Supporting Information

Supplementary Table SI. STROBE-MR checklist of the present study.

[1] Discovery phase

Supplementary Table SII. Screening and MR analysis results of causal relationships between 91 inflammatory proteins and osteomyelitis during the discovery phase.
Supplementary Table SIII. Details of confirmed instrumental variables during the discovery phase.
Supplementary Table SIV. MR Analysis of four inflammatory proteins and osteomyelitis.(discovery phase) (MR-Egger, Weighted median, Inverse variance weighted, Simple mode, Weighted mode)

[2] Replication phase

Supplementary Table SV. Screening and MR analysis results of causal relationships between 91 inflammatory proteins and osteomyelitis during the replication phase.
Supplementary Table SVI. Details of confirmed instrumental variables during the replication phase.
Supplementary Table SVII. MR Analysis of six inflammatory proteins and osteomyelitis.(replication phase) (MR-Egger, Weighted median, Inverse variance weighted, Simple mode, Weighted mode)

[3] Sensitivity analysis and graphical visualization of the MR results

Supplementary Table SVIII. Heterogeneity of MR analysis for serum levels of circulating inflammatory proteins and osteomyelitis.
Supplementary Table SIX. Results of the MR Horizontal pleiotropy analysis between circulating inflammatory proteins and osteomyelitis.
Supplementary Figure S1. (I) Scatter plot of the association of four inflammatory proteins with osteomyelitis. (discovery phase) (II) Scatter plot of the association between six inflammatory proteins and osteomyelitis (replication phase)
Supplementary Figure S2. (I) “Leave-one-out” plot of four inflammatory proteins associated with osteomyelitis (discovery phase) (II) “Leave-one-out” plot of the association between six inflammatory proteins and osteomyelitis (replication phase)

Supplementary Figure S3-S12. PheWAS results for the inflammatory proteins. The bottom dashed line represented the suggestive line and the top dashed line was the significant line. Traits that exceeded the significant line were considered to be significantly associated with the gene regulating inflammatory proteins.

Supplementary Table SI. STROBE-MR checklist of the present study.

No.	Section	Checklist item	Relevant text from manuscript
1	Title and abstract	Indicate MR as the study's design in the title and the abstract as a main purpose of the study	Title, Abstract
2	Background	Explain the scientific background and rationale for the reported study. Explain the exposure and a plausible potential causal relationship between exposure and outcome. Justify why MR is a helpful method to address the study question.	Introduction
3	Objectives	State specific objectives clearly, including prespecified causal hypotheses. State that MR is a method that intends to estimate causal effects.	Introduction
4a	Study design and data sources	Setting: Describe the study design (two-sample MR) and the underlying population . Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection.	Materials and methods: 3.1 Study design
4b		Participants: Report the eligibility criteria and the sources and methods of selection of participants. Report the sample size and whether any power or sample size calculations were carried out prior to the main analysis.	Materials and methods: 3.2 Data Sources
4c		Describe measurement, quality control, and selection of genetic variants.	Materials and methods: 3.3 Selection of Instrumental Variables
4d		For each exposure, outcome, and other relevant variables, describe methods of assessment and diagnostic criteria for diseases.	Materials and methods: 3.2 Data Sources
4e		Provide details of ethics committee approval and participant informed consent, if relevant.	Materials and methods: 3.2 Data Sources
5	Assumptions	Explicitly state the 3 core instrumental variable (IV) assumptions for the main analysis (relevance, independence, and exclusion restriction), as well assumptions for any additional or sensitivity analysis.	Materials and methods: 3.1 Study design
6a	Statistical methods: main analysis	Describe how quantitative variables were handled in the analyses (i.e., scale, units, model)	Materials and methods: 3.4 Statistical analysis
6b		Describe how genetic variants were handled in the analyses and, if applicable, how their weights were selected	Materials and methods: 3.4 Statistical analysis

6c		Describe the MR estimator (e.g. two-stage least squares, Wald ratio) and related statistics. Detail the included covariates and, in case of two-sample MR, whether the same covariate set was used for adjustment in the two samples	Materials and methods: 3.4 Statistical analysis
6d		Explain how missing data were addressed	N/A
6e		If applicable, indicate how multiple testing was addressed	Materials and methods: 3.4 Statistical analysis
7	Assessment of assumptions	Describe any methods or prior knowledge used to assess the assumptions or justify their validity	Materials and methods: 3.4 Statistical analysis
8	Sensitivity analyses and additional analyses	Describe any sensitivity analyses or additional analyses performed (e.g. comparison of effect estimates from different approaches, independent replication, bias analytic techniques, validation of instruments, simulations)	Materials and methods: 3.4 Statistical analysis
9a	Software and pre-registration	Name statistical software and package(s), including version and settings used	R studio(4.3.1), Stata (17.0 version)
9b		State whether the study protocol and details were pre-registered (as well as when and where)	N/A
10a	Descriptive data	Report the numbers of individuals at each stage of included studies and reasons for exclusion. Consider use of a flow diagram	N/A
10b		Report summary statistics for phenotypic exposure(s), outcome(s), and other relevant variables (e.g. means, SDs, proportions)	Supplementary Table SII.
10c		If the data sources include meta-analyses of previous studies, provide the assessments of heterogeneity across these studies	N/A
10d		For two-sample MR: i. Provide justification of the similarity of the genetic variant-exposure associations between the exposure and outcome samples ii. Provide information on the number of individuals who overlap between the exposure and outcome studies	N/A

11a	Main results	Report the associations between genetic variant and exposure, and between genetic variant and outcome, preferably on an interpretable scale	Results: 4.2 MR discovery analysis of 91 inflammatory proteins on OM, and 4.3 MR replication analysis of 91 inflammatory proteins on OM
11b		Report MR estimates of the relationship between exposure and outcome, and the measures of uncertainty from the MR analysis, on an interpretable scale, such as odds ratio or relative risk per SD difference	Results: 4.2 MR discovery analysis of 91 inflammatory proteins on OM, and 4.3 MR replication analysis of 91 inflammatory proteins on OM
11c		If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
11d		Consider plots to visualize results (e.g. forest plot, scatterplot of associations between genetic variants and outcome versus between genetic variants and exposure)	Supplementary Figure S1 and S2
12a	Assessment of assumptions	Report the assessment of the validity of the assumptions	N/A
12b		Report any additional statistics (e.g., assessments of heterogeneity across genetic variants, such as I^2, Q statistic or E-value)	Supplementary Table SVIII and SIX
13a	Sensitivity analyses and additional analyses	Report any sensitivity analyses to assess the robustness of the main results to violations of the assumptions	Supplementary Table SVIII and SIX
13b		Report results from other sensitivity analyses or additional analyses	Supplementary Table SVIII and SIX
13c		Report any assessment of direction of causal relationship (e.g., bidirectional MR)	Supplementary Table SVIII and SIX
13d		When relevant, report and compare with estimates from non-MR analyses	Supplementary Table SVIII and SIX
13e		Consider additional plots to visualize results (e.g., leave-one-out analyses)	Supplementary Figure S2

14	Key results	Summarize key results with reference to study objectives	Discussion: Lines 204 to 214
15	Limitations	Discuss limitations of the study, taking into account the validity of the IV assumptions, other sources of potential bias, and imprecision. Discuss both direction and magnitude of any potential bias and any efforts to address them	5.3 Limitations of the Study
16a	Interpretation	Meaning: Give a cautious overall interpretation of results in the context of their limitations and in comparison with other studies	5.2 Possible Explanations for the Causality
16b		Mechanism: Discuss underlying biological mechanisms that could drive a potential causal relationship between the investigated exposure and the outcome, and whether the gene-environment equivalence assumption is reasonable. Use causal language carefully, clarifying that IV estimates may provide causal effects only under certain assumptions	5.2 Possible Explanations for the Causality
16c		Clinical relevance: Discuss whether the results have clinical or public policy relevance, and to what extent they inform effect sizes of possible interventions	5.2 Possible Explanations for the Causality
17	Generalizability	Discuss the generalizability of the study results (a) to other populations, (b) across other exposure periods/timings, and (c) across other levels of exposure	Discussion
18	Funding	Describe sources of funding and the role of funders in the present study and, if applicable, sources of funding for the databases and original study or studies on which the present study is based	Funding
19	Data and data sharing	Provide the data used to perform all analyses or report where and how the data can be accessed, and reference these sources in the article. Provide the statistical code needed to reproduce the results in the article, or report whether the code is publicly accessible and if so, where	Data availability statement
20	Conflicts of Interest	All authors should declare all potential conflicts of interest	Conflicts of Interest

Supplementary Table SII. Screening and MR analysis results of causal relationships between 91 inflammatory proteins and osteomyelitis during the discovery phase.

	Study accession	Reported trait	p＜5E-08	Clump	Merge	Harmonision	*p*
1	GCST90274848	Vascular endothelial growth factor A	416	6	6	4 (rs6475938, rs6993770)	0.959 (MR Egger); 0.649 (Weighted median); 0.587 (IVW); 0.689 (Simple mode); 0.71 (Weighted mode)
2	GCST90274847	Urokinase-type plasminogen activator	617	8	7	7	0.959 / 0.63 / 0.244 / 0.7 / 0.788
3	GCST90274846	Tumor necrosis factor ligand superfamily member 12	549	8	7	5 (rs73133996, rs9842051)	0.964 / 0.835 / 0.949 / 0.653 / 0.932
4*	**GCST90274845**	**Thymic stromal lymphopoietin**	**1**	**1**	**1**	**1**	**0.808 (Wald ratio)**
5	GCST90274844	TNF-related activation-induced cytokine	552	7	7	7	0.182 / 0.539 / 0.736 / 0.35 / 0.37
6	GCST90274843	TNF-related apoptosis-inducing ligand	720	10	10	9 (rs654488)	0.713 / 0.999 / 0.809 / 0.701 / 0.9
7	GCST90274842	Tumor necrosis factor ligand superfamily member 14	85	4	4	4	0.479 / 0.828 / 0.947 / 0.999 / 0.867
8*	**GCST90274841**	**Tumor necrosis factor receptor superfamily member 9**	**321**	**2**	**2**	**2**	**0.684 (IVW)**
9	GCST90274840	TNF-beta	7077	6	5	4 (rs7310615)	0.092 / 0.101 / 0.391 / 0.894 / 0.081
10*	**GCST90274839**	**Tumor necrosis factor**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
11*	**GCST90274838**	**Transforming growth factor-alpha**	**50**	**2**	**2**	**1 (rs72912115)**	**0.730 (Wald ratio)**

12*	**GCST90274837**	**STAM binding protein**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
13	GCST90274836	Sulfotransferase 1A1	746	3	3	3	0.767 / 0.998 / 0.999 / 0.551 / 0.887
14	GCST90274835	Signaling lymphocytic activation molecule	538	9	7	5 (rs10212190, rs2725405)	0.757 / 0.843 / 0.601 / 0.542 / 0.979
15*	**GCST90274834**	**SIR2-like protein 2**	**8**	**1**	**1**	**1**	**0.320 (Wald ratio)**
16 ¶	GCST90274833	Stem cell factor	967	11	11	10 (rs798893)	**0.05** / 0.472 / 0.705 / 0.557 / 0.472
17*	**GCST90274832**	**Programmed cell death 1 ligand 1**	**53**	**1**	**1**	**1**	**0.136 (Wald ratio)**
18	GCST90274831	Oncostatin-M	282	5	4	4	0.451 / 0.682 / 0.308 / 0.892 / 0.758
19 ¶	GCST90274830	Osteoprotegerin	443	5	4	3 (rs114165349)	0.357 / **0.012** / **0.003** / 0.205 / 0.169
20*	**GCST90274829**	**Neurotrophin-3**	**30**	**2**	**0**	**0 (rs11151953, rs28735437)**	**No SNPs available for MR**
21*	**GCST90274828**	**Neurturin**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
22	GCST90274827	Matrix metalloproteinase-10	1230	6	6	4 (rs516316, rs72699188)	0.466 / 0.124 / 0.087 / 0.262 / 0.294
23	GCST90274826	Matrix metalloproteinase-1	1273	8	8	7 (rs484915)	0.242 / 0.157 / 0.225 / 0.585 / 0.242
24	GCST90274825	Macrophage inflammatory protein 1a	448	6	5	5	0.475 / 0.157 / 0.373 / 0.541 / 0.237
25 ¶	GCST90274824	Monocyte chemoattractant protein-4	1023	6	6	6	0.794 / 0.183 / **0.022** / 0.369 / 0.454
26	GCST90274823	Monocyte chemoattractant protein-3	243	5	5	5	0.105 / 0.458 / 0.312 / 0.866 / 0.09

27	GCST90274822	Monocyte chemoattractant protein 2	727	11	11	9 (rs188234686,	0.941 / 0.765 / 0.917 / 0.688 / 0.828
28	GCST90274821	Monocyte chemoattractant protein-1	1168	4	4	3 (rs1846616)	0.733 / 0.402 / 0.373 / 0.383 / 0.362
29	GCST90274820	Leukemia inhibitory factor receptor	396	3	3	3	0.95 / 0.249 / 0.148 / 0.532 / 0.407
30*	**GCST90274819**	**Leukemia inhibitory factor**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
31*	**GCST90274818**	**Latency-associated peptide transforming growth factor beta 1**	**84**	**2**	**2**	**2**	**0.606 (IVW)**
32*	**GCST90274817**	**Interleukin-8**	**112**	**2**	**2**	**2**	**0.179 (IVW)**
33*	**GCST90274816**	**Interleukin-7**	**145**	**1**	**0**	**0**	**No SNPs available for MR**
34*	**GCST90274815**	**Interleukin-6**	**187**	**1**	**1**	**1**	**0.982 (Wald ratio)**
35*	**GCST90274814**	**Interleukin-5**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
36*	**GCST90274813**	**Interleukin-4**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
37*	**GCST90274812**	**Interleukin-33**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
38*	**GCST90274811**	**Interleukin-2 receptor subunit beta**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
39*	**GCST90274810**	**Interleukin-24**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
40*	**GCST90274809**	**Interleukin-22 receptor subunit alpha-1**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
41*	**GCST90274808**	**Interleukin-20 receptor subunit alpha**	**2**	**1**	**1**	**1**	**0.61 (Wald ratio)**

42*	**GCST90274807**	**Interleukin-20**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
43*	**GCST90274806**	**Interleukin-2**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
44*	**GCST90274805**	**Interleukin-1-alpha**	**497**	**2**	**1**	**1**	**0.326 (Wald ratio)**
45	GCST90274804	interleukin-18 receptor 1	2358	6	6	4 (rs55871806, rs78714574)	0.177 / 0.475 / 0.738 / 0.714 / 0.391
46	GCST90274803	Interleukin-18	1063	4	4	3 (rs12681624)	0.550 / 0.507 / 0.997 / 0.572 / 0.536
47*	**GCST90274802**	**Interleukin-17C**	**39**	**2**	**2**	**1 (rs114882743)**	**0.573 (Wald ratio)**
48*	**GCST90274801**	**Interleukin-17A**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
49	GCST90274800	Interleukin-15 receptor subunit alpha	315	3	3	3	0.37 / 0.66 / 0.635 / 0.535 / 0.831
50*	**GCST90274799**	**Interleukin-13**	**6**	**1**	**1**	**1**	**0.952 (IVW)**
51	GCST90274798	Interleukin-12 subunit beta	2369	14	14	11 (rs12588969, rs516978,	0.423 / 0.845 / 0.299 / 0.808 / 0.983
52	GCST90274797	Interleukin-10 receptor subunit beta	470	3	3	3	0.507 / 0.496 / 0.507 / 0.371 / 0.497
53*	**GCST90274796**	**Interleukin-10 receptor subunit alpha**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
54	GCST90274795	Interleukin-10	798	4	4	4	0.419 / 0.551 / 0.39 / 0.577 / 0.921
55*	**GCST90274794**	**Interferon gamma**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
56*	**GCST90274793**	**Hepatocyte growth factor**	**171**	**2**	**2**	**2**	**0.911 (IVW)**

57*	**GCST90274792**	**Glial cell line-derived neurotrophic factor**	**435**	**5**	**4**	**2 (rs2194229, rs2453338)**	**0.511 (IVW)**
58	GCST90274791	Fms-related tyrosine kinase 3 ligand	416	9	9	7 (rs144317085, rs9554186)	0.693 / 0.667 / 0.801 / 0.869 / 0.594
59	GCST90274790	Fibroblast growth factor 5	412	4	4	3 (rs56373850)	0.989 / 0.904 / 0.925 / 0.891 / 0.876
60*	**GCST90274789**	**Fibroblast growth factor 23**	**57**	**2**	**2**	**0 (rs3811621, rs6127099）**	**No SNPs available for MR**
61	GCST90274788	Fibroblast growth factor 21	432	4	4	4	0.863 / 0.705 / 0.461 / 0.167 / 0.933
62	GCST90274787	Fibroblast growth factor 19	299	3	3	3	0.486 / 0.238 / 0.353 / 0.507 / 0.318
63*	**GCST90274786**	**Protein S100-A12**	**110**	**2**	**2**	**2**	**0.575 (IVW)**
64*	**GCST90274785**	**Delta and Notch-like epidermal growth factor-related receptor**	**649**	**4**	**4**	**2 (rs62193248, rs6517655)**	**0.435 (IVW)**
65	GCST90274784	C-X-C motif chemokine 9	264	4	4	4	0.126 / 0.421 / 0.817 / 0.294 / 0.324
66*	**GCST90274783**	**C-X-C motif chemokine 6**	**447**	**3**	**3**	**2 (rs10021230)**	**0.741 (IVW)**
67	GCST90274782	C-X-C motif chemokine 5	1178	7	6	4 (rs6993770, rs7090111)	0.965 / 0.725 / 0.57 / 0.896 / 0.813
68	GCST90274781	C-X-C motif chemokine 11	693	4	4	4	0.574 / 0.418 / 0.95 / 0.672 / 0.46
69	GCST90274780	C-X-C motif chemokine 10	221	5	5	5	0.877 / 0.443 / 0.219 / 0.617 / 0.486
70*	**GCST90274779**	**C-X-C motif chemokine 1**	**298**	**3**	**1**	**1**	**0.978 (Wald ratio)**
71	GCST90274778	Fractalkine	773	5	5	4 (rs671623)	0.371 / 0.554 / 0.792 / 0.549 / 0.460

72	GCST90274777	Cystatin D	2589	10	9	8 (rs516316)	0.924 / 0.864 / 0.969 / 0.834 / 0.869
73*	**GCST90274776**	**Macrophage colony-stimulating factor 1**	**177**	**1**	**1**	**1**	**0.234 (Wald ratio)**
74	GCST90274775	CUB domain-containing protein 1	1337	5	5	4 (rs2276862)	0.758 / 0.263 / 0.296 / 0.845 / 0.452
75	GCST90274774	T-cell surface glycoprotein CD6 isoform	765	3	3	3	0.367 / 0.912 / 0.784 / 0.576 / 0.862
76	GCST90274773	T-cell surface glycoprotein CD5	366	6	6	4 (rs4939490, rs674379)	0.295 / 0.166 / 0.587 / 0.411 / 0.166
77	GCST90274772	CD40L receptor	451	3	3	3	0.826 / 0.063 / 0.133 / 0.219 / 0.318
78	GCST90274771	Natural killer cell receptor 2B4	521	6	6	6	0.955 / 0.832 / 0.483 / 0.293 / 0.856
79 ¶	GCST90274770	C-C motif chemokine 4	1616	4	4	4	0.823 / 0.108 / **0.05** / 0.298 / 0.187
80	GCST90274769	C-C motif chemokine 28	27	5	5	4 (rs291084)	0.772 / 0.664 / 0.281 / 0.239 / 0.784
81	GCST90274768	C-C motif chemokine 25	1552	7	6	5 (rs516316)	0.604 / 0.225 / 0.130 / 0.273 / 0.301
82	GCST90274767	C-C motif chemokine 23	541	4	3	3	0.367 / 0.085 / 0.179 / 0.378 / 0.238
83*	**GCST90274766**	**C-C motif chemokine 20**	**58**	**2**	**2**	**2**	**0.412 (IVW)**
84*	**GCST90274765**	**C-C motif chemokine 19**	**3119**	**6**	**5**	**2 (rs13010492, rs4766578, rs9469127)**	**0.434 (IVW)**
85	GCST90274764	Eotaxin	339	6	6	6	0.241 / 0.236 / 0.126 / 0.959 / 0.072

86*	**GCST90274763**	**Caspase 8**	**89**	**1**	**1**	**0**	**No SNPs available for MR**
87*	**GCST90274762**	**beta-nerve growth factor**	**46**	**2**	**2**	**2**	**0.822 (IVW)**
88	GCST90274761	Axin-1	9	3	3	3	0.456 / 0.991 / 0.986 / 0.628 / 0.992
89*	**GCST90274760**	**Artemin**	**17**	**4**	**4**	**2 (rs6509909, rs9684768)**	**0.846 (IVW)**
90 ¶	GCST90274759	Adenosine Deaminase	317	3	3	3	0.325 / **0.007** / **0.005** / 0.116 / 0.213
91*	**GCST90274758**	**Eukaryotic translation initiation factor 4E-binding protein 1**	**152**	**2**	**2**	**2**	**0.663 (IVW)**

***** Insufficient available SNPs (SNP≤2); ¶ Significant *p* value in IVW or default method ($p < 0.05$)

Supplementary Table SIII. Details of confirmed instrumental variables during the discovery phase.

	Study accession	SNP	CHR:POS	effect_allele	other_allele	beta	se	*p*
19	GCST90274830	rs112635299	14:94838142	G	T	-0.2117	0.10986	0.0539796
		rs2247769	8:120081031	T	C	-0.069735	0.0315966	0.0273112
		rs704	17:26694861	G	A	0.0360821	0.0312618	0.248422
25	GCST90274824	rs12075	1:159175354	G	A	-0.00578796	0.0309775	0.851783
		rs2721961	8:116657911	T	G	-0.0204429	0.0334965	0.541665
		rs3136676	17:32683289	A	G	0.0517381	0.0684329	0.449625
		rs3917900	17:32587314	G	A	-0.0459839	0.0327106	0.159789
		rs72825017	17:32529710	G	T	0.0386243	0.0686505	0.573692
79	GCST90274770	rs7612912	3:42910621	T	C	0.0829726	0.0324792	0.0106297
		rs113341849	3:46384204	G	A	-0.0508404	0.0465273	0.274524
		rs140505982	3:46459749	C	T	-0.058654	0.156694	0.708164
		rs17692864	17:34945214	T	C	0.104192	0.0735691	0.156703
		rs8064426	17:34819750	G	A	0.050499	0.0376806	0.180185
90	GCST90274759	rs112665079	20:43120683	C	T	-0.136127	0.0738395	0.0652469
		rs12479560	20:43300667	G	A	-0.036693	0.0323539	0.256747
		rs80212763	20:43223930	C	T	-0.260059	0.137537	0.0586476

Supplementary Table SIV. MR Analysis of four inflammatory proteins and osteomyelitis.(discovery phase) (MR-Egger, Weighted median, Inverse variance weighted, Simple mode, Weighted mode)

Exposure-Outcome	SNP(n)	se	OR	95%CI	*p-value*	low	hi
Osteoprotegerin (OPG) levels - Osteomyelitis	3						
MR Egger		0.857	3.921	0.731-21.033	0.357	0.731	21.033
Weighted median		0.149	1.437	1.073-1.925	**0.012**	1.073	1.925
Inverse variance weighted		0.135	1.484	1.139-1.933	**0.003**	1.139	1.933
Simple mode		0.185	1.401	0.975-2.011	0.205	0.975	2.011
Weighted mode		0.173	1.422	1.014-1.994	0.169	1.014	1.994
Monocyte chemoattractant protein-4 (MCP-4) levels - Osteomyelitis	6						
MR Egger		0.259	0.930	0.559-1.546	0.794	0.559	1.546
Weighted median		0.116	1.162	0.926-1.457	0.183	0.926	1.457
Inverse variance weighted		0.088	1.223	1.029-1.453	**0.022**	1.029	1.453
Simple mode		0.166	1.183	0.854-1.638	0.369	0.854	1.638
Weighted mode		0.141	1.123	0.852-1.479	0.454	0.852	1.479
Adenosine Deaminase(ADA) levels - Osteomyelitis	3						
MR Egger		0.092	1.178	0.983-1.410	0.325	0.983	1.410
Weighted median		0.073	1.209	1.047-1.396	**0.010**	1.047	1.396
Inverse variance weighted		0.069	1.209	1.056-1.384	**0.006**	1.056	1.384
Simple mode		0.104	1.333	1.087-1.634	0.110	1.087	1.634
Weighted mode		0.082	1.166	0.993-1.369	0.203	0.993	1.369
C-C motif chemokine 4 (CCL4) levels - Osteomyelitis	4						
MR Egger		0.239	0.941	0.59-1.502	0.823	0.59	1.502
Weighted median		0.066	1.111	0.977-1.264	0.108	0.977	1.264
Inverse variance weighted		0.06	1.121	0.997-1.261	**0.05**	0.997	1.261
Simple mode		0.09	1.119	0.939-1.334	0.298	0.939	1.334
Weighted mode		0.062	1.111	0.984-1.255	0.187	0.984	1.255

Supplementary Table SV. Screening and MR analysis results of causal relationships between 91 inflammatory proteins and osteomyelitis during the replication phase.

	Study accession	Reported trait	p＜5E-08	Clump	Merge	Harmonision	p
1	GCST90274848	Vascular endothelial growth factor A	416	9	7	7	0.754 (MR Egger); 0.534 (Weighted median); 0.449 (IVW); 0.547 (Simple mode); 0.477 (Simple mode)
2	GCST90274847	Urokinase-type plasminogen activator	617	10	10	10	0.416 / 0.206 / 0.382 / 0.454 / 0.372
3	GCST90274846	Tumor necrosis factor ligand superfamily member 12	549	9	7	7	0.894 / 0.338 / 0.354 / 0.295 / 0.399
4*	**GCST90274845**	**Thymic stromal lymphopoietin**	**1**	**1**	**0**	**0**	**No SNPs available for MR**
5	GCST90274844	TNF-related activation-induced cytokine	552	7	7	7	0.603 / 0.082 / 0.078 / 0.413 / 0.279
6	GCST90274843	TNF-related apoptosis-inducing ligand	720	11	9	9	0.342 / 0.944 / 0.423 / 0.953 / 0.452
7	GCST90274842	Tumor necrosis factor ligand superfamily member 14	85	5	5	5	0.375 / 0.564 / 0.58 / 0.544 / 0.616
8*	**GCST90274841**	**Tumor necrosis factor receptor superfamily member 9**	**321**	**2**	**2**	**2**	**0.815 (IVW)**
9 ¶	**GCST90274840**	TNF-beta	7077	13	12	11 (rs7310615)	**0.048** / 0.101 / 0.08 / 0.476 / 0.277
10*	**GCST90274839**	**Tumor necrosis factor**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
11*	**GCST90274838**	**Transforming growth factor-alpha**	**50**	**2**	**2**	**2**	**0.572 (IVW)**
12*	**GCST90274837**	**STAM binding protein**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
13	GCST90274836	Sulfotransferase 1A1	746	4	3	3	0.988 / 0.197 / 0.305 / 0.572 / 0.284

14 ¶	GCST90274835	Signaling lymphocytic activation molecule	538	9	5	4 (rs2725405)	0.214 / **0.028** / 0.06 / 0.236 / 0.161
15*	**GCST90274834**	**SIR2-like protein 2**	**8**	**1**	**1**	**1**	**0.717 (Wald ratio)**
16	GCST90274833	Stem cell factor	967	12	11	11	0.553 / 0.646 / 0.738 / 0.766 / 0.64
17*	**GCST90274832**	**Programmed cell death 1 ligand 1**	**53**	**2**	**2**	**2**	**0.324 (IVW)**
18 ¶	GCST90274831	Oncostatin-M	282	5	3	3	0.593 / **0.049** / 0.11 / 0.189 / 0.208
19	GCST90274830	Osteoprotegerin	443	7	6	6	0.828 / 0.551 / 0.688 / 0.682 / 0.51
20*	**GCST90274829**	**Neurotrophin-3**	**30**	**2**	**2**	**1 (rs11151953)**	**0.551 (Wald ratio)**
21*	**GCST90274828**	**Neurturin**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
22*	**GCST90274827**	**Matrix metalloproteinase-10**	**1230**	**10**	**??**	**0**	**No SNPs available for MR**
23	GCST90274826	Matrix metalloproteinase-1	1273	12	11	10 (rs484915)	0.857 / 0.818 / 0.601 / 0.783 / 0.78
24	GCST90274825	Macrophage inflammatory protein 1a	448	8	8	8	0.994 / 0.924 / 0.944 / 0.521 / 0.722
25	GCST90274824	Monocyte chemoattractant protein-4	1023	10	10	10	0.471 / 0.585 / 0.653 / 0.609 / 0.711
26 ¶	GCST90274823	Monocyte chemoattractant protein-3	243	6	6	6	0.743 / 0.162 / **0.025** / 0.316 / 0.293
27	GCST90274822	Monocyte chemoattractant protein 2	727	16	16	16	0.891 / 0.333 / 0.464 / 0.955 / 0.535
28	GCST90274821	Monocyte chemoattractant protein-1	1168	6	6	6	0.912 / 0.927 / 0.866 / 0.860 / 0.974
29	GCST90274820	Leukemia inhibitory factor receptor	396	3	3	3	0.350 / 0.312 / 0.354 / 0.508 / 0.252
30*	**GCST90274819**	**Leukemia inhibitory factor**	**0**	**0**	**0**	**0**	**No SNPs available for MR**

31*	**GCST90274818**	**Latency-associated peptide transforming growth factor beta 1**	**84**	**2**	**1**	**1**	**0.867 (Wald ratio)**
32*	**GCST90274817**	**Interleukin-8**	**112**	**2**	**2**	**2**	**0.305 (IVW)**
33*	**GCST90274816**	**Interleukin-7**	**145**	**1**	**0**	**0**	**No SNPs available for MR**
34*	**GCST90274815**	**Interleukin-6**	**187**	**1**	**1**	**1**	**0.744 (Wald ratio)**
35*	**GCST90274814**	**Interleukin-5**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
36*	**GCST90274813**	**Interleukin-4**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
37*	**GCST90274812**	**Interleukin-33**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
38*	**GCST90274811**	**Interleukin-2 receptor subunit beta**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
39*	**GCST90274810**	**Interleukin-24**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
40*	**GCST90274809**	**Interleukin-22 receptor subunit alpha-1**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
41*	**GCST90274808**	**Interleukin-20 receptor subunit alpha**	**2**	**1**	**0**	**0**	**No SNPs available for MR**
42*	**GCST90274807**	**Interleukin-20**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
43*	**GCST90274806**	**Interleukin-2**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
44*	**GCST90274805**	**Interleukin-1-alpha**	**497**	**3**	**2**	**2**	**0.862 (IVW)**
45	GCST90274804	interleukin-18 receptor 1	2358	17	15	15	0.291 / 0.604 / 0.725 / 0.211 / 0.878
46	GCST90274803	Interleukin-18	1063	4	4	4	0.7 / 0.867 / 0.692 / 0.954 / 0.897
47*	**GCST90274802**	**Interleukin-17C**	**39**	**2**	**2**	**2**	**0.934 (IVW)**

48*	**GCST90274801**	**Interleukin-17A**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
49 ¶	GCST90274800	Interleukin-15 receptor subunit alpha	315	9	8	8	0.569 / 0.085 / **0.047** / 0.409 / 0.179
50*	**GCST90274799**	**Interleukin-13**	**6**	**1**	**1**	**1**	**0.782 (Wald ratio)**
51	GCST90274798	Interleukin-12 subunit beta	2369	17	14	14	0.3 / 0.62 / 0.3 / 0.72 / 0.8
52	GCST90274797	Interleukin-10 receptor subunit beta	470	6	6	6	0.599 / 0.843 / 0.845 / 0.853 / 0.866
53*	**GCST90274796**	**Interleukin-10 receptor subunit alpha**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
54	GCST90274795	Interleukin-10	798	4	4	4	0.857 / 0.798 / 0.17 / 0.808 / 0.858
55*	**GCST90274794**	**Interferon gamma**	**0**	**0**	**0**	**0**	**No SNPs available for MR**
56*	**GCST90274793**	**Hepatocyte growth factor**	**171**	**2**	**0**	**0**	**No SNPs available for MR**
57	GCST90274792	Glial cell line-derived neurotrophic factor	435	10	8	8	0.322 / 0.558 / 0.582 / 0.371 / 0.611
58	GCST90274791	Fms-related tyrosine kinase 3 ligand	416	9	8	8	0.206 / 0.265 / 0.302 / 0.697 / 0.306
59	GCST90274790	Fibroblast growth factor 5	412	8	8	8	0.437 / 0.583 / 0.818 / 0.413 / 0.449
60*	**GCST90274789**	**Fibroblast growth factor 23**	**57**	**2**	**2**	**2**	**0.724 (IVW)**
61	GCST90274788	Fibroblast growth factor 21	432	4	3	3	0.51 / 0.787 / 0.634 / 0.712 / 0.786
62	GCST90274787	Fibroblast growth factor 19	299	3	3	3	0.571 / 0.429 / 0.638 / 0.485 / 0.494
63*	**GCST90274786**	**Protein S100-A12**	**110**	**2**	**2**	**2**	**0.323 (IVW)**
64	GCST90274785	Delta and Notch-like epidermal growth factor-related receptor	649	7	7	6 (rs2302769)	0.978 / 0.495 / 0.396 / 0.183 / 0.933

65	GCST90274784	C-X-C motif chemokine 9	264	4	3	3	0.73 / 0.321 / 0.824 / 0.451 / 0.344
66	GCST90274783	C-X-C motif chemokine 6	447	8	7	7	0.785 / 0.92 / 0.541 / 0.897 / 0.936
67 ¶	GCST90274782	C-X-C motif chemokine 5	1178	7	6	6	0.26 / **0.01** / **0.03** / 0.332 / 0.069
68	GCST90274781	C-X-C motif chemokine 11	693	6	5	5	0.651 / 0.287 / 0.286 / 0.426 / 0.343
69	GCST90274780	C-X-C motif chemokine 10	221	6	6	6	0.946 / 0.916 / 0.787 / 0.815 / 0.852
70	GCST90274779	C-X-C motif chemokine 1	298	5	3	3	0.695 / 0.491 / 0.552 / 0.932 / 0.523
71	GCST90274778	Fractalkine	773	5	5	4 (rs671623)	0.453 / 0.154 / 0.505 / 0.355 / 0.246
72	GCST90274777	Cystatin D	2589	22	22	21 (rs516316)	0.466 / 0.125 / 0.28 / 0.413 / 0.125
73*	**GCST90274776**	**Macrophage colony-stimulating factor 1**	**177**	**1**	**1**	**1**	**0.952 (Wald ratio)**
74 ¶	GCST90274775	CUB domain-containing protein 1	1337	5	5	5	0.317 / **0.043** / 0.068 / 0.279 / 0.168
75	GCST90274774	T-cell surface glycoprotein CD6 isoform	765	12	12	12	0.597 / 0.637 / 0.834 / 0.605 / 0.612
76	GCST90274773	T-cell surface glycoprotein CD5	366	7	7	7	0.066 / 0.774 / 0.992 / 0.498 / 0.483
77	GCST90274772	CD40L receptor	451	6	5	5	0.2 / 0.078 / 0.111 / 0.462 / 0.141
78	GCST90274771	Natural killer cell receptor 2B4	521	8	7	7	0.705 / 0.811 / 0.922 / 0.926 / 0.804
79 ¶	GCST90274770	C-C motif chemokine 4	1616	11	10	10	0.606 / 0.082 / **0.012** / 0.162 / 0.097
80	GCST90274769	C-C motif chemokine 28	27	5	5	4 (rs291084)	0.948 / 0.461 / 0.764 / 0.397 / 0.437
81	GCST90274768	C-C motif chemokine 25	1552	19	18	17 (rs516316)	0.516 / 0.17 / 0.372 / 0.259 / 0.146

82	GCST90274767	C-C motif chemokine 23	541	9	9	9	0.199 / 0.779 / 0.415 / 0.645 / 0.058
83*	**GCST90274766**	**C-C motif chemokine 20**	**58**	**2**	**2**	**2**	**0.499 (IVW)**
84 ¶	GCST90274765	C-C motif chemokine 19	3119	8	8	6 (rs13010492, rs4766578)	0.69 / 0.183 / **0.03** / 0.381 / 0.428
85	GCST90274764	Eotaxin	339	7	6	6	0.174 / 0.197 / 0.531 / 0.386 / 0.322
86	GCST90274763	**Caspase 8**	89	1	1	1	0.239 (Wald ratio)
87*	**GCST90274762**	**beta-nerve growth factor**	**46**	**2**	**2**	**2**	**0.951 (IVW)**
88	GCST90274761	Axin-1	9	3	3	3	0.698 / 0.48 / 0.484 / 0.533 / 0.487
89 ¶	GCST90274760	Artemin	17	4	3	3	0.871 / 0.092 / **0.034** / 0.298 / 0.318
90	GCST90274759	Adenosine Deaminase	317	7	5	5	0.709 / 0.269 / 0.211 / 0.612 / 0.379
91*	**GCST90274758**	**Eukaryotic translation initiation factor 4E-binding protein 1**	**152**	**2**	**2**	**2**	**0.386 (IVW)**

***** Insufficient available SNPs (SNP≤2); ¶ Significant *p* value in IVW or default method ($p < 0.05$)

Supplementary Table SVI. Details of confirmed instrumental variables during the replication phase.

	Study accession	SNP	CHR:POS	effect_allele	other_allele	beta	se	*p*
26	GCST90274823	rs12075	1:159175354	A	G	0.00906609	0.0213681	0.671360831
		rs2228467	3:42906116	C	T	-0.0444547	0.0437504	0.309582926
		rs4146770	3:151048544	T	C	0.014292	0.0259537	0.581856647
		rs6505401	17:32566418	C	T	-0.0458994	0.0212809	0.031018443
		rs7116054	11:68891695	T	C	0.0216255	0.0265378	0.415132753
		rs7213460	17:32522613	A	G	-0.016776	0.0213447	0.43189383
49	GCST90274800	rs11256272	10:6038217	C	G	0.000698265	0.0332245	0.983232443
		rs11257090	10:6220725	A	G	0.00656616	0.0222188	0.767594758
		rs17144669	10:5874707	G	T	0.0711969	0.0923613	0.440794331
		rs2228059	rs2228059	G	T	-0.0203379	0.0211032	0.33517761
		rs2229135	10:5995052	T	C	0.0153932	0.037818	0.683982515
		rs36055263	10:6018970	G	A	-0.0381666	0.0212548	0.072547091
		rs667373	10:5939434	T	G	-0.0127686	0.0251437	0.611575389
67	GCST90274782	rs7137828	12:111932800	T	C	-0.0361965	0.0211621	0.087184644
		rs10821552	9:136939992	A	C	0.063505	0.022447	0.004667776
		rs425535	4:74863997	C	T	0.0831193	0.0326456	0.010893063
		rs6837786	4:74897105	C	G	0.0212503	0.0225311	0.345602599
		rs6993770	8:106581528	T	A	-0.0226363	0.0233606	0.332546974
		rs7090111	10:65077994	G	C	-0.000147805	0.0214383	0.994499067
		rs7636889	3:56874033	A	G	0.00695857	0.025058	0.781244549

		rs113308217	17:34823005	C	T	-0.0481016	0.0754903	0.524002067
		rs113341849	3:46384204	A	G	0.0460285	0.0334773	0.16915701
		rs12600678	17:34478231	C	T	-0.0152983	0.032462	0.637449816
		rs139925642	17:34823492	T	C	-0.0414734	0.115451	0.71942413
		rs140505982	3:46459749	T	C	0.0492864	0.0674861	0.465194959
79	GCST90274770	rs62069151	17:34986068	A	G	0.0369841	0.0354072	0.296237477
		rs79010839	17:34901949	T	C	0.0483591	0.0401949	0.228931208
		rs8064426	17:34819750	A	G	-0.0362257	0.0320319	0.258086329
		rs8065403	17:34463323	A	G	0.0198081	0.0318043	0.533408584
		rs9330240	17:34974689	C	T	0.0936866	0.0500903	0.061434171
		rs11574915	9:34710084	C	A	-0.0645815	0.0321997	0.044893142
		rs13010492	2:204776176	C	G	0.0386917	0.0211912	0.067875025
		rs150906309	6:32093029	C	T	0.200207	0.102399	0.05056267
84	GCST90274765	rs191795965	6:32455073	C	T	-0.00227475	0.0257469	0.929598041
		rs4766578	12:111904371	A	T	-0.0333311	0.0211452	0.114957418
		rs59142330	6:32624507	C	A	0.0329848	0.0271119	0.223748947
		rs62292952	3:132200719	G	T	0.0407929	0.0334637	0.222837358
		rs9469127	6:32444093	G	C	-0.0305964	0.0675864	0.650764719
		rs1329733	9:92208227	G	A	0.0255173	0.0211846	0.228387852
89	GCST90274760	rs62277657	3:111720183	A	G	0.0229133	0.0257112	0.37283442
		rs9684768	4:156930775	C	G	0.0354048	0.022135	0.109710704

Supplementary Table SVII. MR Analysis of six inflammatory proteins and osteomyelitis.(replication phase) (MR-Egger, Weighted median, Inverse variance weighted, Simple mode, Weighted mode)

Exposure-Outcome	SNP(n)	se	OR	95%CI	*p-value*	low	hi
Monocyte chemoattractant protein-3 (MCP-3) levels - Osteomyelitis	6						
MR Egger		0.196	0.933	0.635-1.371	0.743	0.635	1.371
Weighted median		0.106	0.862	0.7-1.061	0.162	0.7	1.061
Inverse variance weighted		0.088	0.822	0.692-0.976	**0.025**	0.692	0.976
Simple mode		0.139	0.857	0.653-1.124	0.316	0.653	1.124
Weighted mode		0.123	0.865	0.679-1.102	0.293	0.679	1.102
Interleukin-15 receptor subunit alpha (IL15RA) levels - Osteomyelitis	8						
MR Egger		0.082	1.051	0.895-1.233	0.569	0.895	1.233
Weighted median		0.05	1.082	0.982-1.194	0.085	0.982	1.194
Inverse variance weighted		0.042	1.088	1.001-1.183	**0.047**	1.001	1.183
Simple mode		0.087	1.073	0.904-1.274	0.409	0.904	1.274
Weighted mode		0.05	1.081	0.979-1.193	0.179	0.979	1.193
C-X-C motif chemokine 5 (CXCL5) levels - Osteomyelitis	6						
MR Egger		0.122	0.852	0.671-1.083	0.26	0.671	1.083
Weighted median		0.059	0.862	0.767-0.967	**0.01**	0.767	0.967
Inverse variance weighted		0.067	0.865	0.759-0.986	**0.03**	0.759	0.986
Simple mode		0.113	0.881	0.706-1.099	0.332	0.706	1.099
Weighted mode		0.062	0.857	0.759-0.968	0.069	0.759	0.968
C-C motif chemokine 4 (CCL4) levels - Osteomyelitis	10						
MR Egger		0.082	1.045	0.889-1.229	0.606	0.889	1.229
Weighted median		0.049	1.089	0.99-1.198	0.082	0.99	1.198
Inverse variance weighted		0.041	1.108	1.023-1.2	**0.012**	1.023	1.2
Simple mode		0.085	1.128	0.955-1.332	0.162	0.955	1.332
Weighted mode		0.047	1.09	0.994-1.195	0.097	0.994	1.195
C-C motif chemokine 19 (CCL19) levels - Osteomyelitis	6						
MR Egger		0.191	0.921	0.634-1.339	0.69	0.634	1.339
Weighted median		0.093	0.885	0.739-1.061	0.183	0.739	1.061

Inverse variance weighted		0.079	0.843	0.723-0.984	**0.03**	0.723	0.984
Simple mode		0.15	0.874	0.652-1.172	0.381	0.652	1.172
Weighted mode		0.104	0.912	0.744-1.119	0.428	0.744	1.119
Artemin (ARTN) levels - Osteomyelitis	3						
MR Egger		1.976	0.666	0.014-32.017	0.871	0.014	32.017
Weighted median		0.218	1.45	0.945-2.225	0.092	0.945	2.225
Inverse variance weighted		0.181	1.471	1.031-2.098	**0.034**	1.031	2.098
Simple mode		0.273	1.427	0.836-2.437	0.298	0.836	2.437
Weighted mode		0.24	1.415	0.883-2.266	0.318	0.883	2.266

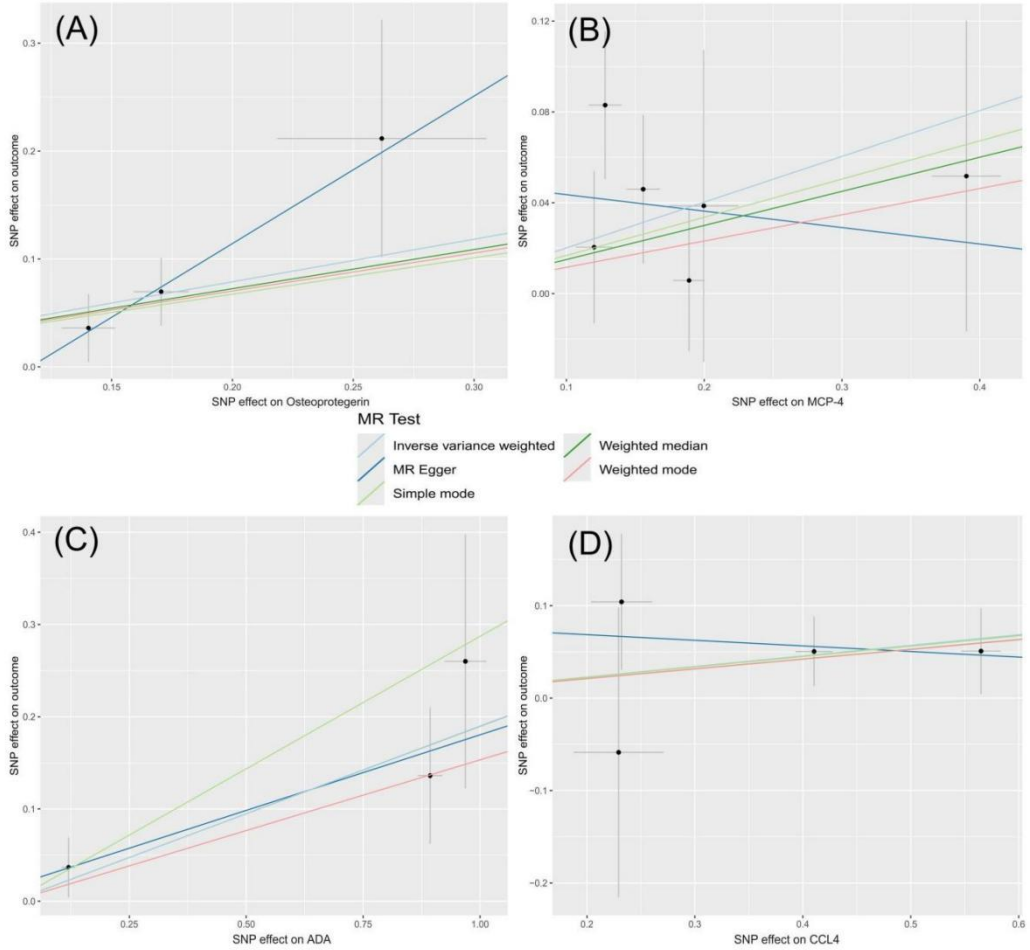
Supplementary Table SVIII. Heterogeneity of MR analysis for serum levels of circulating inflammatory proteins and osteomyelitis.

	Exposure	Outcome	Method	heterogeneity test		
				Q	Q_df	Q_*p value*
Discovery phase	Osteoprotegerin (OPG) levels	Osteomyelitis	MR-Egger	0.043	1	0.836
			Inverse variance weighted	1.361	2	0.506
	Monocyte chemoattractant protein-4 (MCP-4) levels	Osteomyelitis	MR-Egger	3.291	4	0.510
			Inverse variance weighted	4.551	5	0.473
	Adenosine Deaminase(ADA) levels	Osteomyelitis	MR-Egger	0.512	1	0.474
			Inverse variance weighted	0.697	2	0.706
	C-C motif chemokine 4 (CCL4) levels	Osteomyelitis	MR-Egger	0.93	2	0.628
			Inverse variance weighted	1.504	3	0.681
Replication phase	Monocyte chemoattractant protein-3 (MCP-3) levels	Osteomyelitis	MR-Egger	1.9	4	0.754
			Inverse variance weighted	2.428	5	0.787
	Interleukin-15 receptor subunit alpha (IL15RA) levels	Osteomyelitis	MR-Egger	3.982	6	0.679
			Inverse variance weighted	4.235	7	0.752
	C-X-C motif chemokine 5 (CXCL5) levels	Osteomyelitis	MR-Egger	8.386	4	0.078
			Inverse variance weighted	8.439	5	0.133
	C-C motif chemokine 4 (CCL4) levels	Osteomyelitis	MR-Egger	3.911	8	0.865
			Inverse variance weighted	4.571	9	0.87
	C-C motif chemokine 19 (CCL19) levels	Osteomyelitis	MR-Egger	5.316	4	0.256
			Inverse variance weighted	5.674	5	0.339
	Artemin (ARTN) levels	Osteomyelitis	MR-Egger	0.122	1	0.727
			Inverse variance weighted	0.284	2	0.868

Supplementary Table SIX. Results of the MR Horizontal pleiotropy analysis between circulating inflammatory proteins and osteomyelitis.

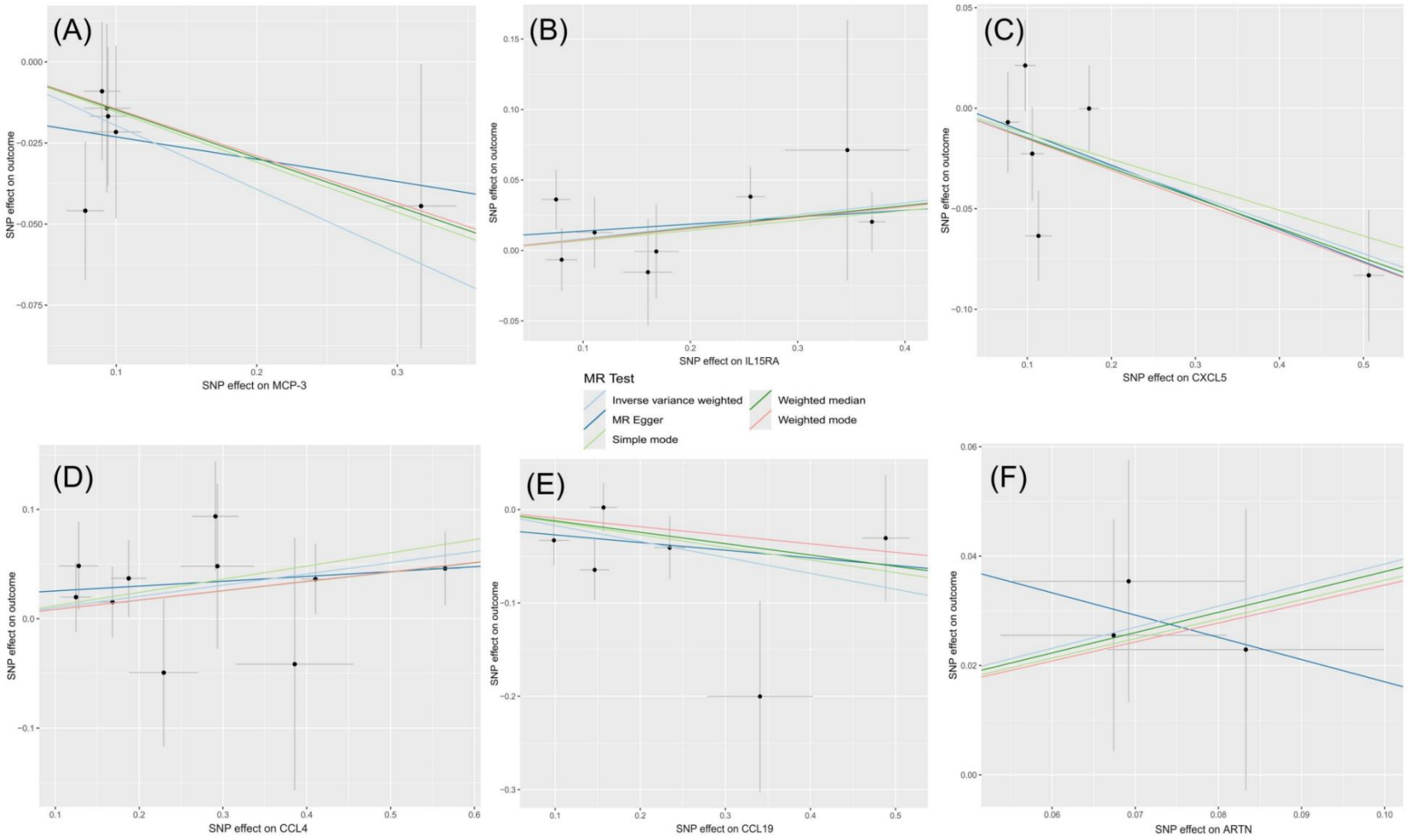
	Exposure	Outcome	horizontal pleiotropy		
			Egger_intercept	SE	*p*
Discovery phase	Osteoprotegerin (OPG) levels	Osteomyelitis	-0.159	0.138	0.456
	Monocyte chemoattractant protein-4 (MCP-4) levels	Osteomyelitis	0.051	0.045	0.324
	Adenosine Deaminase(ADA) levels	Osteomyelitis	0.017	0.039	0.741
	C-C motif chemokine 4 (CCL4) levels	Osteomyelitis	0.081	0.107	0.528
Replication phase	Monocyte chemoattractant protein-3 (MCP-3) levels	Osteomyelitis	-0.016	0.022	0.508
	Interleukin-15 receptor subunit alpha (IL15RA) levels	Osteomyelitis	0.009	0.018	0.633
	C-X-C motif chemokine 5 (CXCL5) levels	Osteomyelitis	0.004	0.023	0.882
	C-C motif chemokine 4 (CCL4) levels	Osteomyelitis	0.021	0.026	0.44
	C-C motif chemokine 19 (CCL19) levels	Osteomyelitis	-0.019	0.036	0.631
	Artemin (ARTN) levels	Osteomyelitis	0.058	0.143	0.756

Supplementary Figure S1. (I) Scatter plot of the association of four inflammatory proteins with osteomyelitis. (discovery phase) (II) Scatter plot of the association between six inflammatory proteins and osteomyelitis (replication phase)



(I) Scatter plot of the association of four inflammatory proteins with osteomyelitis. (discovery phase)

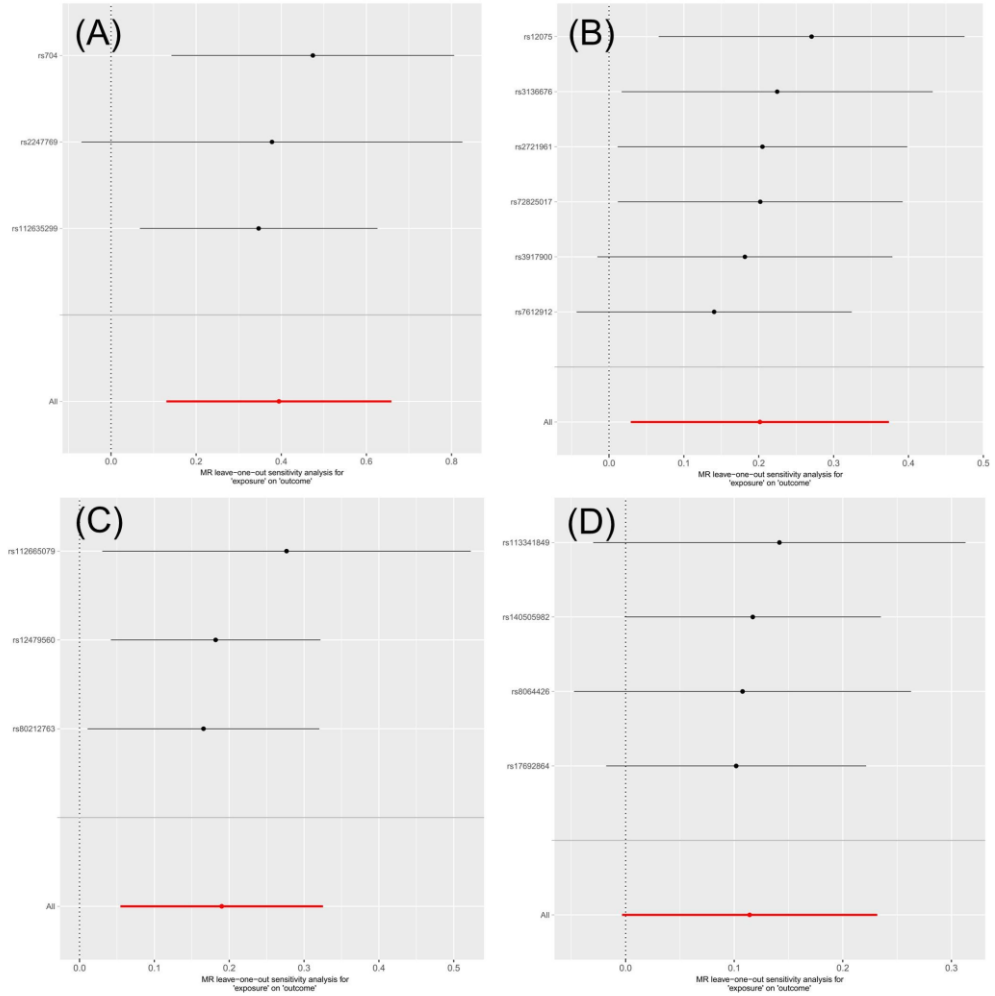
(A) Osteoprotegerin and osteomyelitis. (B) MCP-4 and osteomyelitis. (C) ADA and osteomyelitis. (D) CCL4 and osteomyelitis.



(II) Scatter plot of the association between six inflammatory proteins and osteomyelitis (replication phase).

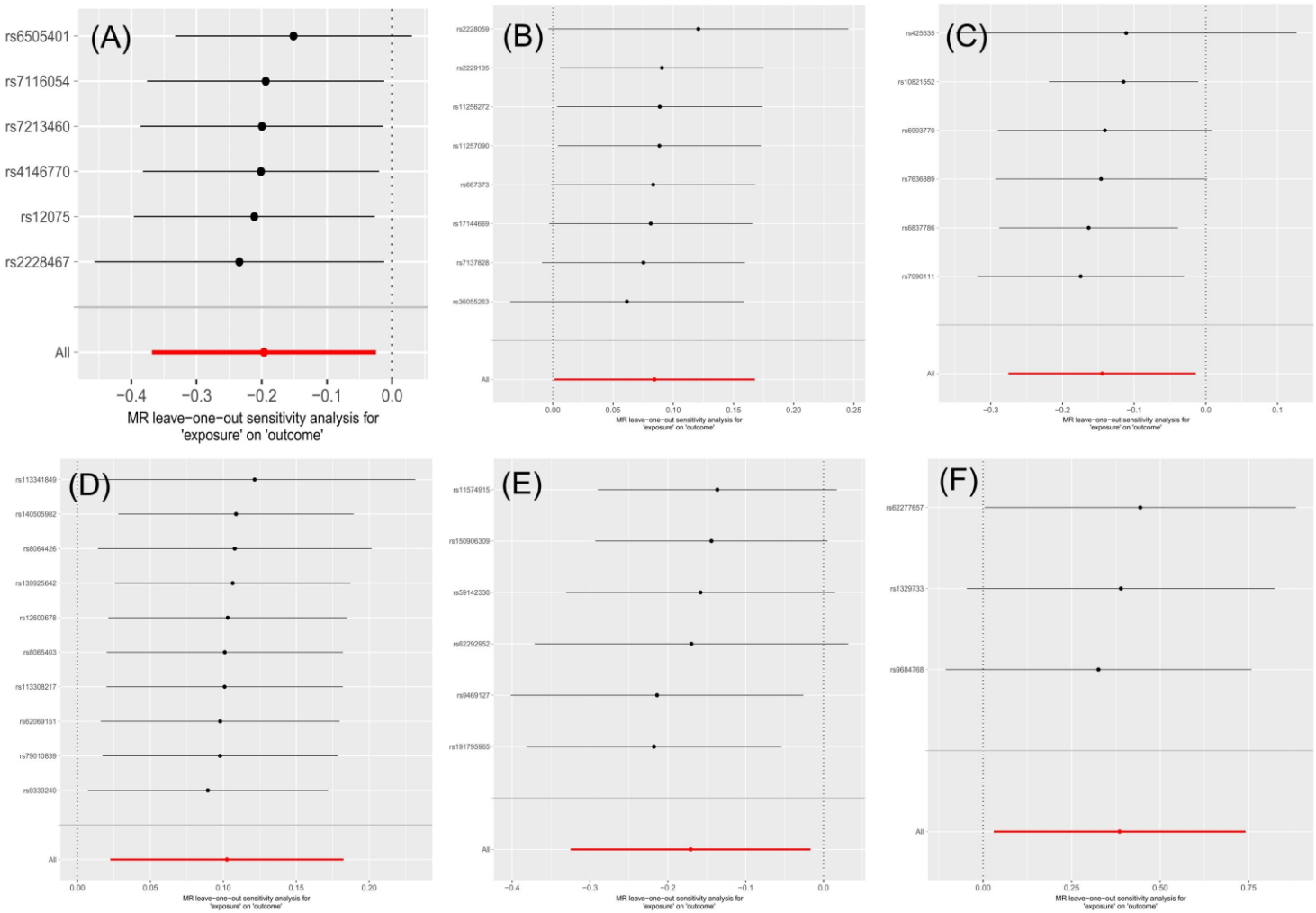
(A) MCP-3 and osteomyelitis. (B) IL15RA and osteomyelitis. (C) CXCL5 and osteomyelitis. (D) CCL4 and osteomyelitis. (E) CCL19 and osteomyelitis. (F) ARTN and osteomyelitis

Supplementary Figure S2. (I) “Leave-one-out” plot of four inflammatory proteins associated with osteomyelitis (discovery phase) (II) “Leave-one-out” plot of the association between six inflammatory proteins and osteomyelitis (replication phase)



(I) “Leave-one-out” plot of four inflammatory proteins associated with osteomyelitis (discovery phase)

(A) Osteoprotegerin on osteomyelitis. (B) MCP-4 on osteomyelitis. (C) ADA on osteomyelitis. (D) CCL4 on osteomyelitis.



(II) "Leave-one-out" plot of the association between six inflammatory proteins and osteomyelitis (replication phase)

(A) MCP-3 on osteomyelitis. (B) IL15RA on osteomyelitis. (C) CXCL5 on osteomyelitis. (D) CCL4 on osteomyelitis. (E) CCL19 on osteomyelitis. (F) ARTN on osteomyelitis.

Supplementary Figure S3-S12. PheWAS results for the inflammatory proteins. The bottom dashed line represented the suggestive line and the top dashed line was the significant line. Traits that exceeded the significant line were considered to be significantly associated with the gene regulating inflammatory proteins.

Figure S3. Binary traits associated with CCL4 in PheWAS

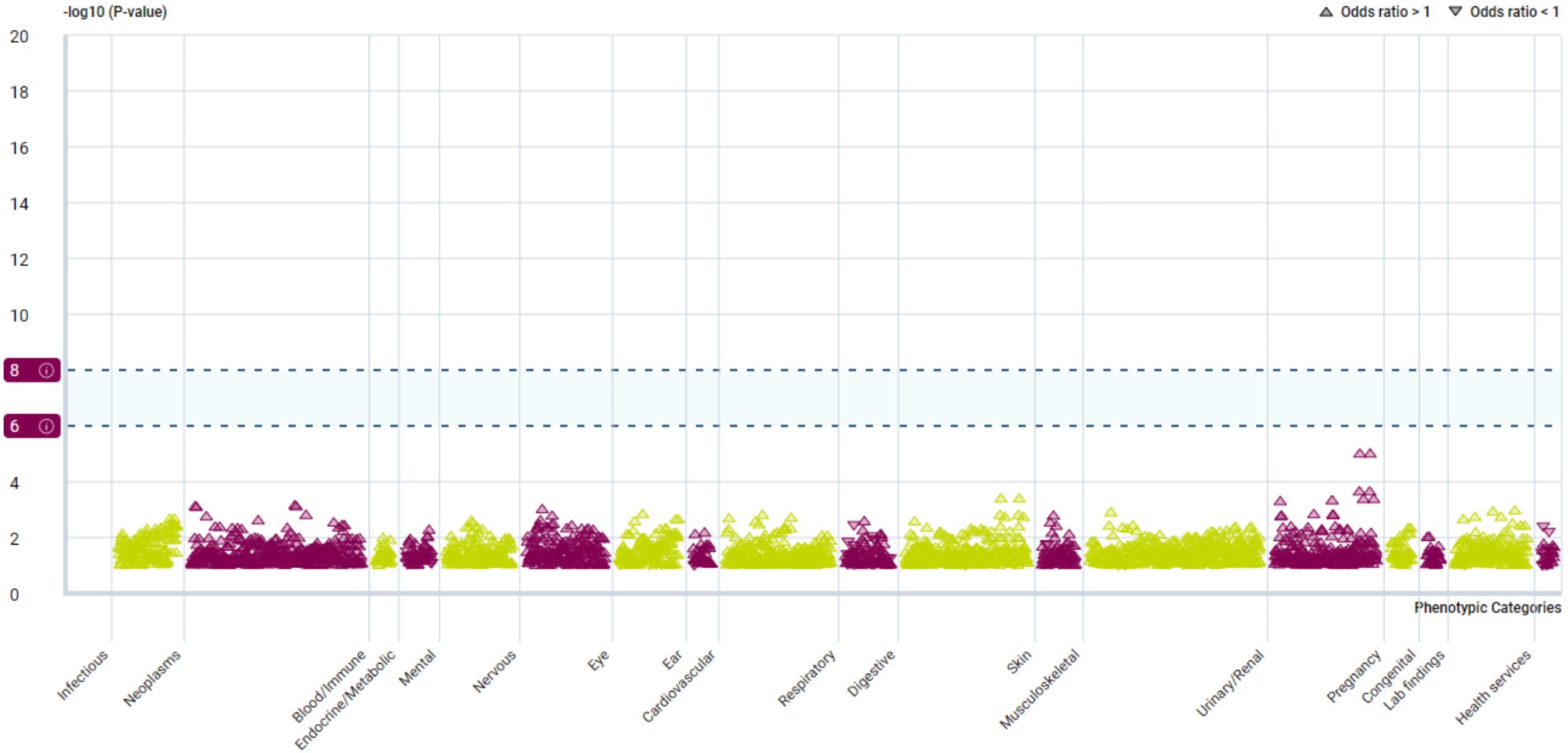


Figure S4. Continuous traits associated with CCL4 in PheWAS

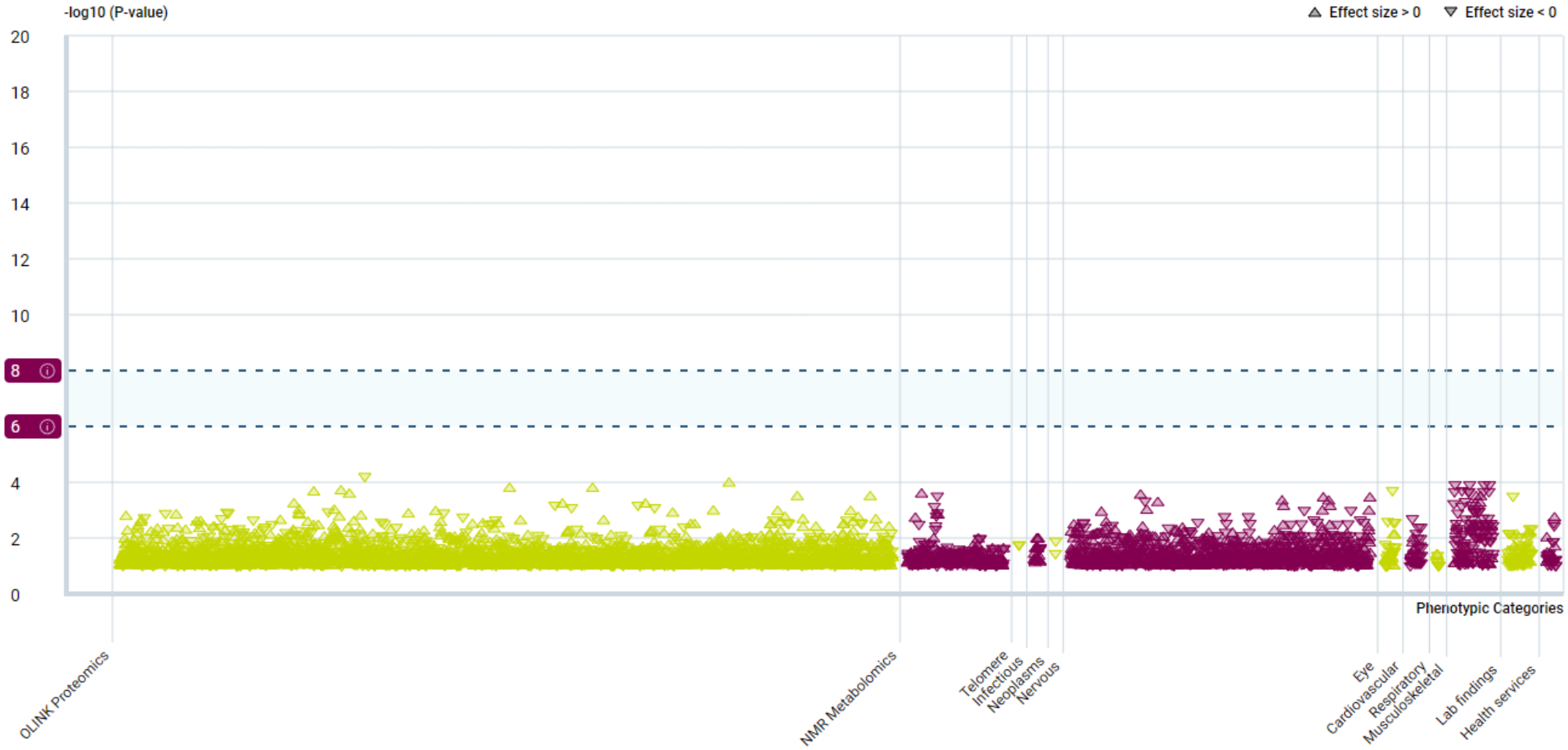


Figure S5. Binary traits associated with IL15RA in PheWAS

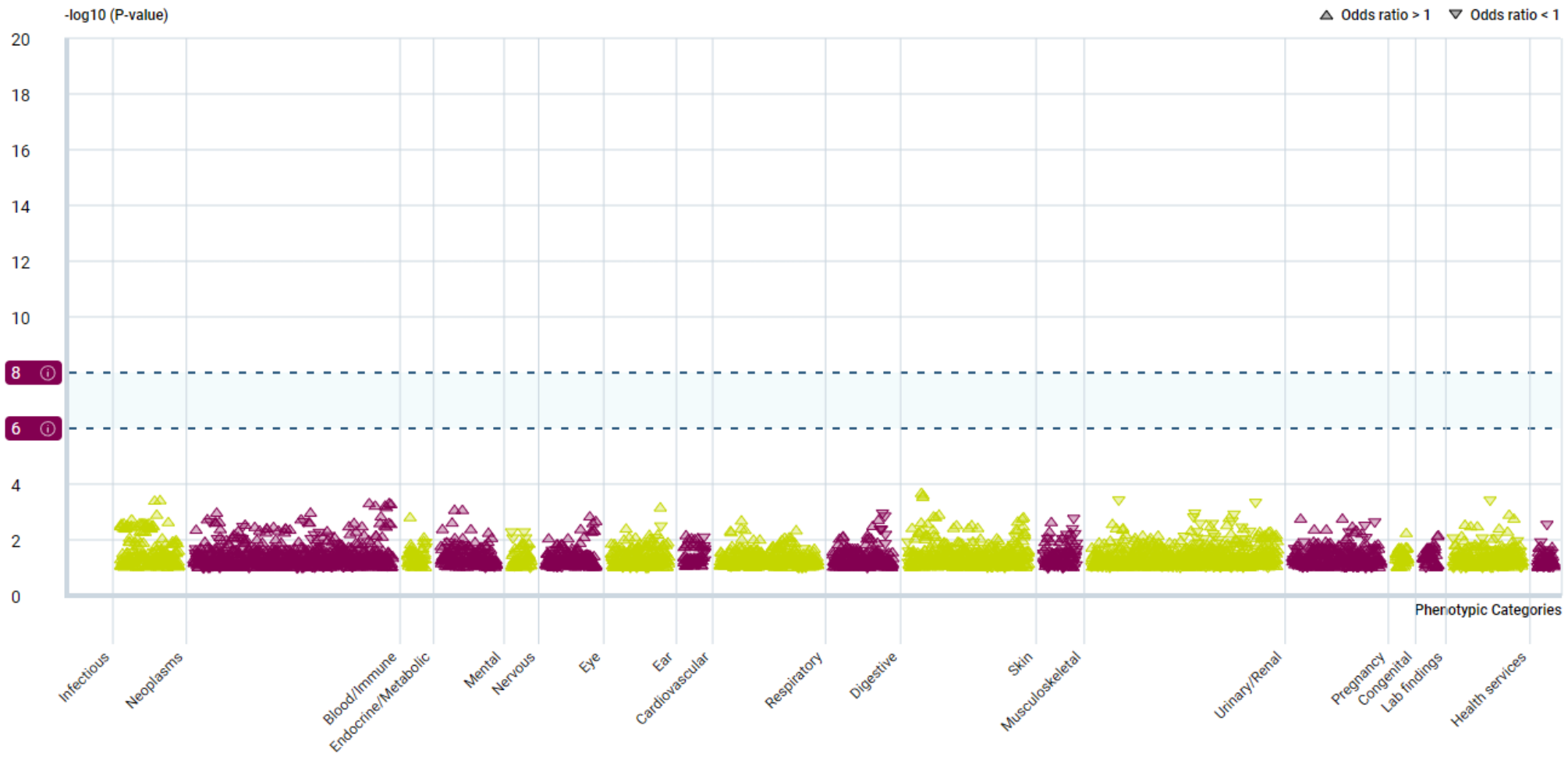


Figure S6. Continuous traits associated with IL15RA in PheWAS

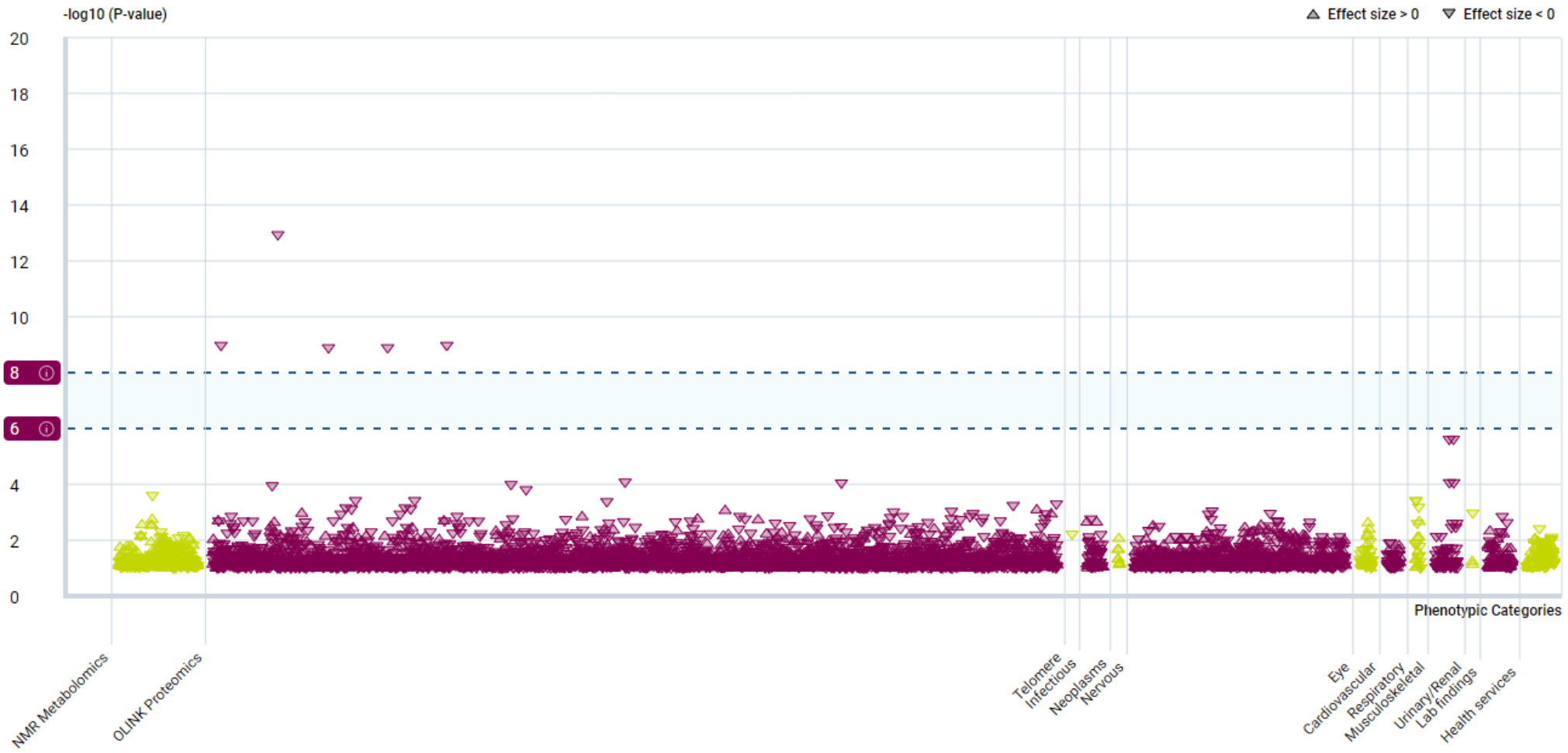


Figure S7. Binary traits associated with CXCL5 in PheWAS

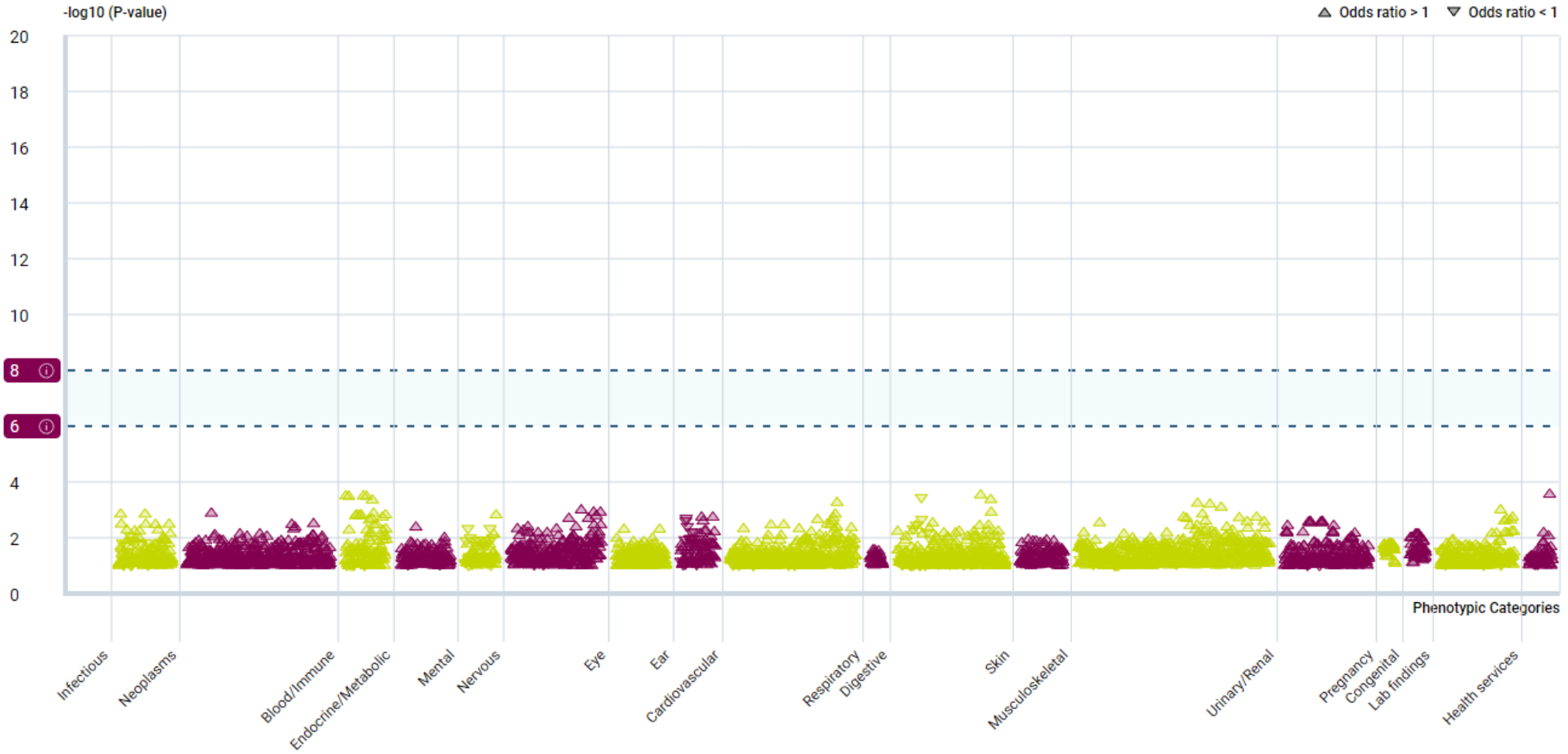


Figure S8. Continuous traits associated with CXCL5 in PheWAS

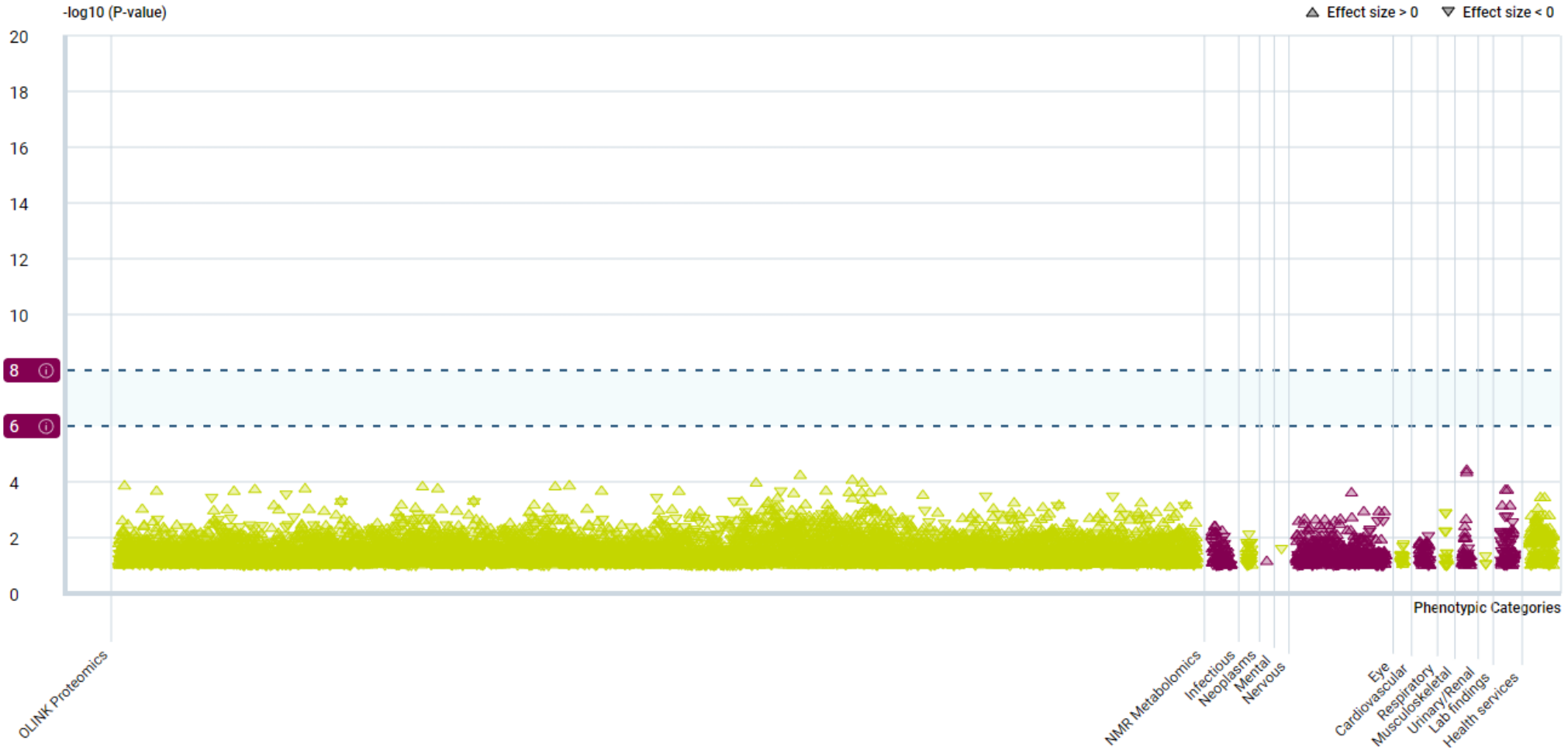


Figure S9. Binary traits associated with CCL19 in PheWAS

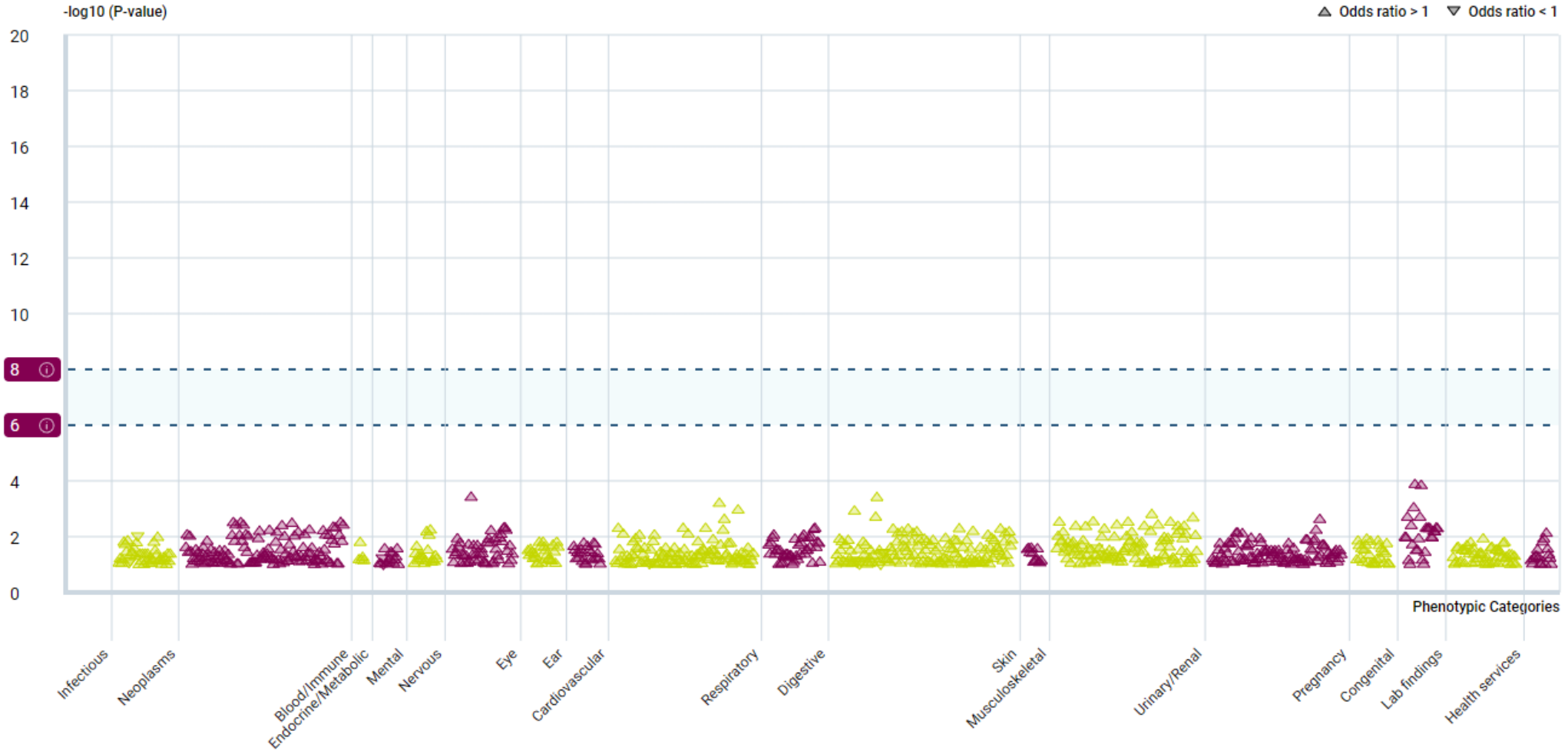


Figure S10. Continuous traits associated with CCL19 in PheWAS

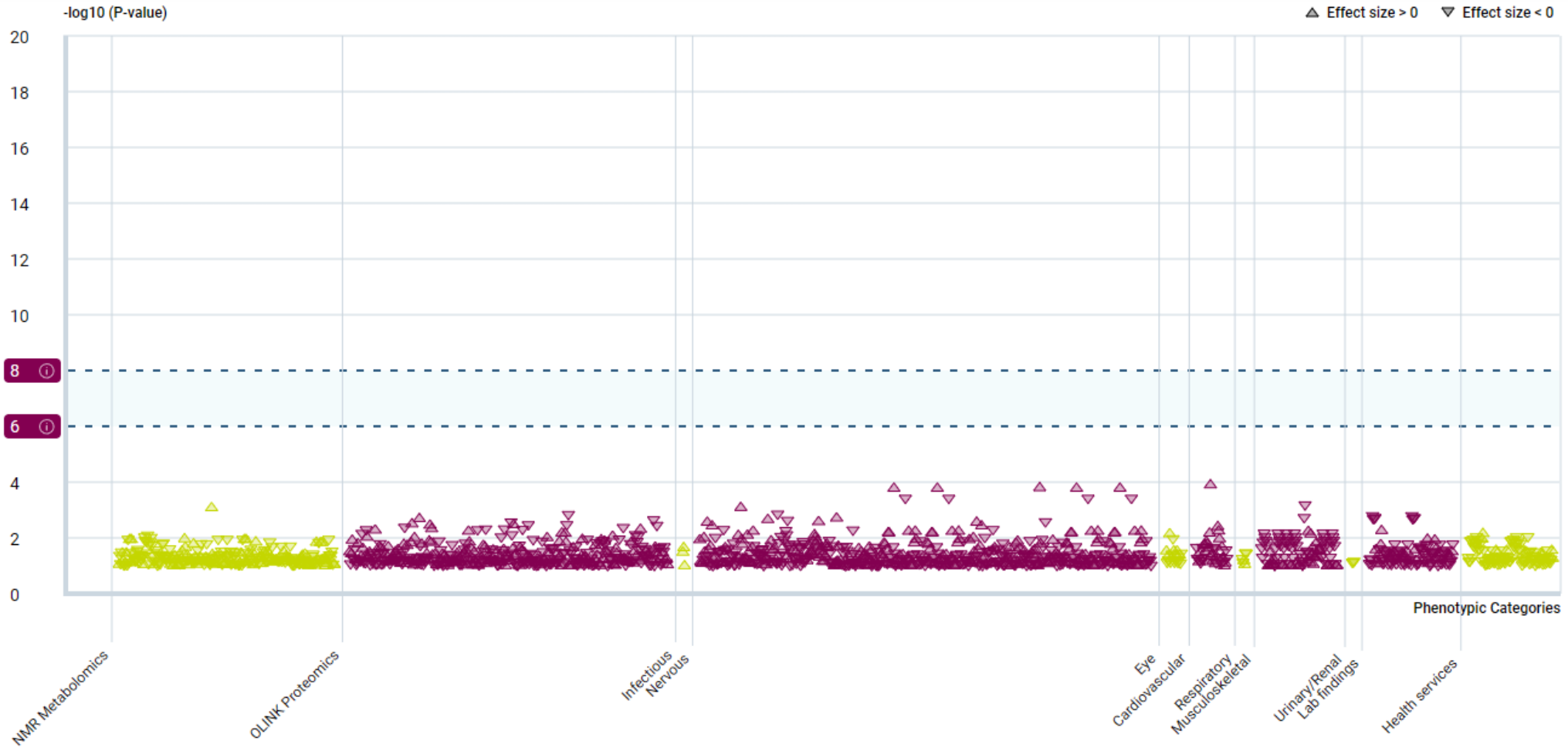


Figure S11. Binary traits associated with ARTN in PheWAS

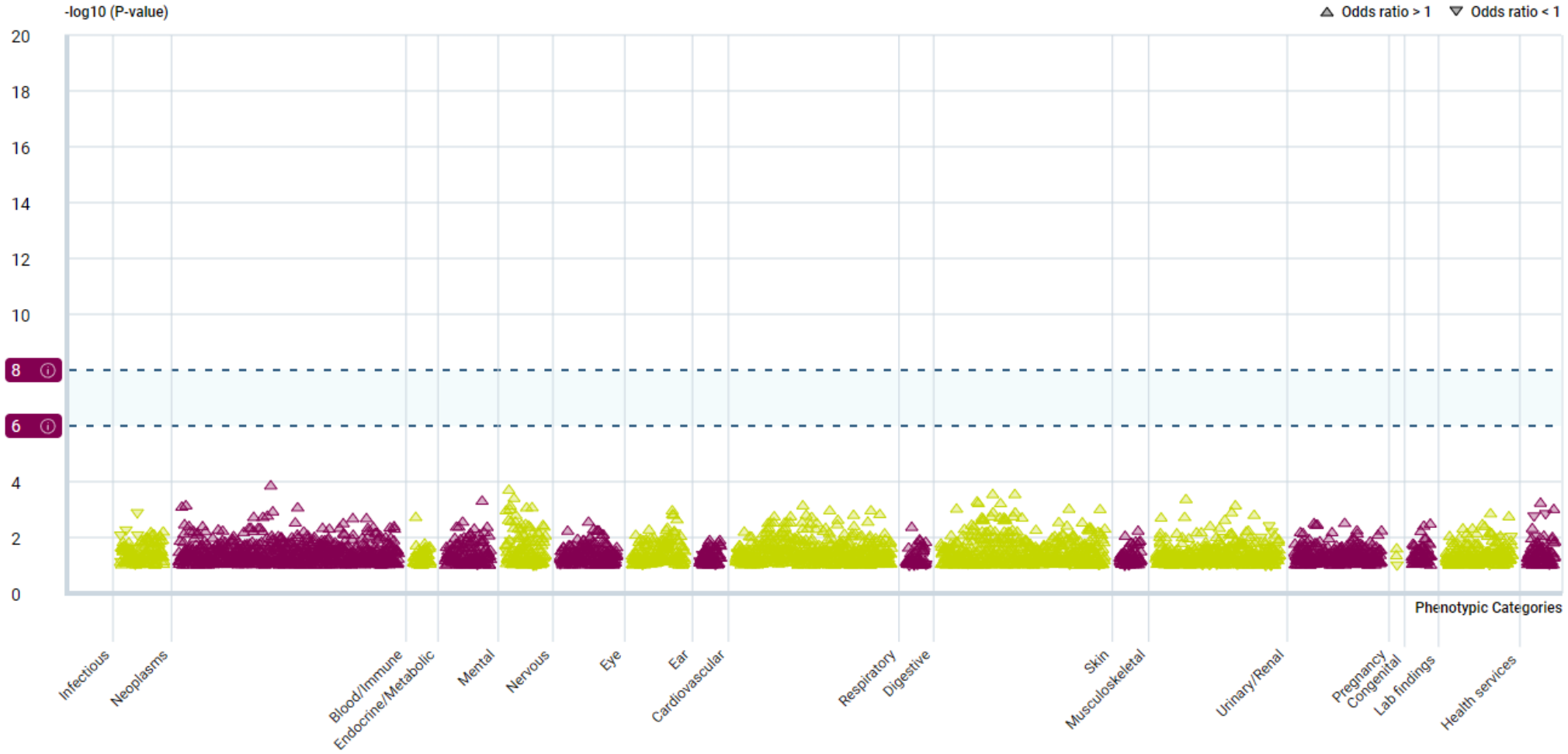
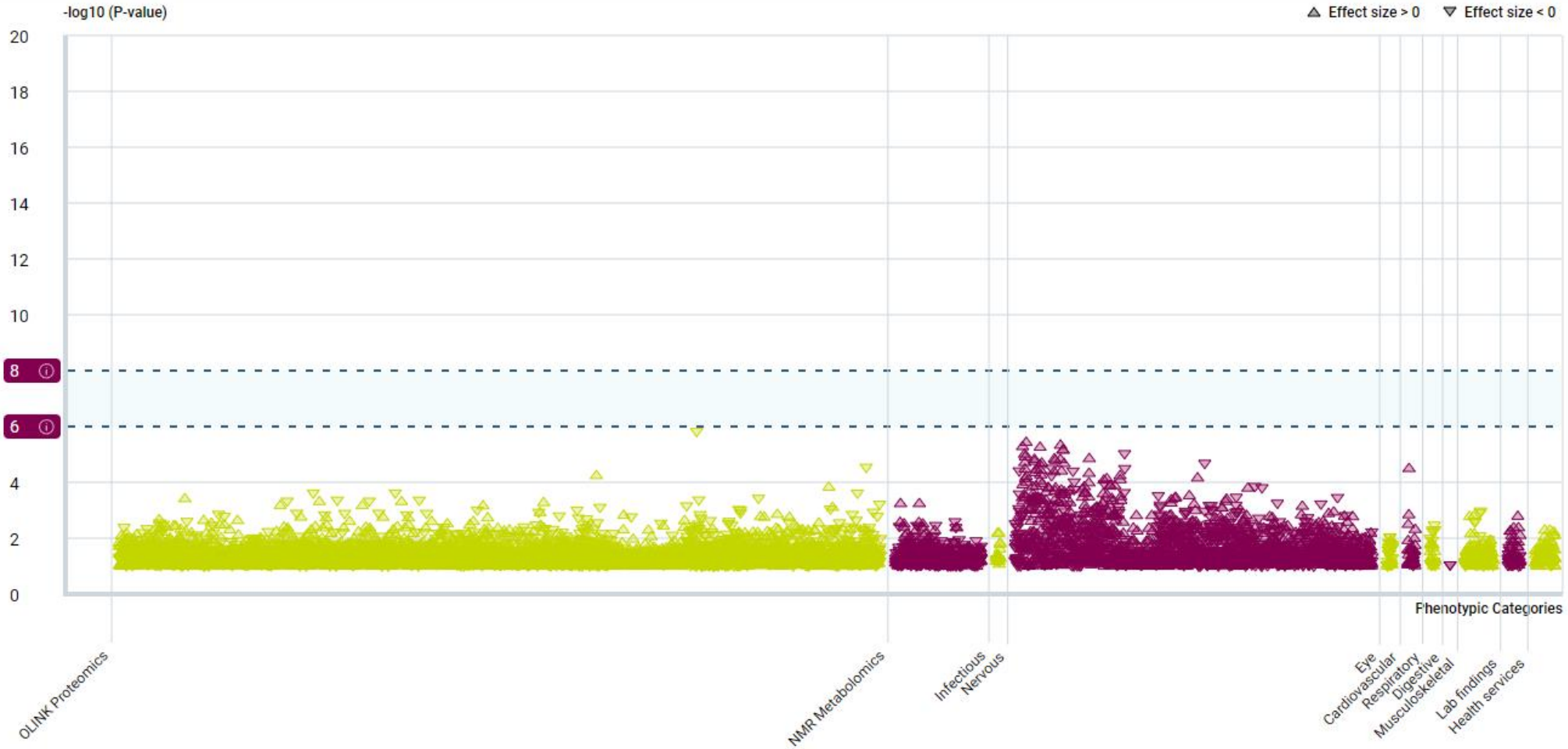



Figure S12. Continuous traits associated with ARTN in PheWAS