

Investigating Pleiotropy Between Depression and Autoimmune Diseases Using the UK Biobank

Supplement 1

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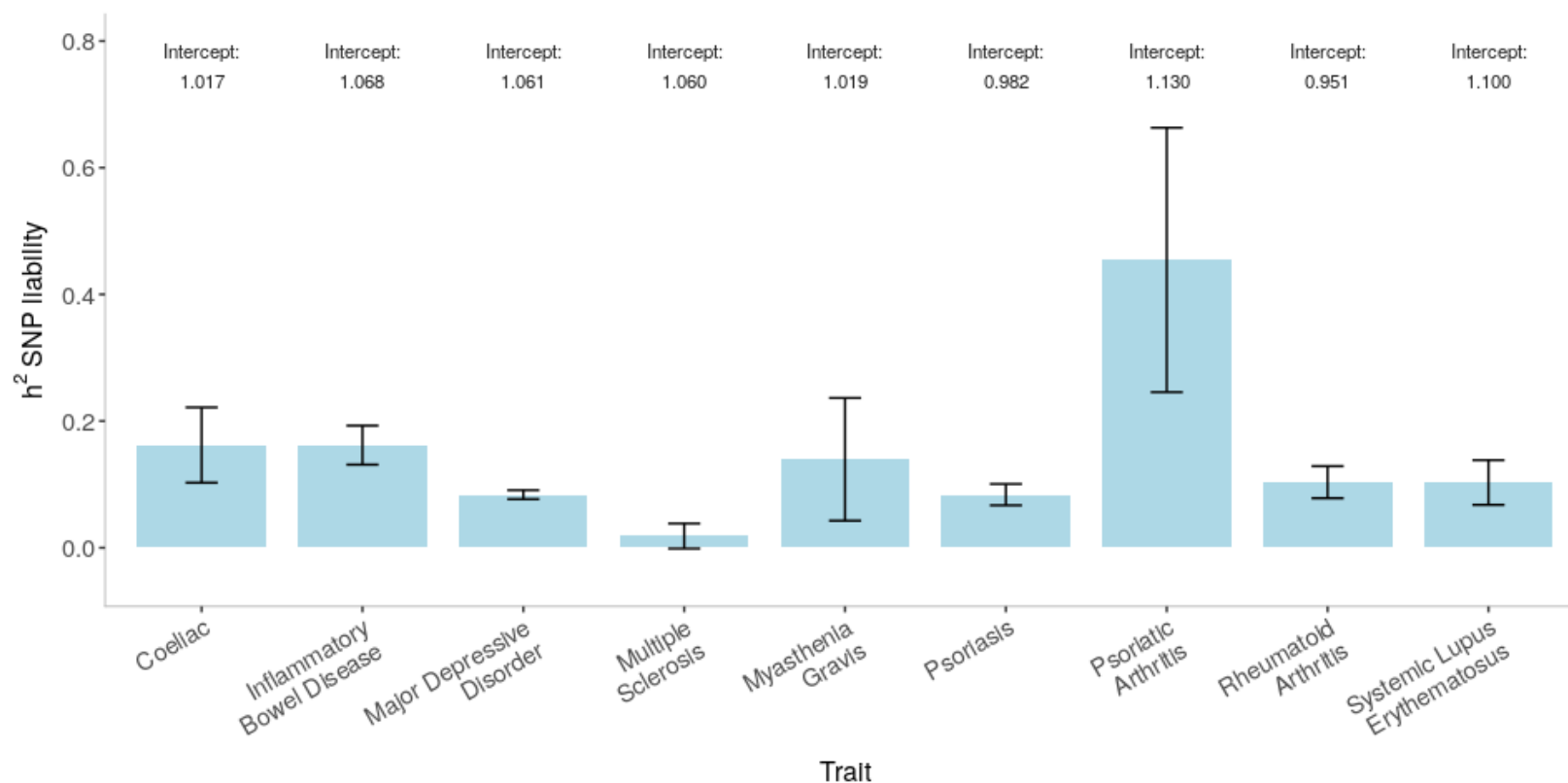
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1 Power calculations

1.1 SNP-based heritability estimates

Estimates of SNP-based heritability are required for power calculations using the AVENGEME software. We estimated SNP-based heritability for depression and the eight autoimmune diseases for which summary statistics were publicly available (summary statistics described in Table 1 of the main paper), and the results are shown in Supplementary Figure 1.

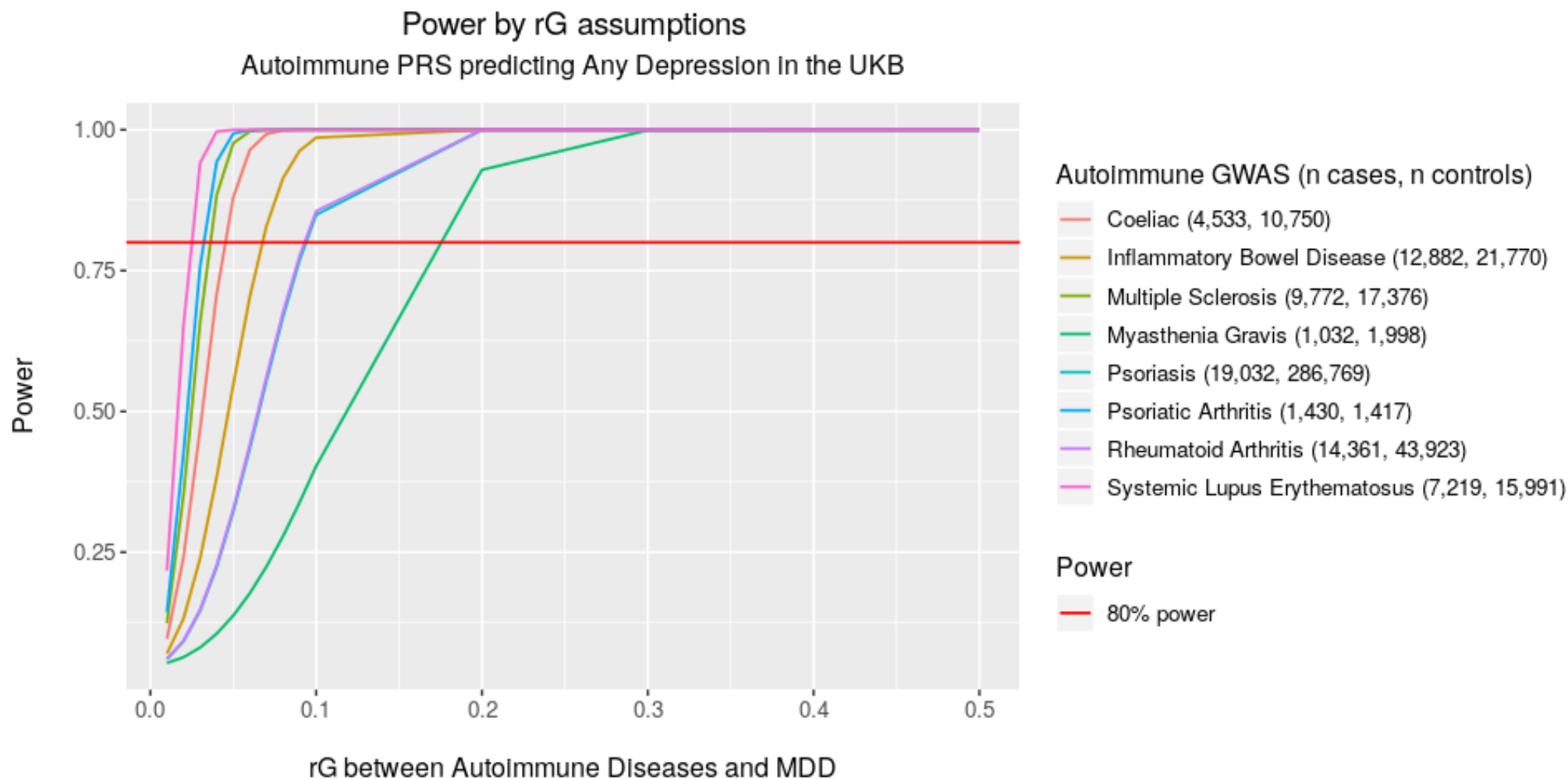


Supplementary Figure S1: SNP-based heritability (h^2_{SNP}) of traits with publicly available summary statistics. Estimated using LDSC after removing variants within the MHC from summary statistics. Transformed to liability scale using population prevalence estimates: Coeliac=1%, IBD=0.5%, MDD=15%, MS=0.1%, MG=0.02%, Psoriasis=2%, PsA=0.5%, RA=1%, SLE=0.1%. Error bars: 95% CIs. Intercepts shown atop bars.

1.2 Power estimates for autoimmune PRS predicting any depression in the UKB

Supplementary Table S1: AVENGEME inputs for calculating power to detect association between PRS for autoimmune diseases and ‘any’ depression case status in the UKB.

BASE GWAS							TARGET TRAIT				
Trait	Total N (case+control)	h^2_{SNP} excluding MHC	Population prevalence	Sample prevalence	Optimal p- value threshold (P_T)	No. SNPs used to construct PRS at (P_T)	Trait	Total N (case+control)	h^2_{SNP} excluding MHC	Population prevalence	Sample prevalence
Coeliac	15,283	16.21%	1.00%	30%	0.200	12,430	Any Depression	297,627	8.38%	15%	22%
Inflammatory Bowel Disease	34,652	16.20%	0.50%	37%	1.000	80,201	Any Depression	297,627	8.38%	15%	22%
Multiple Sclerosis	27,148	1.85%	0.10%	36%	0.050	3,240	Any Depression	297,627	8.38%	15%	22%
Myasthenia Gravis	3,030	13.96%	0.02%	34%	0.300	56,894	Any Depression	297,627	8.38%	15%	22%
Psoriasis	305,801	8.38%	2.00%	6%	1.000	136,084	Any Depression	297,627	8.38%	15%	22%
Psoriatic Arthritis	2,847	45.44%	0.50%	50%	0.050	4,666	Any Depression	297,627	8.38%	15%	22%
Rheumatoid Arthritis	58,284	10.35%	1.00%	25%	1.000	118,649	Any Depression	297,627	8.38%	15%	22%
Systemic Lupus Erythematosus	23,210	10.30%	0.10%	31%	0.001	836	Any Depression	297,627	8.38%	15%	22%

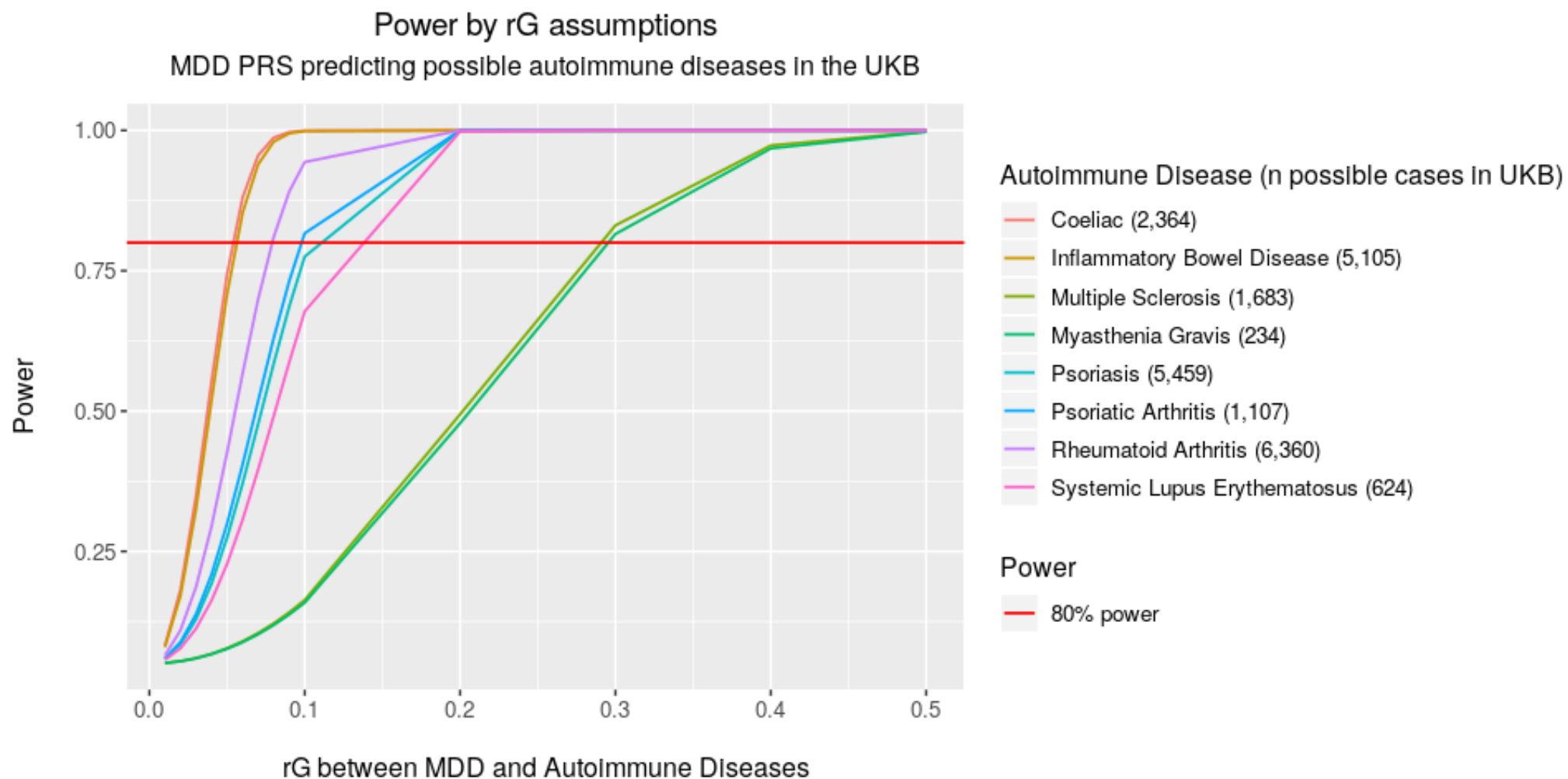


Supplementary Figure S2: Power to detect associations between autoimmune PRS and any depression case status in UKB across different levels of genetic correlation (r_G).

1.3 Power estimates for depression PRS predicting autoimmune disease in the UKB

Supplementary Table S2: AVENGEME inputs for calculating power to detect association between PRS for Major Depressive Disorder (MDD) and possible autoimmune diseases in UKB.

BASE GWAS							TARGET TRAIT				
Trait	Total N (case+control)	h^2_{SNP} excluding MHC	Population prevalence	Sample prevalence	Optimal p- value threshold (P_T)	No. SNPs used to construct PRS at (P_T)	Trait	Total N (case+control)	h^2_{SNP} excluding MHC	Population prevalence	Sample prevalence
MDD	431,394	8.38%	15%	27%	0.001	1,123	Coeliac	326,438	16.21%	1.00%	0.72%
MDD	431,394	8.38%	15%	27%	0.300	48,852	Inflammatory Bowel Disease	329,179	16.20%	0.50%	1.55%
MDD	431,394	8.38%	15%	27%	0.500	67,956	Multiple Sclerosis	325,757	1.85%	0.10%	0.52%
MDD	431,394	8.38%	15%	27%	1.000	99,216	Myasthenia Gravis	324,308	13.96%	0.02%	0.07%
MDD	431,394	8.38%	15%	27%	0.500	67,956	Psoriasis	329,533	8.38%	2.00%	1.66%
MDD	431,394	8.38%	15%	27%	1.000	99,216	Psoriatic Arthritis	325,181	45.44%	0.50%	0.34%
MDD	431,394	8.38%	15%	27%	0.500	67,956	Rheumatoid Arthritis	330,434	10.35%	1.00%	1.92%
MDD	431,394	8.38%	15%	27%	0.050	14,137	Systemic Lupus Erythematosus	324,698	10.30%	0.10%	0.19%

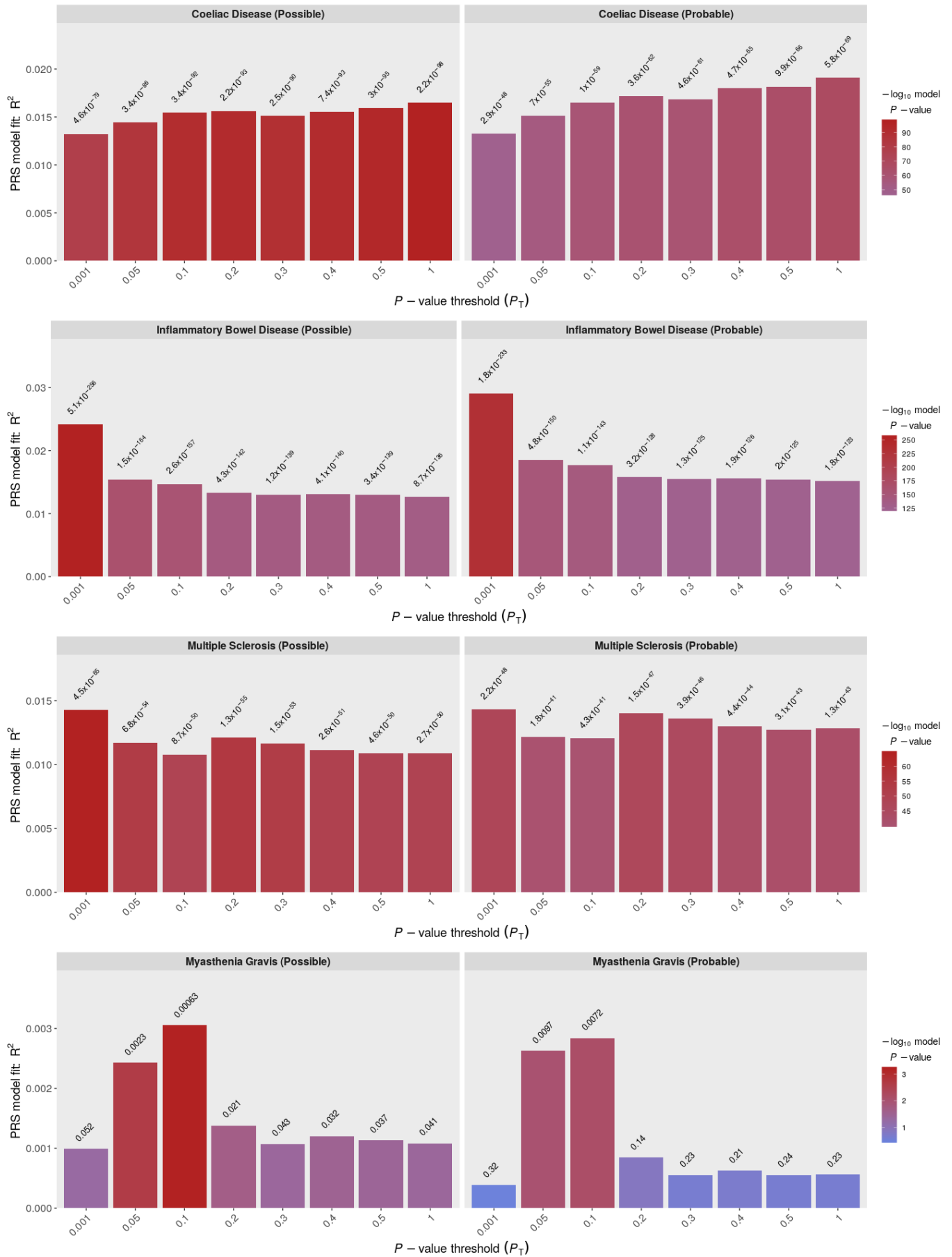


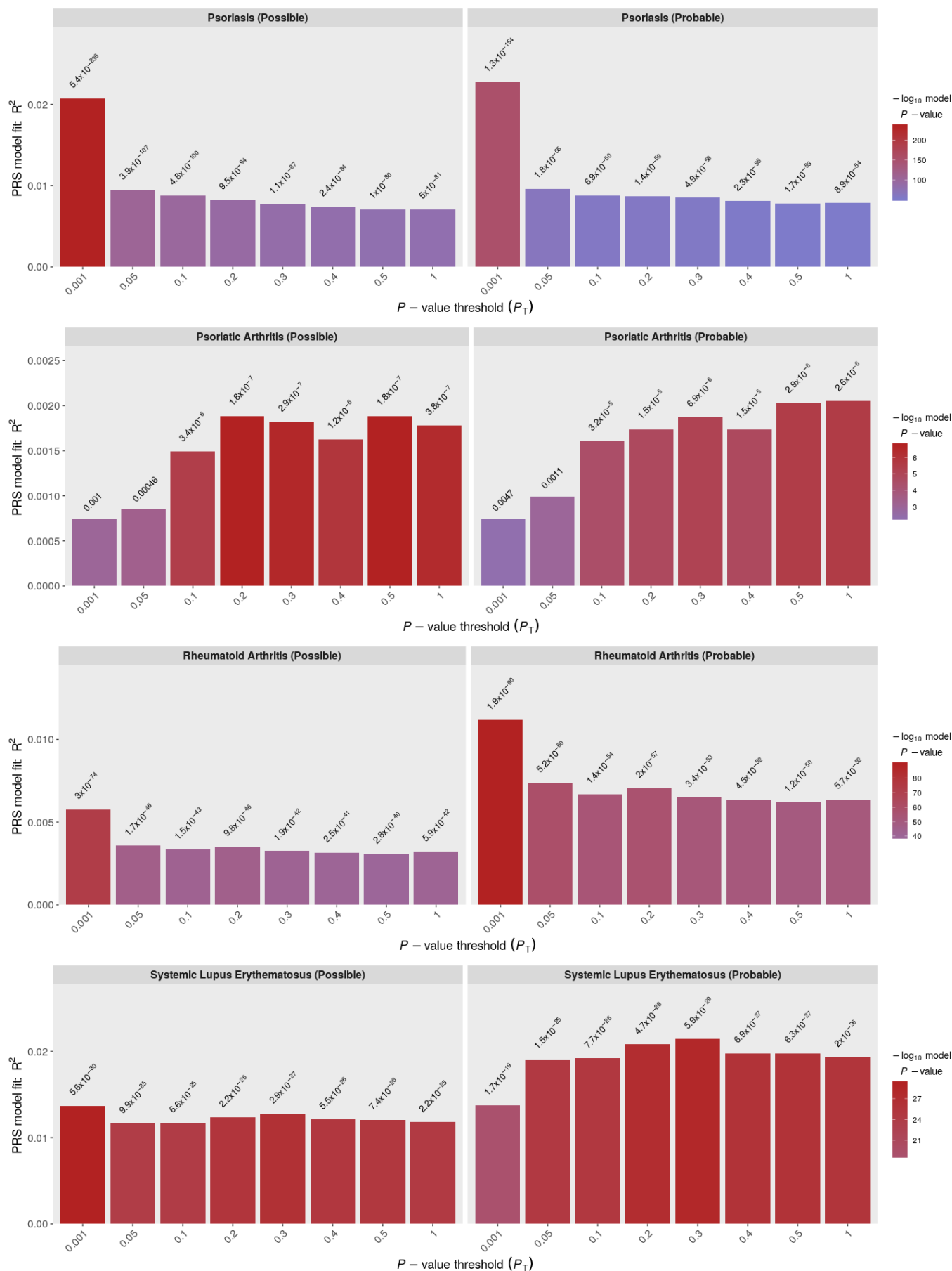
Supplementary Figure S3: Power to detect associations between MDD PRS and possible autoimmune case status in UKB across different levels of genetic correlation (rG).

2 Polygenic risk score analyses

Supplementary Table S3: Within-trait PRS - associations between PRS for autoimmune diseases and autoimmune case/control status (possible/probable) at optimal P_T .

Base GWAS	Target Trait in UKB	Optimal p-value threshold (P_T)	No. SNPs used to construct PRS at (P_T)	Population Prevalence used to convert to liability R^2	Unadjusted Variance explained (Observed R^2)	Adjusted Variance explained (Liability R^2)	Coefficient	Standard Error	P-value
Coeliac	Coeliac (Possible)	1.000	42,731	1.00%	1.65%	2.60%	0.46	0.022	2e-98
Coeliac	Coeliac (Probable)	1.000	42,731	1.00%	1.91%	3.37%	0.52	0.030	6e-69
Inflammatory Bowel Disease	Inflammatory Bowel Disease (Possible)	0.001	676	0.50%	2.41%	2.77%	0.49	0.014	5e-256
Inflammatory Bowel Disease	Inflammatory Bowel Disease (Probable)	0.001	676	0.50%	2.90%	3.62%	0.56	0.017	2e-233
Multiple Sclerosis	Multiple Sclerosis (Possible)	0.001	230	0.10%	1.42%	1.53%	0.42	0.025	4e-65
Multiple Sclerosis	Multiple Sclerosis (Probable)	0.001	230	0.10%	1.43%	1.64%	0.43	0.030	2e-48
Myasthenia Gravis	Myasthenia Gravis (Possible)	0.100	22,895	0.02%	0.31%	0.35%	0.23	0.066	6e-04
Myasthenia Gravis	Myasthenia Gravis (Probable)	0.100	22,895	0.02%	0.28%	0.34%	0.23	0.084	7e-03
Psoriasis	Psoriasis (Possible)	0.001	637	2.00%	2.08%	3.24%	0.44	0.013	5e-236
Psoriasis	Psoriasis (Probable)	0.001	637	2.00%	2.27%	4.11%	0.49	0.019	1e-154
Psoriatic Arthritis	Psoriatic Arthritis (Possible)	0.200	14,198	0.50%	0.19%	0.29%	0.27	0.052	2e-07
Psoriatic Arthritis	Psoriatic Arthritis (Probable)	1.000	45,914	0.50%	0.20%	0.34%	0.31	0.066	3e-06
Rheumatoid Arthritis	Rheumatoid Arthritis (Possible)	0.001	550	1.00%	0.58%	0.73%	0.23	0.013	3e-74
Rheumatoid Arthritis	Rheumatoid Arthritis (Probable)	0.001	550	1.00%	1.12%	1.63%	0.34	0.017	2e-90
Systemic Lupus Erythematosus	Systemic Lupus Erythematosus (Possible)	0.001	836	0.10%	1.37%	1.73%	0.42	0.037	6e-30
Systemic Lupus Erythematosus	Systemic Lupus Erythematosus (Probable)	0.300	74,372	0.10%	2.14%	2.92%	0.58	0.052	6e-29

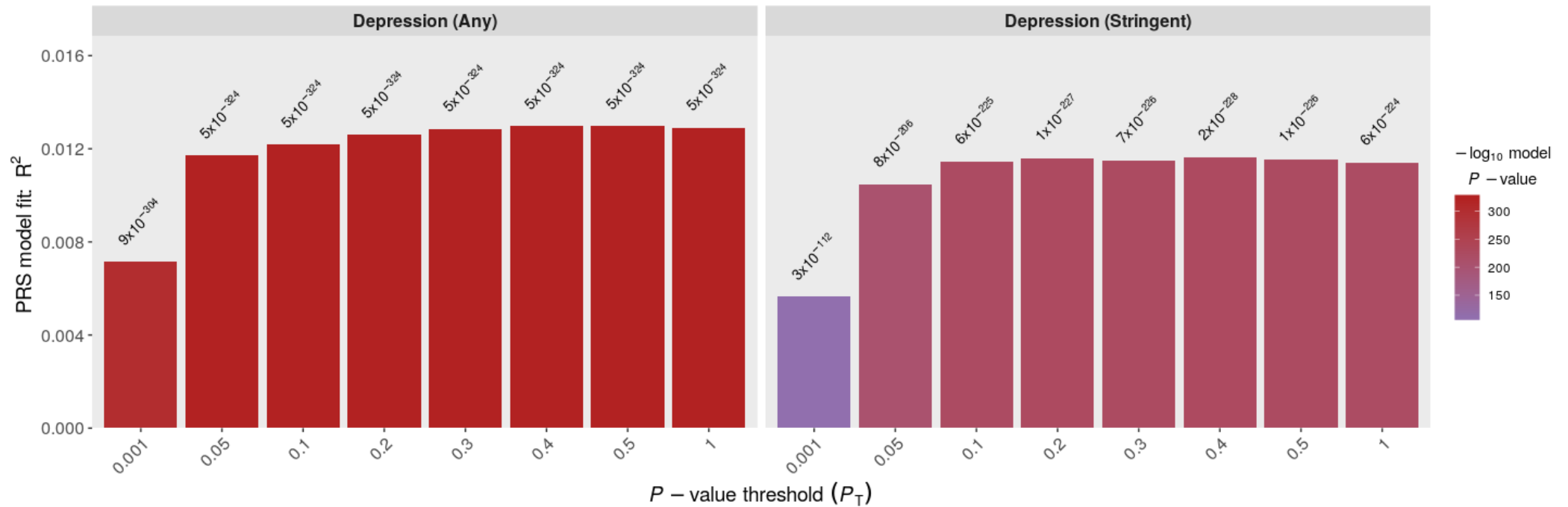




Supplementary Figure S4: Within-trait PRS - associations between PRS for autoimmune diseases and autoimmune case/control status (possible/probable) across eight P_T. Y-axis shows unadjusted R² (observed-scale).

Supplementary Table S4: Within-trait PRS - associations between PRS for MDD and depression case/control status (any/stringent) at optimal P_T .

Base GWAS	Target Trait in UKB	Optimal p-value threshold (P_T)	No. SNPs used to construct PRS at (P_T)	Population Prevalence used to convert to liability R^2	Unadjusted Variance explained (Observed R^2)	Adjusted Variance explained (Liability R^2)	Coefficient	Standard Error	P-value
Major Depressive Disorder	Depression (Any)	0.4	59,001	15%	1.30%	1.48%	0.23	0.005	<5e-324
Major Depressive Disorder	Depression (Stringent)	0.4	59,001	15%	1.16%	2.23%	0.28	0.009	2e-228

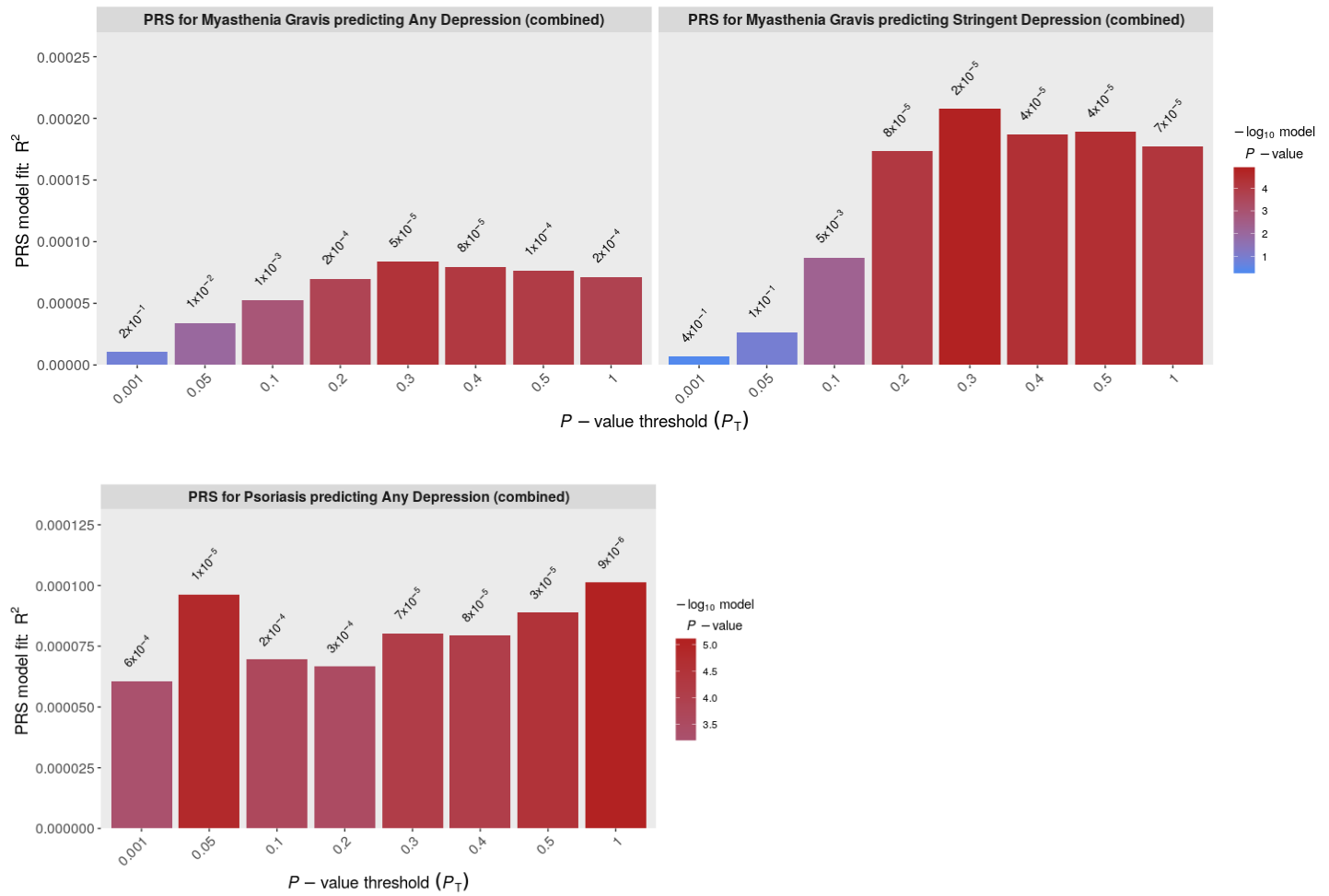


Supplementary Figure S5: Within-trait PRS - associations between PRS for MDD and depression case/control status (any/stringent) across eight P_T . Y-axis shows unadjusted R^2 (observed-scale). Note: p-value for MDD PRS predicting Depression (Any) = 0 for thresholds 0.05 to 1 due to limit on the smallest number on the R platform (5e-324).

Supplementary Table S5: Cross-trait PRS - associations between PRS for autoimmune diseases and depression case/control status (any/stringent) in men and women at optimal P_T . Associations with p-values < 7.1×10^{-5} , meeting Bonferroni correction, highlighted in red.

Base GWAS	Target Trait in UKB	Optimal p-value threshold (P_T)	No. SNPs used to construct PRS at (P_T)	Population Prevalence used to convert to liability R^2	Unadjusted Variance explained (Observed R^2)	Adjusted Variance explained (Liability R^2)	Coefficient	Standard Error	P-value
Coeliac	Any (combined)	0.200	12,430	15%	0.0021%	0.0024%	0.009	0.005	4.4e-02
Coeliac	Any (female)	0.200	12,430	15%	0.0006%	0.0007%	0.005	0.006	4.1e-01
Coeliac	Any (male)	0.050	3,881	15%	0.0045%	0.0060%	0.015	0.008	5.4e-02
Coeliac	Stringent (combined)	0.200	12,430	15%	0.0013%	0.0026%	0.010	0.009	2.7e-01
Coeliac	Stringent (female)	0.001	186	15%	0.0017%	0.0029%	0.010	0.011	3.4e-01
Coeliac	Stringent (male)	0.001	186	15%	0.0034%	0.0075%	-0.016	0.015	2.7e-01
Inflammatory Bowel Disease	Any (combined)	1.000	80,201	15%	0.0051%	0.0058%	0.014	0.005	1.6e-03
Inflammatory Bowel Disease	Any (female)	1.000	80,201	15%	0.0047%	0.0049%	0.013	0.006	2.4e-02
Inflammatory Bowel Disease	Any (male)	1.000	80,201	15%	0.0079%	0.0106%	0.019	0.008	1.0e-02
Inflammatory Bowel Disease	Stringent (combined)	0.300	38,677	15%	0.0173%	0.0333%	0.035	0.009	7.9e-05
Inflammatory Bowel Disease	Stringent (female)	0.050	10,082	15%	0.0238%	0.0406%	0.038	0.011	4.4e-04
Inflammatory Bowel Disease	Stringent (male)	1.000	80,201	15%	0.0230%	0.0510%	0.043	0.015	4.2e-03
Lupus	Any (combined)	0.001	836	15%	0.0029%	0.0034%	-0.011	0.004	1.7e-02
Lupus	Any (female)	0.001	836	15%	0.0026%	0.0027%	-0.010	0.006	9.4e-02
Lupus	Any (male)	0.001	836	15%	0.0056%	0.0075%	-0.016	0.007	3.1e-02
Lupus	Stringent (combined)	0.001	836	15%	0.0018%	0.0035%	-0.011	0.009	2.0e-01
Lupus	Stringent (female)	0.001	836	15%	0.0038%	0.0066%	-0.015	0.011	1.6e-01
Lupus	Stringent (male)	0.050	18,572	15%	0.0020%	0.0045%	0.013	0.015	3.9e-01
Multiple Sclerosis	Any (combined)	0.050	3,240	15%	0.0052%	0.0059%	0.014	0.005	1.5e-03
Multiple Sclerosis	Any (female)	0.050	3,240	15%	0.0066%	0.0068%	0.015	0.006	7.4e-03
Multiple Sclerosis	Any (male)	0.050	3,240	15%	0.0058%	0.0078%	0.016	0.007	2.8e-02
Multiple Sclerosis	Stringent (combined)	0.050	3,240	15%	0.0033%	0.0063%	0.015	0.009	8.6e-02
Multiple Sclerosis	Stringent (female)	0.100	5,974	15%	0.0087%	0.0148%	0.023	0.011	3.4e-02
Multiple Sclerosis	Stringent (male)	0.050	3,240	15%	0.0024%	0.0053%	0.014	0.015	3.6e-01
Myasthenia Gravis	Any (combined)	0.300	56,894	15%	0.0084%	0.0096%	0.018	0.005	5.2e-05
Myasthenia Gravis	Any (female)	0.200	40,875	15%	0.0127%	0.0131%	0.022	0.006	2.1e-04
Myasthenia Gravis	Any (male)	0.300	56,894	15%	0.0073%	0.0098%	0.019	0.008	1.4e-02
Myasthenia Gravis	Stringent (combined)	0.300	56,894	15%	0.0208%	0.0399%	0.038	0.009	1.6e-05
Myasthenia Gravis	Stringent (female)	0.300	56,894	15%	0.0164%	0.0279%	0.032	0.011	3.5e-03
Myasthenia Gravis	Stringent (male)	0.300	56,894	15%	0.0384%	0.0849%	0.055	0.015	2.2e-04

Base GWAS	Target Trait in UKB	Optimal p-value threshold (P_T)	No. SNPs used to construct PRS at (P_T)	Population Prevalence used to convert to liability R^2	Unadjusted Variance explained (Observed R^2)	Adjusted Variance explained (Liability R^2)	Coefficient	Standard Error	P-value
Psoriasis	Any (combined)	1.000	136,084	15%	0.0101%	0.0116%	0.020	0.005	8.7e-06
Psoriasis	Any (female)	1.000	136,084	15%	0.0124%	0.0128%	0.021	0.006	2.5e-04
Psoriasis	Any (male)	0.050	13,899	15%	0.0133%	0.0178%	0.025	0.007	8.9e-04
Psoriasis	Stringent (combined)	0.050	13,899	15%	0.0126%	0.0243%	0.029	0.009	7.6e-04
Psoriasis	Stringent (female)	1.000	136,084	15%	0.0177%	0.0303%	0.033	0.011	2.4e-03
Psoriasis	Stringent (male)	0.050	13,899	15%	0.0093%	0.0207%	0.027	0.015	6.8e-02
Psoriatic Arthritis	Any (combined)	0.050	4,666	15%	0.0013%	0.0015%	-0.010	0.007	1.1e-01
Psoriatic Arthritis	Any (female)	1.000	45,914	15%	0.0026%	0.0027%	0.018	0.011	9.2e-02
Psoriatic Arthritis	Any (male)	0.100	8,135	15%	0.0058%	0.0077%	-0.026	0.012	2.8e-02
Psoriatic Arthritis	Stringent (combined)	0.001	211	15%	0.0018%	0.0036%	0.012	0.009	2.0e-01
Psoriatic Arthritis	Stringent (female)	1.000	45,914	15%	0.0086%	0.0147%	0.042	0.020	3.4e-02
Psoriatic Arthritis	Stringent (male)	0.100	8,135	15%	0.0081%	0.0178%	-0.039	0.023	9.1e-02
Rheumatoid Arthritis	Any (combined)	1.000	118,649	15%	0.0006%	0.0007%	0.005	0.005	2.6e-01
Rheumatoid Arthritis	Any (female)	0.001	550	15%	0.0011%	0.0011%	-0.006	0.006	2.8e-01
Rheumatoid Arthritis	Any (male)	1.000	118,649	15%	0.0059%	0.0079%	0.017	0.008	2.7e-02
Rheumatoid Arthritis	Stringent (combined)	1.000	118,649	15%	0.0095%	0.0183%	0.025	0.009	3.4e-03
Rheumatoid Arthritis	Stringent (female)	0.001	550	15%	0.0047%	0.0080%	0.017	0.011	1.2e-01
Rheumatoid Arthritis	Stringent (male)	1.000	118,649	15%	0.0232%	0.0514%	0.043	0.015	4.1e-03



Supplementary Figure S6: Cross-trait PRS –associations between PRS for autoimmune diseases and depression case/control status (any/stringent) in men and women across eight P_T . Y-axis shows unadjusted R^2 (observed-scale). Bar charts are shown for significant results only.

Supplementary Table S6: Cross-trait PRS - associations between PRS for MDD and autoimmune case/control status (possible/probable) in men and women at optimal P_T . MDD = Major Depressive Disorder. Associations with p-values $< 7.1 \times 10^{-5}$, meeting Bonferroni correction, highlighted in red. Sex*PRS p-value – estimated where significant associations were observed in sex-specific analyses; tested for an interaction between sex and PRS in the full sample (Phenotype \sim sex + PRS + sex*PRS + covariates).

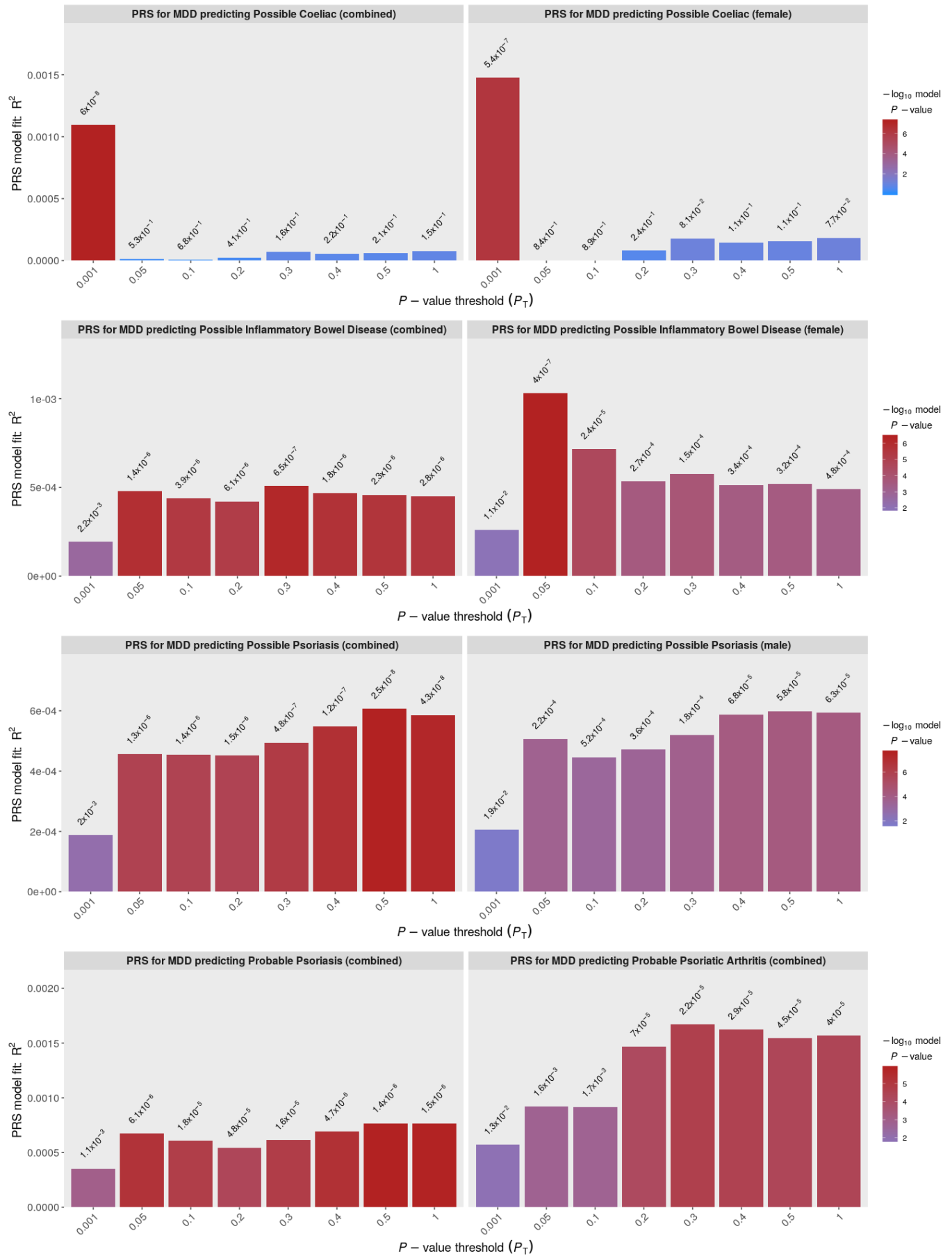
Base GWAS	Target Trait in UKB	Optimal p-value threshold (P_T)	No. SNPs used to construct PRS at (P_T)	Population Prevalence used to convert to liability R^2	Unadjusted Variance explained (Observed R^2)	Adjusted Variance explained (Liability R^2)	Coefficient	Standard Error	P-value	Sex*PRS p-value
MDD	Ankylosing Spondylitis, Possible (combined)	0.050	14,137	0.55%	0.035%	0.054%	0.067	0.027	1.4e-02	NA
MDD	Ankylosing Spondylitis, Possible (female)	0.001	1,123	0.55%	0.130%	0.210%	0.132	0.044	2.8e-03	NA
MDD	Ankylosing Spondylitis, Possible (male)	1.000	99,216	0.55%	0.043%	0.063%	0.072	0.035	3.9e-02	NA
MDD	Ankylosing Spondylitis, Probable (combined)	0.001	1,123	0.55%	0.003%	0.006%	-0.022	0.049	6.5e-01	NA
MDD	Ankylosing Spondylitis, Probable (female)	0.400	59,001	0.55%	0.032%	0.064%	-0.074	0.096	4.5e-01	NA
MDD	Ankylosing Spondylitis, Probable (male)	0.001	1,123	0.55%	0.005%	0.008%	-0.026	0.057	6.5e-01	NA
MDD	Autoimmune Thyroid Disease, Possible (combined)	0.500	67,956	2.00%	0.078%	0.173%	0.104	0.034	2.6e-03	NA
MDD	Autoimmune Thyroid Disease, Possible (female)	0.500	67,956	2.00%	0.075%	0.154%	0.098	0.037	8.8e-03	NA
MDD	Autoimmune Thyroid Disease, Possible (male)	0.500	67,956	2.00%	0.110%	0.278%	0.133	0.087	1.3e-01	NA
MDD	Autoimmune Thyroid Disease, Probable (combined)	0.400	59,001	2.00%	0.083%	0.193%	0.110	0.041	7.3e-03	NA
MDD	Autoimmune Thyroid Disease, Probable (female)	0.400	59,001	2.00%	0.082%	0.178%	0.105	0.044	1.7e-02	NA
MDD	Autoimmune Thyroid Disease, Probable (male)	0.001	1,123	2.00%	0.138%	0.363%	-0.153	0.108	1.5e-01	NA
MDD	Coeliac, Possible (combined)	0.001	1,123	1.00%	0.109%	0.172%	-0.112	0.021	6.0e-08	NA
MDD	Coeliac, Possible (female)	0.001	1,123	1.00%	0.147%	0.221%	-0.127	0.025	5.4e-07	0.33
MDD	Coeliac, Possible (male)	0.001	1,123	1.00%	0.054%	0.091%	-0.082	0.036	2.3e-02	NA
MDD	Coeliac, Probable (combined)	0.001	1,123	1.00%	0.059%	0.104%	-0.087	0.028	2.0e-03	NA
MDD	Coeliac, Probable (female)	0.001	1,123	1.00%	0.066%	0.110%	-0.090	0.034	8.7e-03	NA
MDD	Coeliac, Probable (male)	0.001	1,123	1.00%	0.048%	0.090%	-0.081	0.050	1.1e-01	NA

Base GWAS	Target Trait in UKB	Optimal p-value threshold (P_T)	No. SNPs used to construct PRS at (P_T)	Population Prevalence used to convert to liability R^2	Unadjusted Variance explained (Observed R^2)	Adjusted Variance explained (Liability R^2)	Coefficient	Standard Error	P-value	Sex*PRS p-value
MDD	Inflammatory Bowel Disease, Possible (combined)	0.300	48,852	0.50%	0.051%	0.058%	0.071	0.014	6.5e-07	NA
MDD	Inflammatory Bowel Disease, Possible (female)	0.050	14,137	0.50%	0.103%	0.119%	0.100	0.020	4.0e-07	0.02
MDD	Inflammatory Bowel Disease, Possible (male)	0.300	48,852	0.50%	0.044%	0.051%	0.066	0.020	1.2e-03	NA
MDD	Inflammatory Bowel Disease, Probable (combined)	0.050	14,137	0.50%	0.029%	0.036%	0.055	0.017	1.2e-03	NA
MDD	Inflammatory Bowel Disease, Probable (female)	0.050	14,137	0.50%	0.083%	0.104%	0.094	0.024	9.0e-05	NA
MDD	Inflammatory Bowel Disease, Probable (male)	1.000	99,216	0.50%	0.014%	0.017%	0.038	0.024	1.1e-01	NA
MDD	Multiple Sclerosis, Possible (combined)	0.500	67,956	0.10%	0.047%	0.051%	0.076	0.025	1.9e-03	NA
MDD	Multiple Sclerosis, Possible (female)	0.001	1,123	0.10%	0.058%	0.059%	0.082	0.029	4.4e-03	NA
MDD	Multiple Sclerosis, Possible (male)	0.050	14,137	0.10%	0.115%	0.136%	0.125	0.047	8.1e-03	NA
MDD	Multiple Sclerosis, Probable (combined)	1.000	99,216	0.10%	0.064%	0.073%	0.091	0.030	2.0e-03	NA
MDD	Multiple Sclerosis, Probable (female)	0.001	1,123	0.10%	0.081%	0.088%	0.100	0.035	3.9e-03	NA
MDD	Multiple Sclerosis, Probable (male)	0.050	14,137	0.10%	0.160%	0.201%	0.152	0.057	7.6e-03	NA
MDD	Myasthenia Gravis, Possible (combined)	1.000	99,216	0.02%	0.045%	0.052%	0.087	0.066	1.9e-01	NA
MDD	Myasthenia Gravis, Possible (female)	1.000	99,216	0.02%	0.178%	0.202%	0.171	0.088	5.1e-02	NA
MDD	Myasthenia Gravis, Possible (male)	0.100	22,831	0.02%	0.014%	0.016%	-0.048	0.099	6.3e-01	NA
MDD	Myasthenia Gravis, Probable (combined)	0.001	1,123	0.02%	0.014%	0.017%	0.050	0.082	5.5e-01	NA
MDD	Myasthenia Gravis, Probable (female)	1.000	99,216	0.02%	0.075%	0.092%	0.115	0.119	3.3e-01	NA
MDD	Myasthenia Gravis, Probable (male)	1.000	99,216	0.02%	0.071%	0.085%	-0.112	0.116	3.4e-01	NA
MDD	Pernicious Anemia, Possible (combined)	0.050	14,137	0.10%	0.035%	0.038%	0.066	0.025	9.4e-03	NA

Base GWAS	Target Trait in UKB	Optimal p-value threshold (P_T)	No. SNPs used to construct PRS at (P_T)	Population Prevalence used to convert to liability R^2	Unadjusted Variance explained (Observed R^2)	Adjusted Variance explained (Liability R^2)	Coefficient	Standard Error	P-value	Sex*PRS p-value
MDD	Pernicious Anemia, Possible (female)	0.200	36,975	0.10%	0.030%	0.031%	0.059	0.030	5.0e-02	NA
MDD	Pernicious Anemia, Possible (male)	0.500	67,956	0.10%	0.059%	0.070%	0.090	0.048	6.0e-02	NA
MDD	Pernicious Anemia, Probable (combined)	0.050	14,137	0.10%	0.113%	0.150%	0.131	0.049	7.2e-03	NA
MDD	Pernicious Anemia, Probable (female)	0.100	22,831	0.10%	0.064%	0.082%	0.097	0.057	9.3e-02	NA
MDD	Pernicious Anemia, Probable (male)	0.050	14,137	0.10%	0.380%	0.544%	0.250	0.093	6.9e-03	NA
MDD	Polymyalgia Rheumatica/GCA, Possible (combined)	0.200	36,975	0.85%	0.058%	0.095%	0.085	0.025	6.8e-04	NA
MDD	Polymyalgia Rheumatica/GCA, Possible (female)	0.200	36,975	0.85%	0.114%	0.177%	0.116	0.031	1.5e-04	NA
MDD	Polymyalgia Rheumatica/GCA, Possible (male)	0.001	1,123	0.85%	0.007%	0.012%	0.030	0.043	4.8e-01	NA
MDD	Polymyalgia Rheumatica/GCA, Probable (combined)	0.200	36,975	0.85%	0.074%	0.132%	0.100	0.034	2.8e-03	NA
MDD	Polymyalgia Rheumatica/GCA, Probable (female)	0.200	36,975	0.85%	0.110%	0.189%	0.120	0.041	3.3e-03	NA
MDD	Polymyalgia Rheumatica/GCA, Probable (male)	0.001	1,123	0.85%	0.113%	0.214%	0.128	0.059	3.0e-02	NA
MDD	Psoriasis, Possible (combined)	0.500	67,956	2.00%	0.061%	0.095%	0.076	0.014	2.5e-08	NA
MDD	Psoriasis, Possible (female)	0.500	67,956	2.00%	0.062%	0.100%	0.079	0.020	1.0e-04	NA
MDD	Psoriasis, Possible (male)	0.500	67,956	2.00%	0.060%	0.091%	0.075	0.019	5.8e-05	0.86
MDD	Psoriasis, Probable (combined)	0.500	67,956	2.00%	0.077%	0.139%	0.093	0.019	1.4e-06	NA
MDD	Psoriasis, Probable (female)	0.500	67,956	2.00%	0.118%	0.223%	0.117	0.030	7.9e-05	NA
MDD	Psoriasis, Probable (male)	0.050	14,137	2.00%	0.061%	0.106%	0.081	0.025	1.3e-03	NA
MDD	Psoriatic Arthritis, Possible (combined)	1.000	99,216	0.50%	0.105%	0.163%	0.118	0.030	9.7e-05	NA
MDD	Psoriatic Arthritis, Possible (female)	1.000	99,216	0.50%	0.159%	0.248%	0.145	0.043	6.5e-04	NA
MDD	Psoriatic Arthritis, Possible (male)	0.001	1,123	0.50%	0.069%	0.107%	0.095	0.043	2.6e-02	NA
MDD	Psoriatic Arthritis, Probable (combined)	0.300	48,852	0.50%	0.167%	0.274%	0.153	0.036	2.2e-05	NA

Base GWAS	Target Trait in UKB	Optimal p-value threshold (P_T)	No. SNPs used to construct PRS at (P_T)	Population Prevalence used to convert to liability R^2	Unadjusted Variance explained (Observed R^2)	Adjusted Variance explained (Liability R^2)	Coefficient	Standard Error	P-value	Sex*PRS p-value
MDD	Psoriatic Arthritis, Probable (female)	1.000	99,216	0.50%	0.212%	0.349%	0.173	0.051	6.4e-04	NA
MDD	Psoriatic Arthritis, Probable (male)	0.001	1,123	0.50%	0.153%	0.250%	0.146	0.051	4.4e-03	NA
MDD	Rheumatoid Arthritis, Possible (combined)	0.500	67,956	1.00%	0.065%	0.082%	0.078	0.013	1.1e-09	NA
MDD	Rheumatoid Arthritis, Possible (female)	0.300	48,852	1.00%	0.060%	0.071%	0.072	0.016	3.5e-06	0.68
MDD	Rheumatoid Arthritis, Possible (male)	1.000	99,216	1.00%	0.090%	0.125%	0.096	0.022	1.6e-05	0.26
MDD	Rheumatoid Arthritis, Probable (combined)	0.100	22,831	1.00%	0.065%	0.095%	0.083	0.017	1.2e-06	NA
MDD	Rheumatoid Arthritis, Probable (female)	0.300	48,852	1.00%	0.070%	0.096%	0.084	0.021	4.5e-05	0.90
MDD	Rheumatoid Arthritis, Probable (male)	1.000	99,216	1.00%	0.075%	0.121%	0.094	0.032	2.9e-03	NA
MDD	Sjögren Syndrome, Possible (combined)	0.200	36,975	0.10%	0.064%	0.080%	0.096	0.040	1.5e-02	NA
MDD	Sjögren Syndrome, Possible (female)	0.200	36,975	0.10%	0.041%	0.047%	0.073	0.042	7.9e-02	NA
MDD	Sjögren Syndrome, Possible (male)	0.050	14,137	0.10%	0.517%	0.799%	0.305	0.128	1.8e-02	NA
MDD	Sjögren Syndrome, Probable (combined)	1.000	99,216	0.10%	0.042%	0.057%	0.081	0.051	1.1e-01	NA
MDD	Sjögren Syndrome, Probable (female)	0.200	36,975	0.10%	0.028%	0.035%	0.064	0.054	2.4e-01	NA
MDD	Sjögren Syndrome, Probable (male)	0.500	67,956	0.10%	0.375%	0.605%	0.265	0.158	9.3e-02	NA
MDD	Systemic Lupus Erythematosus, Possible (combined)	0.050	14,137	0.10%	0.097%	0.123%	0.119	0.040	3.2e-03	NA
MDD	Systemic Lupus Erythematosus, Possible (female)	0.050	14,137	0.10%	0.111%	0.130%	0.122	0.044	5.3e-03	NA
MDD	Systemic Lupus Erythematosus, Possible (male)	1.000	99,216	0.10%	0.180%	0.265%	0.175	0.102	8.7e-02	NA
MDD	Systemic Lupus Erythematosus, Probable (combined)	0.050	14,137	0.10%	0.170%	0.231%	0.163	0.053	2.1e-03	NA

Base GWAS	Target Trait in UKB	Optimal p-value threshold (P_T)	No. SNPs used to construct PRS at (P_T)	Population Prevalence used to convert to liability R^2	Unadjusted Variance explained (Observed R^2)	Adjusted Variance explained (Liability R^2)	Coefficient	Standard Error	P-value	Sex*PRS p-value
MDD	Systemic Lupus Erythematosus, Probable (female)	0.050	14,137	0.10%	0.190%	0.242%	0.166	0.057	3.5e-03	NA
MDD	Systemic Lupus Erythematosus, Probable (male)	0.500	67,956	0.10%	0.154%	0.243%	0.168	0.141	2.3e-01	NA
MDD	Type 1 Diabetes, Possible (combined)	0.400	59,001	0.30%	0.082%	0.098%	0.096	0.019	6.0e-07	NA
MDD	Type 1 Diabetes, Possible (female)	1.000	99,216	0.30%	0.126%	0.156%	0.121	0.030	4.5e-05	0.18
MDD	Type 1 Diabetes, Possible (male)	0.300	48,852	0.30%	0.066%	0.075%	0.084	0.025	8.7e-04	NA
MDD	Type 1 Diabetes, Probable (combined)	0.500	67,956	0.30%	0.089%	0.110%	0.102	0.021	1.4e-06	NA
MDD	Type 1 Diabetes, Probable (female)	1.000	99,216	0.30%	0.117%	0.149%	0.119	0.032	2.2e-04	NA
MDD	Type 1 Diabetes, Probable (male)	0.300	48,852	0.30%	0.081%	0.097%	0.095	0.028	6.1e-04	NA





Supplementary Figure S7: Cross-trait PRS associations between PRS for MDD and autoimmune case/control status (possible/probable) in men and women across eight P_T . Y-axis shows unadjusted R^2 (observed-scale). Bar charts are shown for significant results only.

3 Genetic correlations

Supplementary Table S7: Genetic correlations between autoimmune traits and ‘any’ and ‘stringent’ depression in the UKB. Associations with p-values $< 4.1 \times 10^{-3}$, meeting Bonferroni correction, highlighted in red.

	r_G	95% CIs	P-value	r_G	95% CIs	P-value
Autoimmune Disease	Any depression			Stringent depression		
Coeliac Disease	0.017	-0.10 - 0.14	7.8e-01	0.048	-0.10 - 0.19	5.2e-01
Inflammatory Bowel Disease	0.106	0.03 - 0.18	3.8e-03	0.157	0.07 - 0.24	3.0e-04
Multiple Sclerosis	0.302	0.06 - 0.55	1.6e-02	0.375	0.07 - 0.68	1.5e-02
Psoriasis	0.064	-0.01 - 0.14	9.0e-02	0.161	0.06 - 0.26	1.1e-03
Rheumatoid Arthritis	0.004	-0.06 - 0.07	9.0e-01	0.104	0.02 - 0.19	1.7e-02
Systemic Lupus Erythematosus	-0.001	-0.11 - 0.10	9.9e-01	0.126	0.00 - 0.25	5.1e-02