

Causal relationship of obstructive sleep apnea with bone mineral density and the role of BMI

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Table S1: Statistical power calculations for the results of OSA on BMD

Exposure	Outcome	Instrumental variable	Sample size	R2 of exposure by genetic variants	Causal effect (β according to IVW)	Significance level	Power
OSA	TB-BMD	5	217,955	0.09%	-0.053	0.05	11.20%
OSA	TB-BMD (age 0–15)	5	217,955	0.09%	0.033	0.05	6.70%
OSA	TB-BMD (age 15–30)	5	217,955	0.09%	0.053	0.05	11.20%
OSA	TB-BMD (age 30–45)	5	217,955	0.09%	-0.080	0.05	20.10%
OSA	TB-BMD (age 45–60)	5	217,955	0.09%	-0.116	0.05	36.90%
OSA	TB-BMD (age ≥ 60)	5	217,955	0.09%	-0.069	0.05	16%
OSA	LS-BMD	4	217,955	0.09%	0.079	0.05	19.70%
OSA	FN-BMD	4	217,955	0.09%	-0.022	0.05	4.90%
OSA	FA-BMD	4	217,955	0.09%	0.236	0.05	91.10%
OSA	HBMD	5	217,955	0.09%	0.097	0.05	27.40%

OSA: Obstructive sleep apnea; TB-BMD: total body bone mineral density; LS-BMD: Lumbar spine bone mineral density; FN-BMD: Femoral neck bone mineral density; FA-BMD: Forearm bone mineral density; HBMD: Heel bone mineral density; IVW: inverse-variance weighted

Table S2. 5 SNPs represented genetically predicted OSA

SNP	A1	A2	EAF	Beta	SE	P value	r2	F-statistic
rs10928560	T	C	0.1949	-0.0878	0.0158	2.80E-08	0.00014166	30.88
rs4837016	A	G	0.4662	-0.0706	0.0125	1.53E-08	0.00014634	31.90
rs10507084	T	C	0.1793	0.1085	0.0163	2.80E-11	0.00020325	44.31
rs9937053	A	G	0.4298	0.102	0.0125	4.32E-16	0.00030541	66.59
rs142006783	C	T	0.0377	0.1783	0.0327	4.81E-08	0.00013639	29.73

SNP, single nucleotide polymorphism; A1, effect allele; A2, other allele; EAF, effect allele frequency; SE, standard error; OSA, obstructive sleep apnea;

Table S3: MR analysis results of OSA on BMD.

Exposure	Outcome	IVs	IVW		MR-Egger		Weighted Median		Weighted Mode	
			β (95% CI)	<i>P</i> value	β (95% CI)	<i>P</i> value	β (95% CI)	<i>P</i> value	β (95% CI)	<i>P</i> value
OSA	TB-BMD	5	-0.05 (-0.13,0.03)	0.187	-0.05 (-0.54,0.43)	0.841	-0.09 (-0.19,0.01)	0.072	-0.11(-0.22,0.00)	0.133
OSA	TB-BMD (age 0–15)	5	0.03 (-0.13,0.20)	0.688	0.19 (-0.66,1.05)	0.690	0.00 (-0.20,0.20)	0.990	-0.01 (-0.24,0.22)	0.917
OSA	TB-BMD (age 15–30)	5	0.05 (-0.28,0.38)	0.751	-0.3 (-2.31,1.71)	0.788	0.05 (-0.36, 0.46)	0.808	-0.30 (-0.08,0.20)	0.305
OSA	TB-BMD (age 30–45)	5	-0.08 (-0.25,0.19)	0.554	-0.61 (-2.04,0.83)	0.469	-0.10 (-0.34,0.14)	0.434	-0.07 (-0.31,0.17)	0.597
OSA	TB-BMD (age 45–60)	5	-0.12 (-0.27,0.04)	0.147	-0.12 (-1.05,0.82)	0.819	-0.17 (-0.35,0.02)	0.078	-0.21 (-0.40, -0.01)	0.105
OSA	TB-BMD (age \geq 60)	5	-0.07 (-0.19,0.06)	0.280	0.14 (-0.53,0.82)	0.710	-0.08 (-0.22,0.06)	0.281	-0.08 (-0.24,0.08)	0.396
OSA	LS-BMD	4	0.08 (-0.08,0.24)	0.337	0.40 (-0.39,1.19)	0.429	0.08 (-0.10,0.26)	0.380	0.07 (-0.13,0.27)	0.551
OSA	FN-BMD	4	-0.02 (-0.21,0.16)	0.813	0.15 (-0.85,1.15)	0.796	0.00 (-0.17,0.17)	0.999	-0.01 (-0.23,0.21)	0.938
OSA	FA-BMD	4	0.26 (0.06,0.41)	0.009	-0.32 (-1.39,0.75)	0.619	0.22 (0.03,0.40)	0.023	0.27 (0.06,0.48)	0.084
OSA	HBMD	5	0.10 (0.02,0.18)	0.018	0.07 (-0.43,0.57)	0.791	0.07 (0.01,0.13)	0.041	0.01(-0.16,0.17)	0.946

OSA: Obstructive sleep apnea; TB-BMD: total body bone mineral density; LS-BMD: Lumbar spine bone mineral density; FN-BMD: Femoral neck bone mineral density; FA-BMD: Forearm bone mineral density; HBMD: Heel bone mineral density; IVs: Instrumental variable; CI: Confidence Interval.

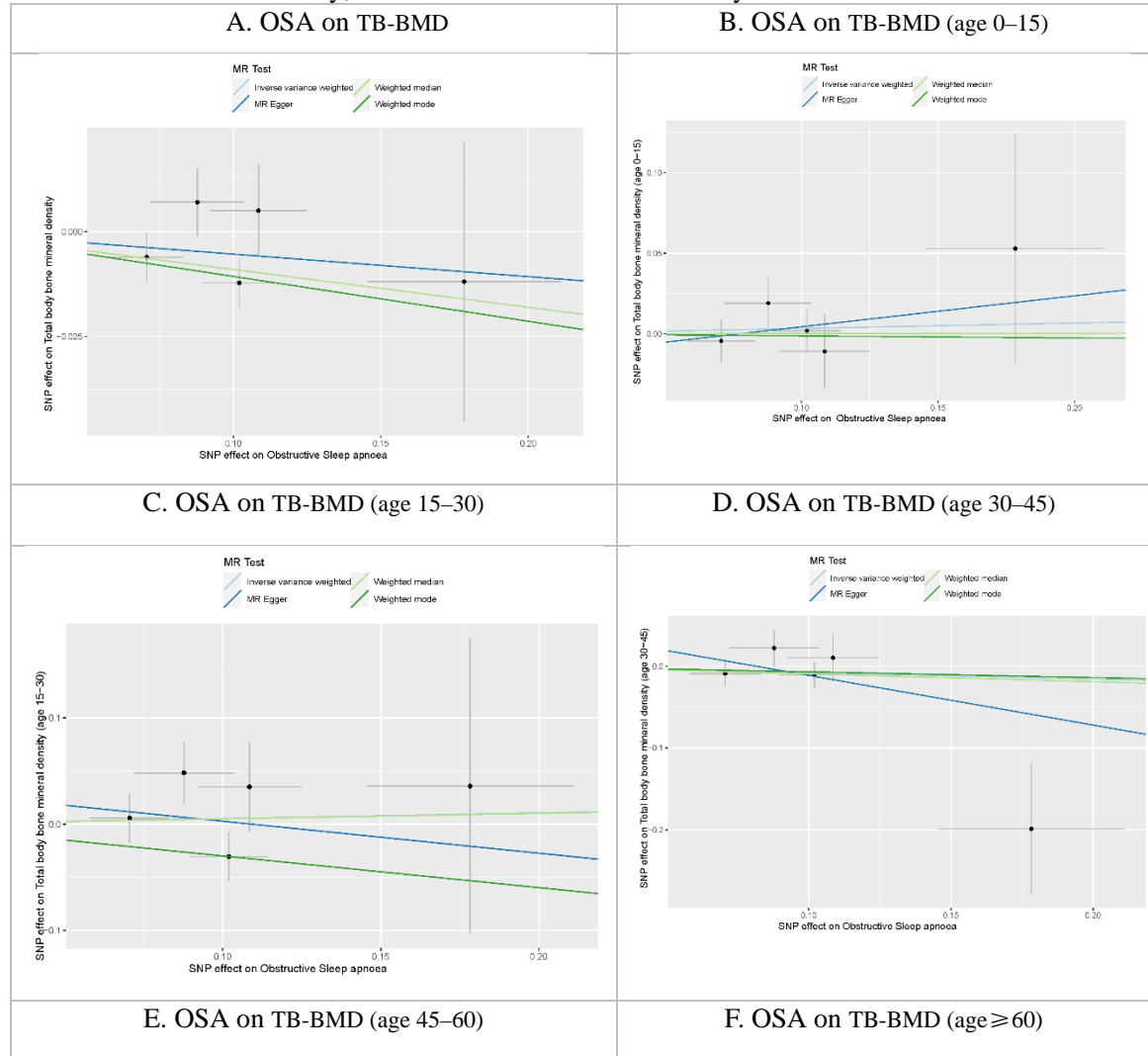
Table S4: Pleiotropy assessment for the results of OSA on BMD

Exposure	Outcome	MR-PRESSO global test		MR-Egger intercept		Cochrane's Q test	
		Observed RSS	P value	Effect size	P value	Q' test	P value
OSA	TB-BMD	8.98	0.328	0.000	1.000	4.62	0.330
OSA	TB-BMD (age 0–15)	2.91	0.766	-0.015	0.736	2.05	0.727
OSA	TB-BMD (age 15–30)	11.36	0.278	0.033	0.749	5.19	0.268
OSA	TB-BMD (age 30–45)	8.87	0.253	0.049	0.517	7.45	0.114
OSA	TB-BMD (age 45–60)	0.72	0.310	0.000	0.994	4.79	0.310
OSA	TB-BMD (age ≥60)	1.02	0.969	-0.019	0.579	0.87	0.929
OSA	LS-BMD	5.54	0.452	-0.028	0.505	3.62	0.307
OSA	FN-BMD	11.60	0.219	-0.015	0.762	6.26	0.100
OSA	FA-BMD	7.89	0.316	0.051	0.412	4.98	0.173
OSA	HBMD	31.59	0.069	0.002	0.931	15.09	0.005

OSA: Obstructive sleep apnea; TB-BMD: total body bone mineral density; LS-BMD: Lumbar spine bone mineral density; FN-BMD: Femoral neck bone mineral density; FA-BMD: Forearm bone mineral density; HBMD: Heel bone mineral density;

Figure S1. Scatter plots of estimates about obstructive sleep apnea on bone mineral density. A. Scatter plots of estimates about OSA on TB-BMD; B. Scatter plots of estimates about OSA on TB-BMD (age 0–15); C. Scatter plots of estimates about OSA on TB-BMD (age 15–30); D. Scatter plots of estimates about OSA on TB-BMD (age 30–45); E. Scatter plots of estimates about OSA on TB-BMD (age 45–60); F. Scatter plots of estimates about OSA on TB-BMD (age ≥60); G. Scatter plots of estimates about OSA on LS-BMD; H. Scatter plots of estimates about OSA on FN-BMD; I. Scatter plots of estimates about OSA on FA-BMD; J. OSA on HBMD.

Abbreviation: OSA: Obstructive sleep apnea; TB-BMD: total body bone mineral density; LS-BMD: Lumbar spine bone mineral density; FN-BMD: Femoral neck bone mineral density; FA-BMD: Forearm bone mineral density; HBMD: Heel bone mineral density.



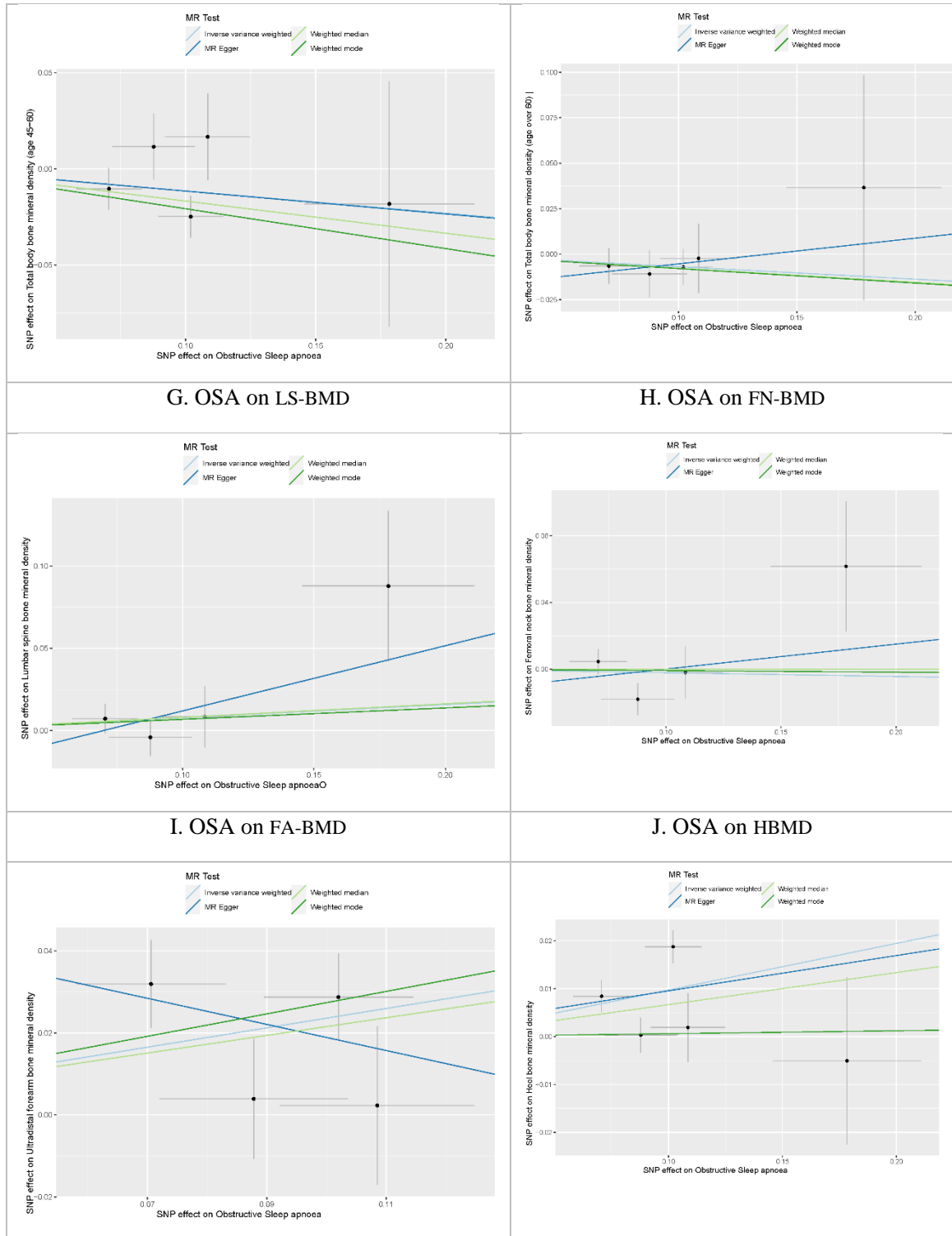
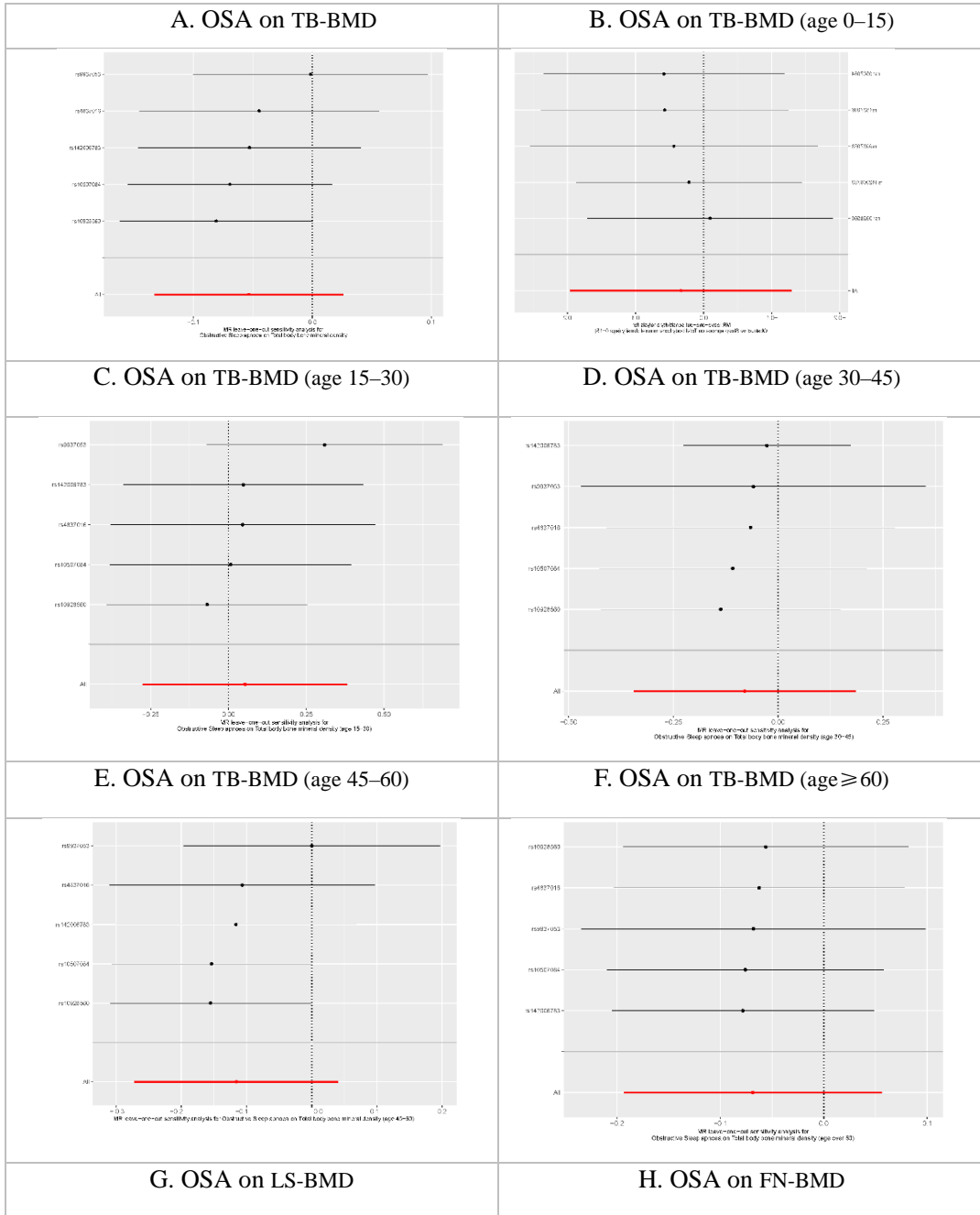
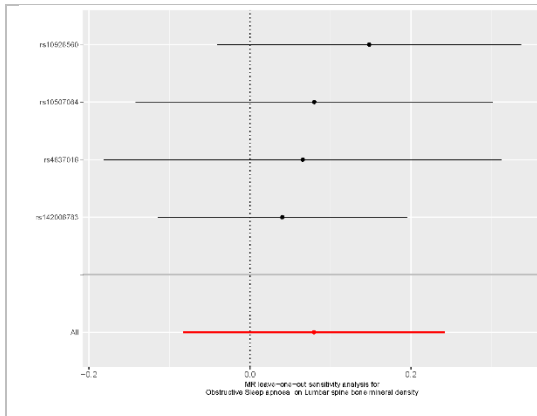


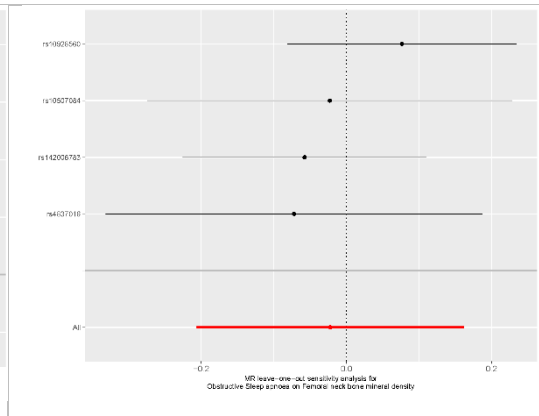
Figure S2. Leave-one-out plots of estimates about obstructive sleep apnoea on bone mineral density. A. Leave-one-out plots of estimates about OSA on TB-BMD; B. Leave-one-out plots of estimates about OSA on TB-BMD (age 0–15); C. Leave-one-out plots of estimates about OSA on TB-BMD (age 15–30); D. Leave-one-out plots of estimates about OSA on TB-BMD (age 30–45); E. Leave-one-out plots of estimates about OSA on TB-BMD (age 45–60); F. Leave-one-out plots of estimates about OSA on TB-BMD (age ≥ 60); G. Leave-one-out plots of estimates about OSA on LS-BMD; H. Leave-one-out plots of estimates about OSA on FN-BMD; I. Leave-one-out plots of estimates about OSA on FA-BMD; J. OSA on HBMD.

Abbreviation: OSA: Obstructive sleep apnea; TB-BMD: total body bone mineral density; LS-BMD: Lumbar spine bone mineral density; FN-BMD: Femoral neck bone mineral density; FA-BMD: Forearm bone mineral density; HBMD: Heel bone mineral density.





I. OSA on FA-BMD



J. OSA on HBMD

