0.47		
	Inverse variance Weighted	13	1.08(0.86-1.35)	0.12	0.54	5.38(0.94)	
	Simple mode	13	1.02(0.64-1.62)	0.24	0.94		
	Weighted mode	13	1.10(0.72-1.66)	0.21	0.67		
RA	MR-egger	13	1.25(0.93-1.70)	0.15	0.17	18.54(0.07)	-0.03(0.02)
	Weighted median	13	1.01(0.85-1.20)	0.09	0.92		
	Inverse variance Weighted	13	0.95(0.81-1.12)	0.08	0.57	25.37(0.01)	
	Simple mode	13	1.09(0.82-1.46)	0.15	0.56		
	Weighted mode	13	1.07(0.83-1.38)	0.13	0.62		
SS	MR-egger	13	1.28(0.77-2.12)	0.26	0.36	4.19(0.96)	-0.02(0.43)
	Weighted median	13	1.01(0.73-1.39)	0.16	0.95		
	Inverse variance Weighted	13	1.07(0.84-1.36)	0.12	0.61	4.85(0.96)	
	Simple mode	13	0.89(0.52-1.50)	0.27	0.66		
	Weighted mode	13	0.97(0.59-1.59)	0.25	0.91		
SLE	MR-egger	13	0.79(0.29-2.15)	0.51	0.66	17.71(0.09)	0.01(0.79)
	Weighted median	13	0.74(0.42-1.30)	0.29	0.29		
	Inverse variance Weighted	13	0.89(0.56-1.42)	0.24	0.63	17.83(0.12)	
	Simple mode	13	0.60(0.22-1.62)	0.51	0.33		
	Weighted mode	13	0.60(0.24-1.53)	0.48	0.31		

Supplemental Figure 1. Funnel plots for autoimmune diseases and sepsis.



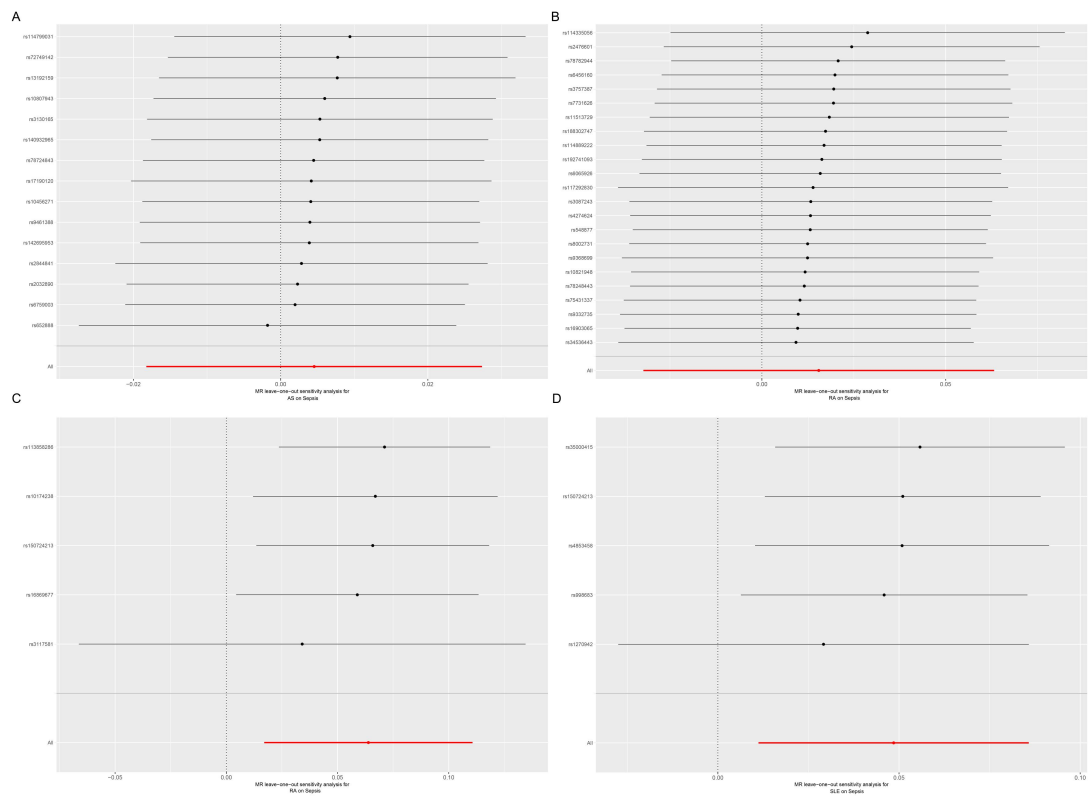
A, ankylosing spondylitis (AS); B, rheumatoid arthritis (RA); C, sicca syndrome (SS); D, systemic lupus erythematosus (SLE)

Supplemental Figure 2. Funnel plots for sepsis and autoimmune diseases.



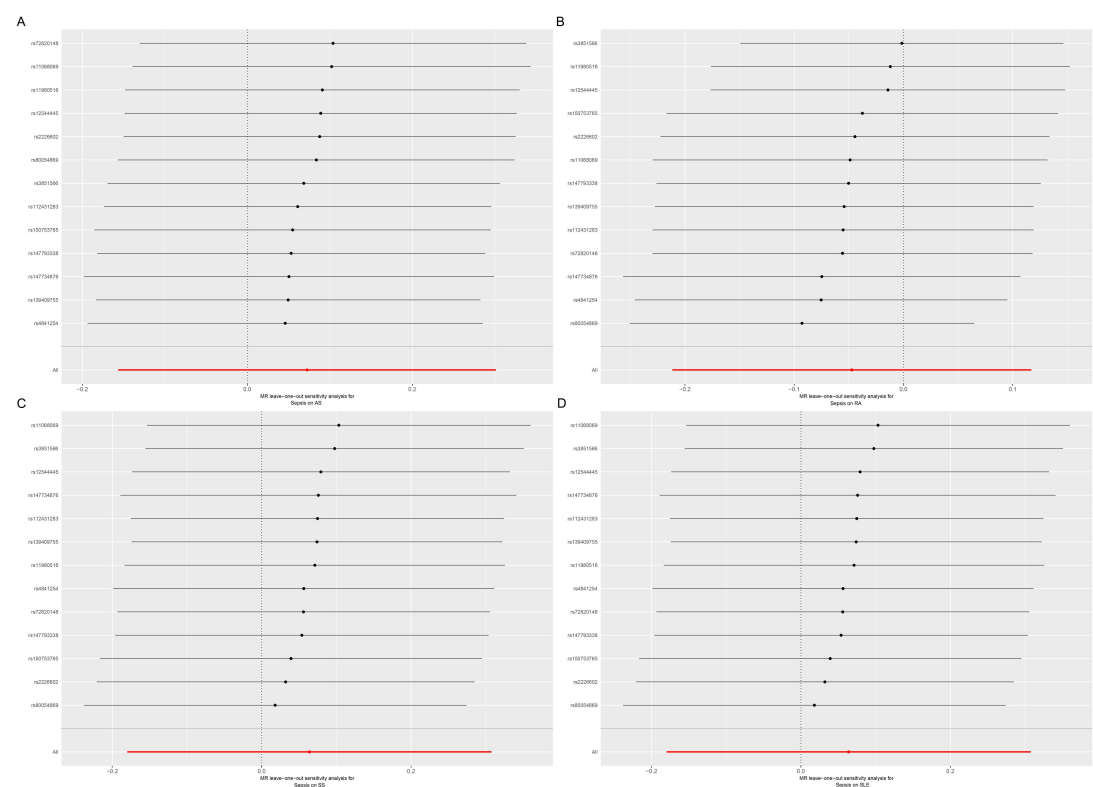
A, ankylosing spondylitis (AS); B, rheumatoid arthritis (RA); C, sicca syndrome (SS); D, systemic lupus erythematosus (SLE)

Supplemental Figure 3. Leave-one-out analysis for autoimmune diseases and sepsis.



A, ankylosing spondylitis (AS); B, rheumatoid arthritis (RA); C, sicca syndrome (SS); D, systemic lupus erythematosus (SLE)

Supplemental Figure 4. Leave-one-out analysis for sepsis and autoimmune diseases.



A, ankylosing spondylitis (AS); B, rheumatoid arthritis (RA); C, sicca syndrome (SS); D, systemic lupus erythematosus (SLE)