Supplementary Material

Supplementary Table 1. Data sources of the Mendelian randomization study

Trait	Instrumental SNPs	Sample Size	Ancestry	Access Link
MMP-1	7	16,889	European	https://www.ebi.ac.uk/gwas/studies/GCST90012033
MMP-3	8	20,791	European	https://www.ebi.ac.uk/gwas/studies/GCST90012027
MMP-7	5	18,245	European	https://www.ebi.ac.uk/gwas/studies/GCST90012056
MMP-8	2	6,049	European	https://www.ebi.ac.uk/gwas/studies/GCST005187
MMP-10	3	16,933	European	https://www.ebi.ac.uk/gwas/studies/GCST90012050
MMP-12	6	19,178	European	https://www.ebi.ac.uk/gwas/studies/GCST90012070
FA-BMD	–	8,143	European	https://www.ebi.ac.uk/gwas/studies/GCST005546
FN-BMD	–	32,735	European	https://www.ebi.ac.uk/gwas/studies/GCST005544
LS-BMD	–	28,498	European	https://www.ebi.ac.uk/gwas/studies/GCST005545

Abbreviations: BMD, bone mineral density; FA, forearm; FN, femoral neck; LS, lumbar spine; MMP; matrix metalloproteinase; SNP, single nucleotide polymorphism.

Supplementary Table 2. Summary statistics utilized in the Mendelian randomization study of MMP-1 on BMD

Site-specific BMD	SNP	Position	EA/ OA	*F*-statistic	Association with MMP-1			Association with BMD		
					Beta	Se	*P*-value	Beta	Se	*P*-value
FA-BMD	rs12141791	1:156419786	A/G	49	0.083	0.013	6.40×10^{-10}	0.018	0.017	0.301
FA-BMD	rs12290253	11:102642261	T/C	211	-0.200	0.015	2.00×10^{-41}	0.005	0.019	0.812
FA-BMD	rs17297226	11:102795639	A/G	144	0.150	0.013	5.80×10^{-29}	0.023	0.019	0.228
FA-BMD	rs186356272	11:102190948	T/G	141	0.460	0.064	9.90×10^{-13}	-0.077	0.088	0.389
FA-BMD	rs2958130*	12:57140506	A/G	44	0.076	0.012	4.60×10^{-11}	0.002	0.016	0.907
FA-BMD	rs471994	11:102697731	A/G	1086	-0.360	0.011	3.50×10^{-228}	-0.007	0.016	0.685
FA-BMD	rs6993770	8:106581528	A/T	96	0.120	0.012	4.60×10^{-23}	-0.002	0.017	0.903
FN-BMD	rs12141791	1:156419786	A/G	49	0.083	0.013	6.40×10^{-10}	0.011	0.008	0.201
FN-BMD	rs12290253	11:102642261	T/C	211	-0.200	0.015	2.00×10^{-41}	0.008	0.009	0.384
FN-BMD	rs17297226	11:102795639	A/G	144	0.150	0.013	5.80×10^{-29}	-0.007	0.009	0.416
FN-BMD	rs186356272	11:102190948	T/G	141	0.460	0.064	9.90×10^{-13}	-0.062	0.042	0.152
FN-BMD	rs2958130*	12:57140506	A/G	44	0.076	0.012	4.60×10^{-11}	-0.017	0.008	0.034
FN-BMD	rs471994	11:102697731	A/G	1086	-0.360	0.011	3.50×10^{-228}	0.001	0.008	0.884
FN-BMD	rs6993770	8:106581528	A/T	96	0.120	0.012	4.60×10^{-23}	0.002	0.008	0.788
LS-BMD	rs12141791	1:156419786	A/G	49	0.083	0.013	6.40×10^{-10}	0.003	0.010	0.768

LS-BMD	rs12290253	11:102642261	T/C	211	-0.200	0.015	2.00×10^{-41}	-0.009	0.011	0.415
LS-BMD	rs17297226	11:102795639	A/G	144	0.150	0.013	5.80×10^{-29}	-0.009	0.010	0.419
LS-BMD	rs186356272	11:102190948	T/G	141	0.460	0.064	9.90×10^{-13}	-0.060	0.048	0.224
LS-BMD	rs2958130*	12:57140506	A/G	44	0.076	0.012	4.60×10^{-11}	0.004	0.009	0.674
LS-BMD	rs471994	11:102697731	A/G	1086	-0.360	0.011	3.50×10^{-228}	0.006	0.009	0.507
LS-BMD	rs6993770	8:106581528	A/T	96	0.120	0.012	4.60×10^{-23}	0.008	0.010	0.401

Note: To measure the strength of instrumental variables of MMP-1, nested functions in the *TwoSampleMR* package were utilized to calculate *F*-statistic and I^2_{GX}(99.5%), where $F < 10$ and $I^2 < 90\%$ indicated that overall MR estimates from multiple variants should be interpreted with caution due to potential bias. * For rs2958130, a proxy SNP (rs7980317, chr12:57158183, $r^2 = 0.92$) in the summary statistics of BMD was utilized.

Abbreviations: BMD, bone mineral density; FA, forearm; FN, femoral neck; EA/OA, effect allele/Other allele; LS, lumbar spine; MMP-1; matrix metalloproteinase 1; SE, standard error; SNP, single nucleotide polymorphism.

Supplementary Table 3. Summary statistics utilized in the Mendelian randomization study of MMP-3 on BMD

Site-specific BMD	SNP	Position	EA/ OA	*F*-statistic	Association with MMP-3			Association with BMD		
					Beta	Se	*P*-value	Beta	Se	*P*-value
FA-BMD	rs11225452	11:102760774	A/T	44	-0.077	0.012	2.40×10^{-11}	-0.020	0.019	0.293
FA-BMD	rs11668189	19:54754103	A/C	1086	-0.056	0.010	2.70×10^{-8}	-0.010	0.016	0.527
FA-BMD	rs1291326	11:102556321	T/C	96	-0.170	0.016	6.40×10^{-28}	-0.002	0.027	0.943
FA-BMD	rs145541733	11:102677129	T/C	45	-0.390	0.054	8.80×10^{-13}	0.074	0.078	0.352
FA-BMD	rs2267373	22:38600542	T/C	30	0.057	0.010	3.00×10^{-9}	0.035	0.017	0.037
FA-BMD	rs4614414	11:103535890	T/C	89	-0.086	0.014	2.30×10^{-10}	0.031	0.019	0.113
FA-BMD	rs632478	11:102715681	T/G	63	-0.480	0.009	5.4×10^{-647}	0.004	0.015	0.822
FA-BMD	rs74973608	11:103244932	A/G	33	-0.120	0.017	5.50×10^{-12}	0.003	0.032	0.936
FN-BMD	rs11225452	11:102760774	A/T	55	-0.077	0.012	2.40×10^{-11}	-0.001	0.009	0.934
FN-BMD	rs11668189	19:54754103	A/C	2705	-0.056	0.010	2.70×10^{-8}	-0.011	0.008	0.193
FN-BMD	rs1291326	11:102556321	T/C	41	-0.170	0.016	6.40×10^{-28}	-0.005	0.013	0.732
FN-BMD	rs145541733	11:102677129	T/C	45	-0.390	0.054	8.80×10^{-13}	0.029	0.040	0.475
FN-BMD	rs2267373	22:38600542	T/C	30	0.057	0.010	3.00×10^{-9}	0.019	0.009	0.049
FN-BMD	rs4614414	11:103535890	T/C	89	-0.086	0.014	2.30×10^{-10}	0.017	0.010	0.079
FN-BMD	rs632478	11:102715681	T/G	63	-0.480	0.009	5.4×10^{-647}	-0.003	0.008	0.713

FN-BMD	rs74973608	11:103244932	A/G	33	-0.120	0.017	5.50×10^{-12}	-0.005	0.015	0.739
LS-BMD	rs11225452	11:102760774	A/T	55	-0.077	0.012	2.40×10^{-11}	-0.006	0.011	0.606
LS-BMD	rs11668189	19:54754103	A/C	2705	-0.056	0.010	2.70×10^{-8}	0.010	0.009	0.313
LS-BMD	rs1291326	11:102556321	T/C	41	-0.170	0.016	6.40×10^{-28}	-0.008	0.016	0.612
LS-BMD	rs145541733	11:102677129	T/C	45	-0.390	0.054	8.80×10^{-13}	0.012	0.047	0.808
LS-BMD	rs2267373	22:38600542	T/C	30	0.057	0.010	3.00×10^{-9}	0.012	0.011	0.284
LS-BMD	rs4614414	11:103535890	T/C	89	-0.086	0.014	2.30×10^{-10}	0.006	0.011	0.565
LS-BMD	rs632478	11:102715681	T/G	63	-0.480	0.009	5.4×10^{-647}	-0.006	0.009	0.475
LS-BMD	rs74973608	11:103244932	A/G	33	-0.120	0.017	5.50×10^{-12}	-0.010	0.018	0.597

Note: To measure the strength of instrumental variables of MMP-3, nested functions in the *TwoSampleMR* package were utilized to calculate *F*-statistic and I^2_{GX}(99.7%), where $F < 10$ and $I^2 < 90\%$ indicated that overall MR estimates from multiple variants should be interpreted with caution due to potential bias.

Abbreviation: BMD, bone mineral density; FA, forearm; FN, femoral neck; EA/OA, effect allele/Other allele; LS, lumbar spine; MMP-3; matrix metalloproteinase 3; SE, standard error; SNP, single nucleotide polymorphism.

Supplementary Table 4. Summary statistics utilized in the Mendelian randomization study of MMP-7 on BMD

Site-specific BMD	SNP	Position	EA/ OA	*F*-statistic	Association with MMP-7			Association with BMD		
					Beta	Se	*P*-value	Beta	Se	*P*-value
FA-BMD	rs11607749	11:102446374	T/C	45	-0.077	0.012	4.20×10^{-10}	0.009	0.017	0.607
FA-BMD	rs17884405	11:102398434	T/C	308	-0.220	0.018	1.90×10^{-37}	0.250	0.103	0.018
FA-BMD	rs62133135	19:54753202	T/C	37	0.065	0.011	9.30×10^{-9}	0.011	0.016	0.510
FA-BMD	rs7946641	11:102415001	A/G	109	0.110	0.012	5.90×10^{-19}	-0.038	0.016	0.016
FA-BMD	rs9427716	1:202012252	T/C	69	0.087	0.012	2.00×10^{-12}	-0.012	0.016	0.449
FN-BMD	rs11607749	11:102446374	T/C	45	-0.077	0.012	4.20×10^{-10}	-0.006	0.008	0.488
FN-BMD	rs17884405	11:102398434	T/C	308	-0.220	0.018	1.90×10^{-37}	0.003	0.048	0.954
FN-BMD	rs62133135	19:54753202	T/C	37	0.065	0.011	9.30×10^{-9}	0.012	0.008	0.132
FN-BMD	rs7946641	11:102415001	A/G	109	0.110	0.012	5.90×10^{-19}	-0.002	0.008	0.755
FN-BMD	rs9427716	1:202012252	T/C	69	0.087	0.012	2.00×10^{-12}	-0.004	0.008	0.637
LS-BMD	rs11607749	11:102446374	T/C	45	-0.077	0.012	4.20×10^{-10}	-0.017	0.010	0.086
LS-BMD	rs17884405	11:102398434	T/C	308	-0.220	0.018	1.90×10^{-37}	-0.046	0.053	0.399
LS-BMD	rs62133135	19:54753202	T/C	37	0.065	0.011	9.30×10^{-9}	-0.006	0.009	0.509
LS-BMD	rs7946641	11:102415001	A/G	109	0.110	0.012	5.90×10^{-19}	-0.004	0.009	0.631

LS-BMD	rs9427716	1:202012252	T/C	69	0.087	0.012	2.00×10^{-12}	0.003	0.009	0.709

Note: To measure the strength of instrumental variables of MMP-7, nested functions in the *TwoSampleMR* package were utilized to calculate *F*-statistic and I^2_{GX} (99.3%), where $F < 10$ and $I^2 < 90\%$ indicated that overall MR estimates from multiple variants should be interpreted with caution due to potential bias.

Abbreviation: BMD, bone mineral density; FA, forearm; FN, femoral neck; EA/OA, effect allele/Other allele; LS, lumbar spine; MMP-7; matrix metalloproteinase 7; SE, standard error; SNP, single nucleotide polymorphism.

Supplementary Table 5. Summary statistics utilized in the Mendelian randomization study of MMP-8 on BMD

Site-specific BMD	SNP	Position	EA/ OA	*F*-statistic	Association with MMP-8			Association with BMD		
					Beta	Se	*P*-value	Beta	Se	*P*-value
FA-BMD	rs1560833	1:153334525	A/G	59	-0.155	0.020	5.31×10^{-15}	0.007	0.017	0.693
FA-BMD	rs800292*	1:196642233	A/G	151	-0.241	0.020	2.42×10^{-35}	0.085	0.019	0.001
FN-BMD	rs1560833	1:153334525	A/G	59	-0.155	0.020	5.31×10^{-15}	0.001	0.008	0.990
FN-BMD	rs800292*	1:196642233	A/G	151	-0.241	0.020	2.42×10^{-35}	0.025	0.009	0.005
LS-BMD	rs1560833	1:153334525	A/G	59	-0.155	0.020	5.31×10^{-15}	0.006	0.010	0.521
LS-BMD	rs800292*	1:196642233	A/G	151	-0.241	0.020	2.42×10^{-35}	0.033	0.010	0.002

Note: To measure the strength of instrumental variables of MMP-8, nested functions in the *TwoSampleMR* package were utilized to calculate *F*-statistic and I^2_{GX} (89.5%), where $F < 10$ and $I^2 < 90\%$ indicated that overall MR estimates from multiple variants should be interpreted with caution due to potential bias. * For rs800292, a proxy SNP (rs559350, chr1:196642533, $r^2 = 1.0$) in the summary statistics of BMD was utilized.

Abbreviation: BMD, bone mineral density; FA, forearm; FN, femoral neck; EA/OA, effect allele/Other allele; LS, lumbar spine; MMP-8; matrix metalloproteinase 8; SE, standard error; SNP, single nucleotide polymorphism.

Supplementary Table 6. Summary statistics utilized in the Mendelian randomization study of MMP-10 on BMD

Site-specific BMD	SNP	Position	EA/ OA	*F*-statistic	Association with MMP-10			Association with BMD		
					Beta	Se	*P*-value	Beta	Se	*P*-value
FA-BMD	rs3129886	6:32410576	T/C	32	-0.071	0.013	4.40×10^{-8}	0.037	0.021	0.085
FA-BMD	rs55930209	11:102608999	A/C	84	-0.260	0.032	4.10×10^{-16}	0.014	0.042	0.742
FA-BMD	rs601338*	19:49206674	A/G	122	0.120	0.011	6.30×10^{-28}	-0.044	0.016	0.006
FN-BMD	rs55930209	11:102608999	A/C	84	-0.260	0.032	4.10×10^{-16}	0.064	0.020	0.002
FN-BMD	rs601338*	19:49206674	A/G	122	0.120	0.011	6.30×10^{-28}	-0.007	0.009	0.432
LS-BMD	rs55930209	11:102608999	A/C	84	-0.260	0.032	4.10×10^{-16}	0.015	0.024	0.534
LS-BMD	rs601338*	19:49206674	A/G	122	0.120	0.011	6.30×10^{-28}	-0.017	0.011	0.126

Note: To measure the strength of instrumental variables of MMP-10, nested functions in the *TwoSampleMR* package were utilized to calculate *F*-statistic and I^2_{GX}(99.6%), where $F < 10$ and $I^2 < 90\%$ indicated that overall MR estimates from multiple variants should be interpreted with caution due to potential bias. * For rs601338, a proxy SNP (rs676388, chr19:49211969, $r^2 = 0.85$) in the summary statistics of BMD was utilized.

Abbreviation: BMD, bone mineral density; FA, forearm; FN, femoral neck; EA/OA, effect allele/Other allele; LS, lumbar spine; MMP-10; matrix metalloproteinase 10; SE, standard error; SNP, single nucleotide polymorphism.

Supplementary Table 7. Summary statistics utilized in the Mendelian randomization study of MMP-12 on BMD

Site-specific BMD	SNP	Position	EA/ OA	*F*-statistic	Association with MMP-12			Association with BMD		
					Beta	Se	*P*-value	Beta	Se	*P*-value
FA-BMD	rs111850229	11:102789864	T/C	118	0.270	0.026	4.90×10^{-26}	0.031	0.037	0.422
FA-BMD	rs117953762	13:72450627	T/C	47	-0.250	0.046	3.40×10^{-8}	-0.048	0.063	0.453
FA-BMD	rs12975366*	19:54759361	T/C	59	0.080	0.011	3.70×10^{-14}	-0.008	0.016	0.626
FA-BMD	rs185686655	11:102787261	T/C	300	0.270	0.018	9.20×10^{-50}	-0.050	0.036	0.175
FA-BMD	rs72981675	11:102721251	T/C	3194	-0.770	0.014	4.8×10^{-640}	0.016	0.023	0.506
FA-BMD	rs72987587	11:102907759	T/G	96	-0.210	0.022	8.70×10^{-21}	-0.035	0.034	0.314
FN-BMD	rs111850229	11:102789864	T/C	118	0.270	0.026	4.90×10^{-26}	-0.020	0.018	0.289
FN-BMD	rs117953762	13:72450627	T/C	47	-0.250	0.046	3.40×10^{-8}	0.000	0.031	0.989
FN-BMD	rs12975366*	19:54759361	T/C	59	0.080	0.011	3.70×10^{-14}	0.006	0.008	0.485
FN-BMD	rs185686655	11:102787261	T/C	300	0.270	0.018	9.20×10^{-50}	-0.003	0.018	0.871
FN-BMD	rs72981675	11:102721251	T/C	3194	-0.770	0.014	4.8×10^{-640}	0.009	0.011	0.449
FN-BMD	rs72987587	11:102907759	T/G	96	-0.210	0.022	8.70×10^{-21}	0.030	0.017	0.073
LS-BMD	rs111850229	11:102789864	T/C	118	0.270	0.026	4.90×10^{-26}	0.006	0.021	0.796
LS-BMD	rs117953762	13:72450627	T/C	47	-0.250	0.046	3.40×10^{-8}	-0.024	0.036	0.524
LS-BMD	rs12975366*	19:54759361	T/C	59	0.080	0.011	3.70×10^{-14}	-0.010	0.009	0.264

LS-BMD	rs185686655	11:102787261	T/C	300	0.270	0.018	9.20×10^{-50}	0.012	0.022	0.582
LS-BMD	rs72981675	11:102721251	T/C	3194	-0.770	0.014	4.8×10^{-640}	0.005	0.013	0.700
LS-BMD	rs72987587	11:102907759	T/G	96	-0.210	0.022	8.70×10^{-21}	0.007	0.019	0.706

Note: To measure the strength of instrumental variables of MMP-10, nested functions in the *TwoSampleMR* package were utilized to calculate *F*-statistic and I^2_{GX}(99.8%), where $F < 10$ and $I^2 < 90\%$ indicated that overall MR estimates from multiple variants should be interpreted with caution due to potential bias. * For rs12975366, a proxy SNP (rs10405357, chr19:54759666, $r^2 = 0.80$) in the summary statistics of BMD was utilized.

Abbreviation: BMD, bone mineral density; FA, forearm; FN, femoral neck; EA/OA, effect allele/Other allele; LS, lumbar spine; MMP-12; matrix metalloproteinase 12; SE, standard error; SNP, single nucleotide polymorphism.

Supplementary Table 8. Mendelian randomization results for causal effects of matrix metalloproteinases on FA-BMD

Traits	No. of SNPs	Effect (95% CI)	*P*-value	Heterogeneity I^2	*P*-value	MR-Egger intercept	*P*-value
MMP-1							
Inverse-variance weighted	7	0.021 (-0.048, 0.091)	0.549	0	0.771		
Weighted median	7	0.014 (-0.068, 0.095)	0.742				
MR-Egger regression	7	-0.024 (-0.156, 0.108)	0.738			0.011	0.466
MMP-3							
Inverse-variance weighted	8	-0.005 (-0.074, 0.065)	0.896	27.55%	0.209		
Weighted median	8	-0.007 (-0.071, 0.057)	0.828				
MR-Egger regression	8	-0.044 (-0.140, 0.053)	0.410			0.013	0.306
MMP-7							
Inverse-variance weighted	5	-0.218 (-0.461, 0.025)	0.079	46.45%	0.113		
Weighted median	5	-0.180 (-0.407, 0.048)	0.122				
MR-Egger regression	5	-1.247 (-2.045, -0.449)	0.055			0.093	0.081

MMP-8							
Inverse-variance weighted	2	-0.252 (-0.535, 0.032)	0.082	80.72%	0.023		
Weighted median	2	NA	NA				
MR-Egger regression	2	NA	NA			NA	NA
MMP-10							
Inverse-variance weighted	3	-0.271 (-0.504, -0.038)	0.023	35.31%	0.213		
Weighted median	3	-0.272 (-0.496, -0.049)	0.017				
MR-Egger regression	3	0.105 (-0.374, 0.583)	0.743			-0.051	0.344
MMP-12							
Inverse-variance weighted	6	-0.016 (-0.070, 0.039)	0.575	0	0.464		
Weighted median	6	-0.017 (-0.076, 0.041)	0.558				
MR-Egger regression	6	-0.017 (-0.102, 0.068)	0.720			0.001	0.971

Note: Weighted median and MR-Egger regression methods were available when there were sufficient instrumental variables ($n \geq 3$).

Abbreviations: BMD, bone mineral density; FA, forearm; MMP, matrix metalloproteinase; SNP, single nucleotide polymorphism.

Supplementary Table 9. Mendelian randomization results for causal effects of matrix metalloproteinases on FN-BMD

Traits	No. of SNPs	Effect (95% CI)	*P*-value	Heterogeneity I^2	*P*-value	MR-Egger intercept	*P*-value
MMP-1							
Inverse-variance weighted	7	-0.018 (-0.059, 0.024)	0.402	33.98%	0.169		
Weighted median	7	-0.012 (-0.050, 0.025)	0.511				
MR-Egger regression	7	-0.004 (-0.089, 0.080)	0.922			-0.003	0.732
MMP-3							
Inverse-variance weighted	8	0.006 (-0.027, 0.040)	0.708	28.30%	0.202		
Weighted median	8	0.006 (-0.024, 0.036)	0.694				
MR-Egger regression	8	-0.009 (-0.058, 0.041)	0.748			0.005	0.440
MMP-7							
Inverse-variance weighted	5	0.017 (-0.070, 0.104)	0.697	0	0.549		
Weighted median	5	-0.021 (-0.130, 0.089)	0.713				
MR-Egger regression	5	-0.237 (-0.624, 0.150)	0.316			0.023	0.278

MMP-8							
Inverse-variance weighted	2	-0.073 (-0.168, 0.023)	0.135	61.17%	0.109		
Weighted median	2	NA	NA				
MR-Egger regression	2	NA	NA			NA	NA
MMP-10							
Inverse-variance weighted	3	-0.145 (-0.327, 0.038)	0.120	67.14%	0.081		
Weighted median	2	NA	NA				
MR-Egger regression	2	NA	NA			NA	NA
MMP-12							
Inverse-variance weighted	6	-0.016 (-0.042, 0.010)	0.238	0	0.511		
Weighted median	6	-0.011 (-0.039, 0.017)	0.430				
MR-Egger regression	6	-0.016 (-0.056, 0.024)	0.469			0.001	0.982

Note: Weighted median and MR-Egger regression methods were available when there were sufficient instrumental variables ($n \geq 3$).

Abbreviations: BMD, bone mineral density; FN, femoral neck; MMP, matrix metalloproteinase; SNP, single nucleotide polymorphism.

Supplementary Table 10. **Mendelian randomization results for causal effects of matrix metalloproteinases on LS-BMD**

Traits	No. of SNPs	Effect (95% CI)	*P*-value	Heterogeneity I^2	*P*-value	MR-Egger intercept	*P*-value
MMP-1							
Inverse-variance weighted	7	-0.007 (-0.046, 0.032)	0.718	0	0.639		
Weighted median	7	-0.006 (-0.051, 0.039)	0.792				
MR-Egger regression	7	-0.042 (-0.116, 0.032)	0.319			0.008	0.330
MMP-3							
Inverse-variance weighted	8	0.013 (-0.020, 0.047)	0.430	0	0.842		
Weighted median	8	0.014 (-0.021, 0.050)	0.437				
MR-Egger regression	8	0.014 (-0.034, 0.062)	0.584			0.000	0.973
MMP-7							
Inverse-variance weighted	5	0.028 (-0.077, 0.134)	0.599	8.68%	0.357		
Weighted median	5	0.000 (-0.124, 0.124)	1.000				
MR-Egger regression	5	0.038 (-0.496, 0.572)	0.898			-0.001	0.973

MMP-8							
Inverse-variance weighted	2	-0.107 (-0.194, -0.019)	0.017	37.98%	0.204		
Weighted median	2	NA	NA				
MR-Egger regression	2	NA	NA			NA	NA
MMP-10							
Inverse-variance weighted	3	-0.099 (-0.223, 0.025)	0.118	0	0.521		
Weighted median	2	NA	NA				
MR-Egger regression	2	NA	NA			NA	NA
MMP-12							
Inverse-variance weighted	6	-0.006 (-0.036, 0.025)	0.721	0	0.806		
Weighted median	6	-0.005 (-0.038, 0.027)	0.746				
MR-Egger regression	6	0.006 (-0.038, 0.051)	0.800			-0.006	0.519

Note: Weighted median and MR-Egger regression methods were available when there were sufficient instrumental variables ($n \geq 3$).

Abbreviations: BMD, bone mineral density; MMP, matrix metalloproteinase; LS, lumbar spine; SNP, single nucleotide polymorphism.