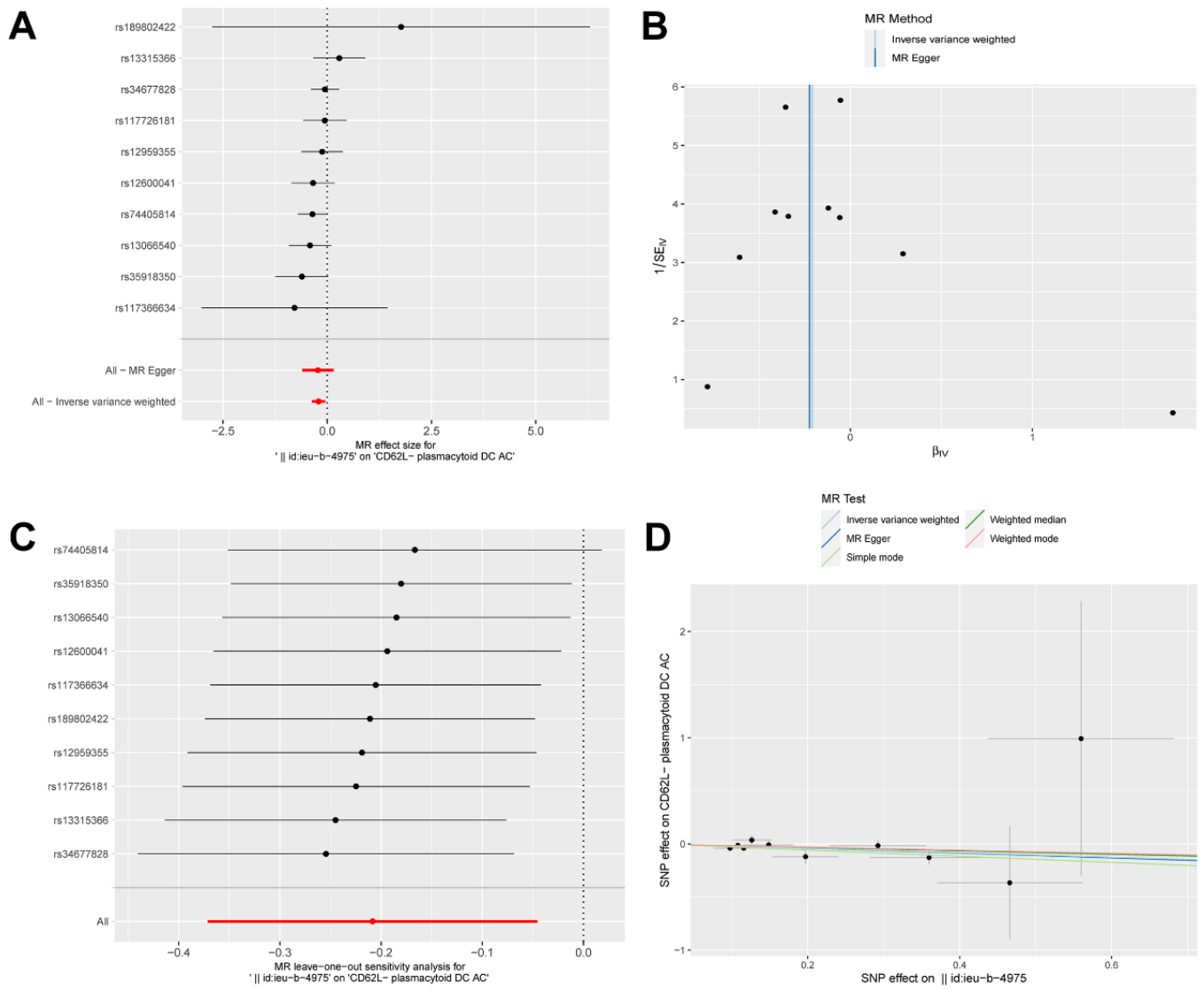


**Supplementary Figure S1. A** – MR leave-one-out sensitivity analysis and MR effect size for CD27 on switched memory B cells on osteomyelitis (OM). **B** – MR leave-one-out sensitivity analysis and MR effect size for CD62L- plasmacytoid dendritic cell absolute count on OM. **C** – MR leave-one-out sensitivity analysis and MR effect size for CD127 on CD8+ T cells on OM



**Supplementary Figure S2. A** – MR effect size for osteomyelitis (OM) on CD27 on switched memory B cells. **B** – Heterogeneity test. **C** – MR leave-one-out sensitivity analysis. **D** – Scatter plot

**Supplementary Table SI.** Pleiotropy tests in the causal relationship between the three immunophenotypes and OM

id.exposure	id.outcome	outcome	exposure	egger_intercept	se	pval
ebi-a-GCST90001927	ieu-b-4975	Osteomyelitis	CD127 on CD8br	-0.009620043	0.010021 3	0.348537 4
ebi-a-GCST90001470	ieu-b-4975	Osteomyelitis	CD62L- plasmacytoid DC AC	-0.022433362	0.011997 9	0.074883 4
ebi-a-GCST90001808	ieu-b-4975	Osteomyelitis	CD27 on sw mem	-0.024025256	0.013583 1	0.087828 9

**Supplementary Table SII.** Heterogeneity tests in the causal relationship between the three immunophenotypes and OM

id.exposure	id.outcome	outcome	exposure	method	Q	Q_df	Q_pval
ebi-a-GCST90001927	ieu-b-4975	Osteomyelitis	CD127 on CD8br	MR Egger	17.549 01	20	0.6170 902
ebi-a-GCST90001927	ieu-b-4975	Osteomyelitis	CD127 on CD8br	Inverse variance weighted	18.470 535	21	0.6190 64
ebi-a-GCST90001808	ieu-b-4975	Osteomyelitis	CD27 on sw mem	MR Egger	17.008 851	28	0.9484 138
ebi-a-GCST90001808	ieu-b-4975	Osteomyelitis	CD27 on sw mem	Inverse variance weighted	20.137 346	29	0.8886 064
ebi-a-GCST90001470	ieu-b-4975	Osteomyelitis	CD62L- plasmacytoid DC AC	MR Egger	9.6539 612	22	0.9891 801
ebi-a-GCST90001470	ieu-b-4975	Osteomyelitis	CD62L- plasmacytoid DC AC	Inverse variance weighted	13.149 998	23	0.9486 622

**Supplementary Table SIII.** Pleiotropy tests in the causal relationship between the nine plasma metabolites and OM

id.exposure	id.outcome	outcome	exposure	egger_intercept	se	pval
GCST9019-9636	ieu-b-4975	Osteomyelitis	Kynurenine levels	0.0080054	0.0199 789	0.6923 433
GCST9019-9713	ieu-b-4975	Osteomyelitis	Docosapentaenoate n3 DPA; 22:5n3 levels	0.016481	0.0153 558	0.2959 279
GCST9019-9958	ieu-b-4975	Osteomyelitis	1-linolenoyl-GPC (18:3) levels	0.0097542	0.0132 842	0.4691 127
GCST9019-9964	ieu-b-4975	Osteomyelitis	Etiocolanolone glucuronide levels	-0.002332	0.0103 603	0.8242 241
GCST9020-0049	ieu-b-4975	Osteomyelitis	Myristoyl dihydro sphingomyelin (d18:0/14:0) levels	-0.018701	0.0130 266	0.1622 04
GCST9020-0133	ieu-b-4975	Osteomyelitis	Heneicosapentaenoate (21:5n3) levels	-0.000213	0.0215 245	0.9922 429
GCST9020-0149	ieu-b-4975	Osteomyelitis	Ximenoylcarnitine (C26:1) levels	0.0112162	0.0130 68	0.3982 834
GCST9020-0237	ieu-b-4975	Osteomyelitis	Palmitoyl-sphingosine-phosphoethanolamine (d18:1/16:0) levels	0.0102072	0.0142 645	0.4811 637
GCST9020-0777	ieu-b-4975	Osteomyelitis	Uridine to cytidine ratio	0.0147402	0.0188 297	0.4433 823

**Supplementary Table SIV.** Heterogeneity tests in the causal relationship between the nine plasma metabolites and OM

id.exposure	id.outcome	outcome	exposure	method	Q	Q <sub>df</sub>	Q <sub>pval</sub>
GCST901-99636	ieu-b-4975	Osteomyelitis	Kynurenine levels	MR Egger	27.23 6449	23	0.246 0373
GCST901-99636	ieu-b-4975	Osteomyelitis	Kynurenine levels	Inverse variance weighted	27.42 6578	24	0.284 9653
GCST901-99713	ieu-b-4975	Osteomyelitis	Docosapentaenoate n3 DPA; 22:5n3 levels	MR Egger	15.08 3094	20	0.771 6334
GCST901-99713	ieu-b-4975	Osteomyelitis	Docosapentaenoate n3 DPA; 22:5n3 levels	Inverse variance weighted	16.23 5011	21	0.756 3047
GCST901-99958	ieu-b-4975	Osteomyelitis	1-linolenoyl-GPC (18:3) levels	MR Egger	23.69 1045	27	0.647 3933
GCST901-99958	ieu-b-4975	Osteomyelitis	1-linolenoyl-GPC (18:3) levels	Inverse variance weighted	24.23 0199	28	0.669 3285
GCST901-99964	ieu-b-4975	Osteomyelitis	Etiocolanolone glucuronide levels	MR Egger	18.31 9025	20	0.566 4014
GCST901-99964	ieu-b-4975	Osteomyelitis	Etiocolanolone glucuronide levels	Inverse variance weighted	18.36 9673	21	0.625 5053
GCST902-00049	ieu-b-4975	Osteomyelitis	Myristoyl dihydro sphingomyelin (d18:0/14:0) levels	MR Egger	21.35 0249	28	0.810 4466
GCST902-00049	ieu-b-4975	Osteomyelitis	Myristoyl dihydro sphingomyelin (d18:0/14:0) levels	Inverse variance weighted	23.41 1097	29	0.757 4026
GCST902-00133	ieu-b-4975	Osteomyelitis	Heneicosapentaenoate (21:5n3) levels	MR Egger	18.99 9615	14	0.164 964
GCST902-00133	ieu-b-4975	Osteomyelitis	Heneicosapentaenoate (21:5n3) levels	Inverse variance weighted	18.99 9748	15	0.213 7453
GCST902-00149	ieu-b-4975	Osteomyelitis	Ximenoylcarnitine (C26:1) levels	MR Egger	21.18 2179	27	0.777 682
GCST902-00149	ieu-b-4975	Osteomyelitis	Ximenoylcarnitine (C26:1) levels	Inverse variance weighted	21.91 8855	28	0.785 034
GCST902-00237	ieu-b-4975	Osteomyelitis	Palmitoyl-sphingosine-phosphoethanolamine (d18:1/16:0) levels	MR Egger	24.69 4299	24	0.422 522
GCST902-00237	ieu-b-4975	Osteomyelitis	Palmitoyl-sphingosine-phosphoethanolamine (d18:1/16:0) levels	Inverse variance weighted	25.22 1146	25	0.450 0362
GCST902-00777	ieu-b-4975	Osteomyelitis	Uridine to cytidine ratio	MR Egger	22.74 5958	19	0.248 7167
GCST902-00777	ieu-b-4975	Osteomyelitis	Uridine to cytidine ratio	Inverse variance weighted	23.47 958	20	0.265 864

**Supplementary Table SV. Mediated effect and mediated proportion**

<b>Immune cell</b>	<b>Metabolite</b>	<b>Outcome</b>	<b>Mediated effect</b>	<b>Mediated proportion</b>	<b>pvalue</b>
CD27 on sw mem	Palmitoyl-sphingosine-phosphoethanolamine (d18:1/16:0) levels	Osteomyelitis	0.00687 (0.000407, 0.0133)	11.2% (0.665%, 21.8%)	0.0372 189
CD127 on CD8br	Docosapentaenoate n3 DPA; 22:5n3 levels	Osteomyelitis	-0.00966 (-0.0179, -0.00143)	12.4% (22.9%, 1.84%)	0.0213 44
CD127 on CD8br	Ximenoylcarnitine (C26:1) levels	Osteomyelitis	-0.00562 (-0.011, -0.000251)	7.19% (14.1%, 0.322%)	0.0401 887