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Table S1. Sensitivity analysis: Association between WQS regression index and osteoporosis/BMD, NHAES.

outcomes	Model I		Model II		Model III	
	OR/ β (95%CI)	<i>P</i>	OR/ β (95%CI)	<i>P</i>	OR/ β (95%CI)	<i>P</i>
Male						
osteoporosis	1.16(0.74,1.82)	0.53	1.14(0.73,1.79)	0.57	1.14(0.73,1.78)	0.56
FN-BMD	-0.01(-0.02,0.00)	0.09	-0.01(-0.02,0.00)	0.11	-0.01(-0.02,0.00)	0.08
LS-BMD	0.00(-0.01,0.01)	0.69	0.00(-0.01,0.01)	0.69	0.00(-0.01,0.01)	0.62
Female						
osteoporosis	1.10(0.47,2.58)	0.82	1.01(0.42,2.43)	0.99	1.06(0.44,2.57)	0.90
FN-BMD	-0.01(-0.03,0.00)	0.04	-0.02(-0.03,0.00)	0.03	-0.02(-0.03,0.00)	0.06
LS-BMD	-0.02(-0.03,0.00)	0.05	-0.02(-0.03,0.00)	0.05	-0.02(-0.03,0.00)	0.07
Age \geq 60						
osteoporosis	1.20(0.87,1.67)	0.27	1.21(0.87,1.68)	0.26	1.23(0.88,1.71)	0.23
FN-BMD	0.01(-0.02,0.01)	0.32	0.01(-0.02,0.01)	0.28	0.01(-0.03,0.01)	0.26
LS-BMD	-0.01(-0.03,0.02)	0.64	-0.01(-0.03,0.02)	0.65	-0.01(-0.03,0.01)	0.46
Age<60						
osteoporosis	1.32(0.93,1.87)	0.11	1.32(0.93,1.88)	0.12	1.30(0.91,1.84)	0.15
FN-BMD	-0.02(-0.02,-0.01)	0.00	-0.01(-0.02,-0.01)	0.00	1.32(0.93,1.87)	0.00
LS-BMD	-0.01(-0.02,0.00)	0.01	-0.01(-0.02,0.00)	0.01	-0.01(-0.02,0.00)	0.02
BMI \geq 25kg/m ²						
osteoporosis	1.05(0.74,1.49)	0.77	1.07(0.76, 1.52)	0.70	1.08(0.76, 1.55)	0.66
FN-BMD	-0.02(-0.03,-0.01)	0.00	-0.02(-0.03,-0.01)	0.00	-0.02(-0.03, -0.01)	0.00
LS-BMD	-0.02(-0.03, 0.00)	0.01	-0.02(-0.03, 0.00)	0.02	-0.02(-0.03, 0.00)	0.01
BMI<25kg/m ²						
osteoporosis	1.17(0.83, 1.66)	0.37	1.15(0.81, 1.64)	0.43	1.16(0.81, 1.67)	0.41
FN-BMD	0.00(-0.02, 0.01)	0.73	0.00(-0.02, 0.01)	0.73	0.00(-0.02, 0.01)	0.69
LS-BMD	-0.02(-0.03, 0.00)	0.04	-0.02(-0.03, 0.00)	0.04	-0.02(-0.03, 0.00)	0.04
Exclusion of medication use						
osteoporosis	1.37(1.07,1.75)	0.04	1.33(1.04,1.70)	0.02	1.33(1.04,1.70)	0.03
FN-BMD	-0.01(-0.02,0.00)	0.00	-0.01(-0.02,0.00)	0.00	-0.01(-0.02,0.00)	0.00
LS-BMD	-0.02(-0.03,-0.01)	0.00	-0.02(-0.03,-0.01)	0.00	-0.02(-0.03,-0.01)	0.00
Exclusion of history of fracture						
osteoporosis	1.23(0.96,1.56)	0.10	1.23(0.96,1.56)	0.10	1.21(0.95,1.54)	0.12
FN-BMD	-0.02(-0.02,-0.01)	0.00	1.23(0.96,1.56)	0.00	1.23(0.96,1.56)	0.00
LS-BMD	-0.01(-0.02,-0.01)	0.00	-0.01(-0.02,-0.01)	0.00	-0.01(-0.02,-0.01)	0.00

FN-BMD: femoral neck bone mineral density; LS-BMD: lumbar spine bone mineral density; β estimates represents mean differences in BMD when the WQS index was increased by one quartile; OR: odds ratio; 95%CI: 95% Confidence interval.

Model I: Adjusting for age, sex, race, education level, marital status, FIR, and BMI.

Model II: Model I + adjusted for smoking and drinking.

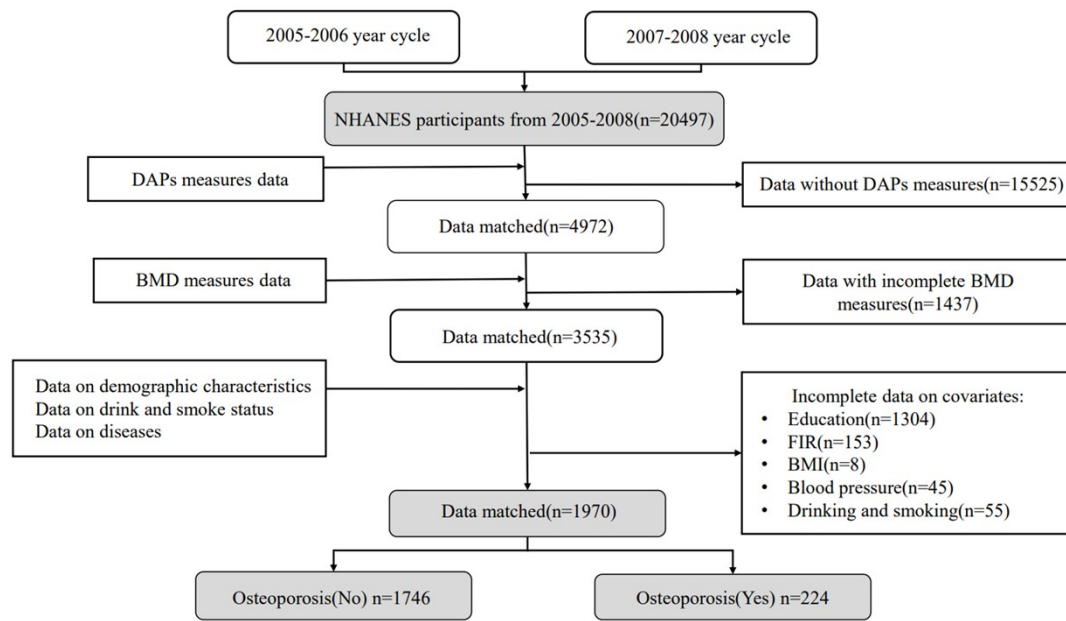
Model III: Model II + adjusted for hypertension, diabetes, and cardiovascular diseases.

Table S2. Estimates for the causal association of pesticides-exposure and BMD.

exposure	outcome	SNPs	Method	OR(95%CI)	<i>P</i>	Heterogeneity	Pleiotropy	
							MR-Egger intercept	MR-PRESSO
Worked with pesticides:	FN-BMD	5	IVW	1.23(0.62,2.43)	0.627			
			Weighted median	1.50(0.52,4.27)	0.487			
						0.014	0.039	0.069
			MR-ML	1.24(0.61,2.52)	0.375			
			Weighted mode	2.81(0.26,30.27)	0.178			
			Simple mode	0.63(0.06,6.54)	0.169			
	LS-BMD	5	IVW	4.01(0.16,98.98)	0.396			
			Weighted median	4.36(0.07,254.42)	0.478			
			MR-ML	4.09(0.16,102.74)	0.392	0.567	0.250	0.590
			Weighted mode	17.36(0.11,2695.82)	0.330			
			Simple mode	0.29(0.00,101.49)	0.698			
Rarely/never	FN-BMD	11	IVW	2.97(1.03,8.59)	0.045			
			Weighted median	3.57(0.82,15.59)	0.076			
						0.471	0.769	0.850
			MR-ML	3.03(1.02,8.97)	0.045			
			Weighted mode	4.55(0.59,35.35)	0.192			
			Simple mode	5.16(0.53,50.43)	0.184			
	LS-BMD	11	IVW	3.09(0.91,10.56)	0.072			
			Weighted median	3.94(0.74,21.02)	0.109			
			MR-ML	3.23(0.91,11.43)	0.069	0.423	0.581	0.523
			Weighted mode	10.27(0.50,211.47)	0.162			
			Simple mode	11.66(0.64,210.98)	0.127			

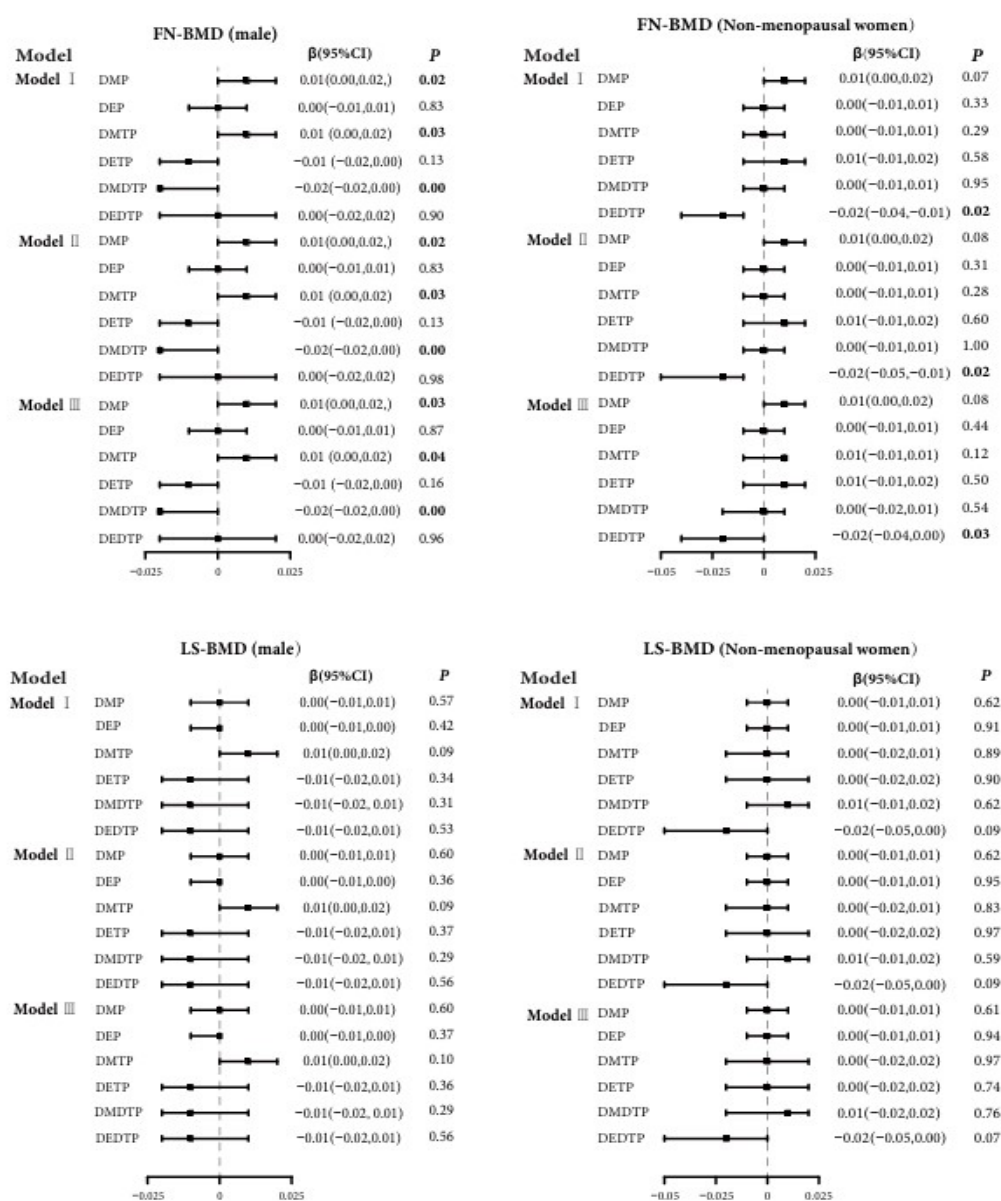
SNP: single-nucleotide polymorphism; FN-BMD: femoral neck bone mineral density; LS-BMD: lumbar spine bone mineral density; OR: odds ratio; 95%CI: 95% confidence interval; IVW: inverse-variance weighted; MR-ML: mendelian randomization maximum likelihood.

Fig S1. Flow chart of exclusion criteria employed in the Study.



NHANES: National Health and Nutrition Examination Survey; BMD: bone mineral density;
DAPs: dialkyl phosphates; FIR: family income to poverty ratio; BMI: body mass index.

Fig S2. Subgroup analysis by gender: Comparison between different models of the weighted relationship between organophosphate pesticides metabolites in urine and osteoporosis /BMD.



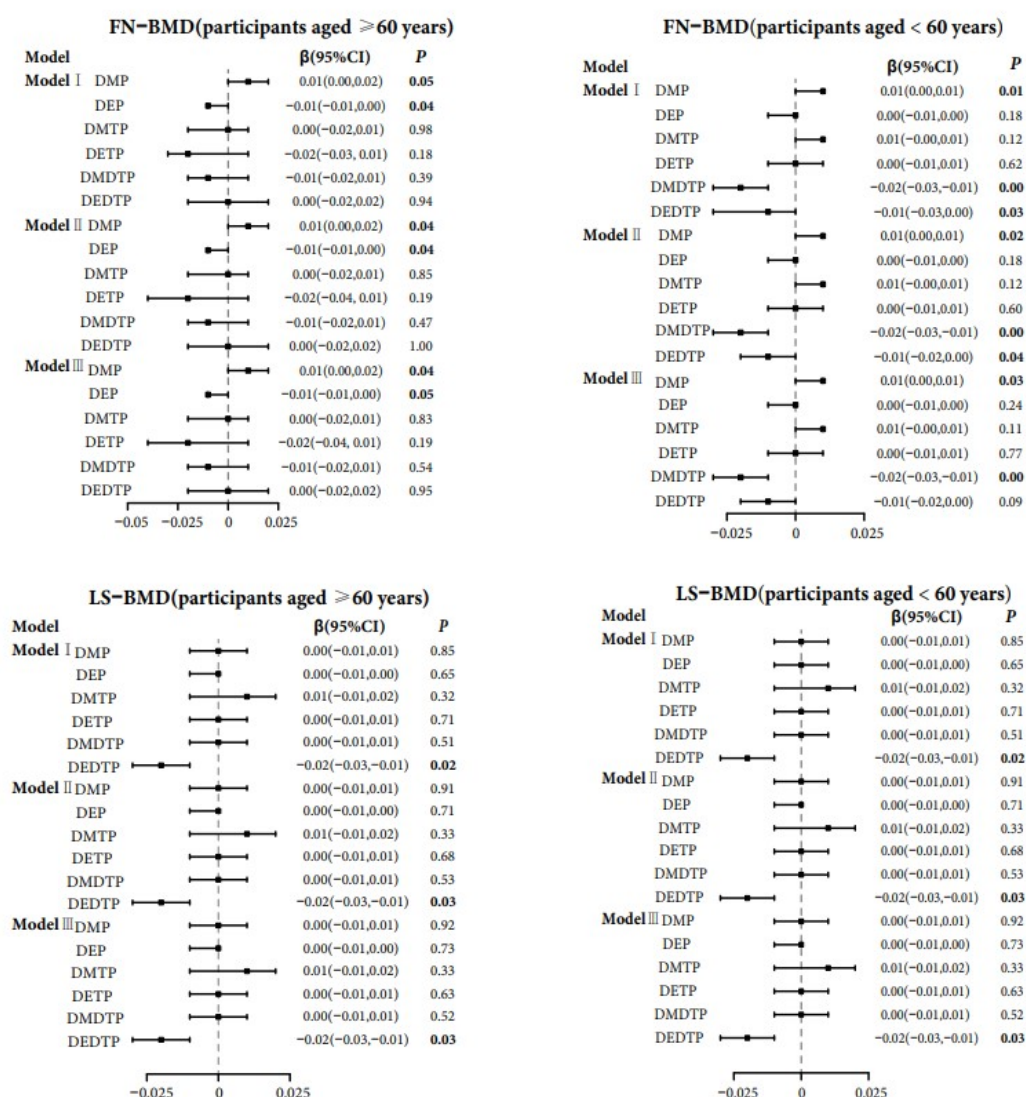
DMP: dimethyl phosphate; DMTP: dimethyl thiophosphate; DMDTP: dimethyl dithiophosphate; DEP: diethyl phosphate; DETP: diethyl thiophosphate, DEDTP: diethyl dithiophosphate; FN-BMD: femoral neck bone mineral density; LS-BMD: lumbar spine bone mineral density.

Model I: Adjusting for age, sex, race, education level, marital status, FIR, and BMI.

Model II: Model I + adjusted for smoking and drinking.

Model III: Model II + adjusted for hypertension, diabetes, and cardiovascular diseases.

Fig S3. Subgroup analysis by age: Comparison between different models of the weighted relationship between organophosphate pesticides metabolites in urine and osteoporosis /BMD.



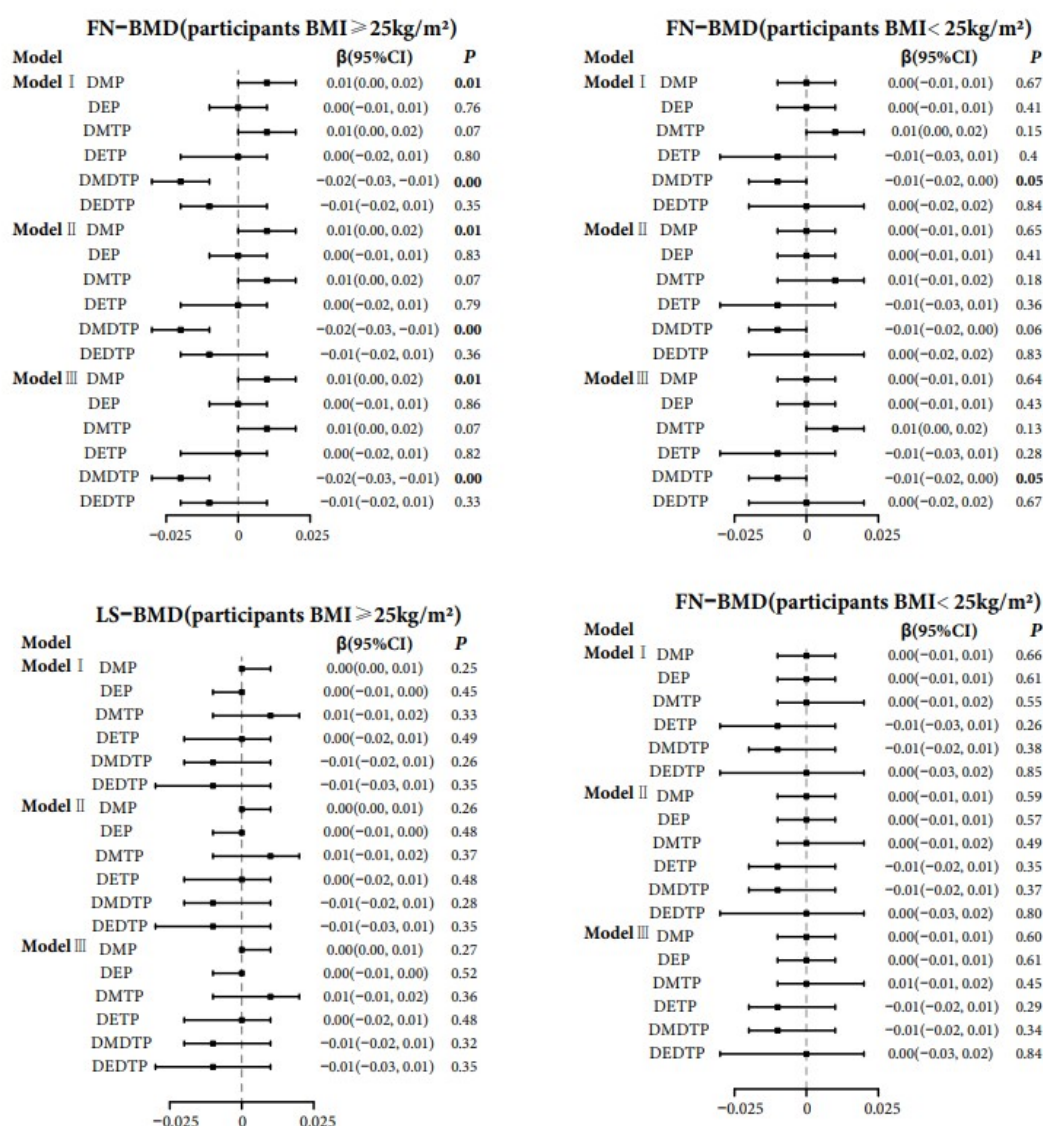
DMP: dimethyl phosphate; DMTP: dimethyl thiophosphate; DMDTP: dimethyl dithiophosphate; DEP: diethyl phosphate; DETP: diethyl thiophosphate, DEDTP: diethyl dithiophosphate; FN-BMD: femoral neck bone mineral density; LS-BMD: lumbar spine bone mineral density.

Model I: Adjusting for age, sex, race, education level, marital status, FIR, and BMI.

Model II: Model I + adjusted for smoking and drinking.

Model III: Model II + adjusted for hypertension, diabetes, and cardiovascular diseases.

Fig S4. Subgroup analysis by BMI: Comparison between different models of the weighted relationship between organophosphorus pesticide metabolites in urine and osteoporosis /BMD.



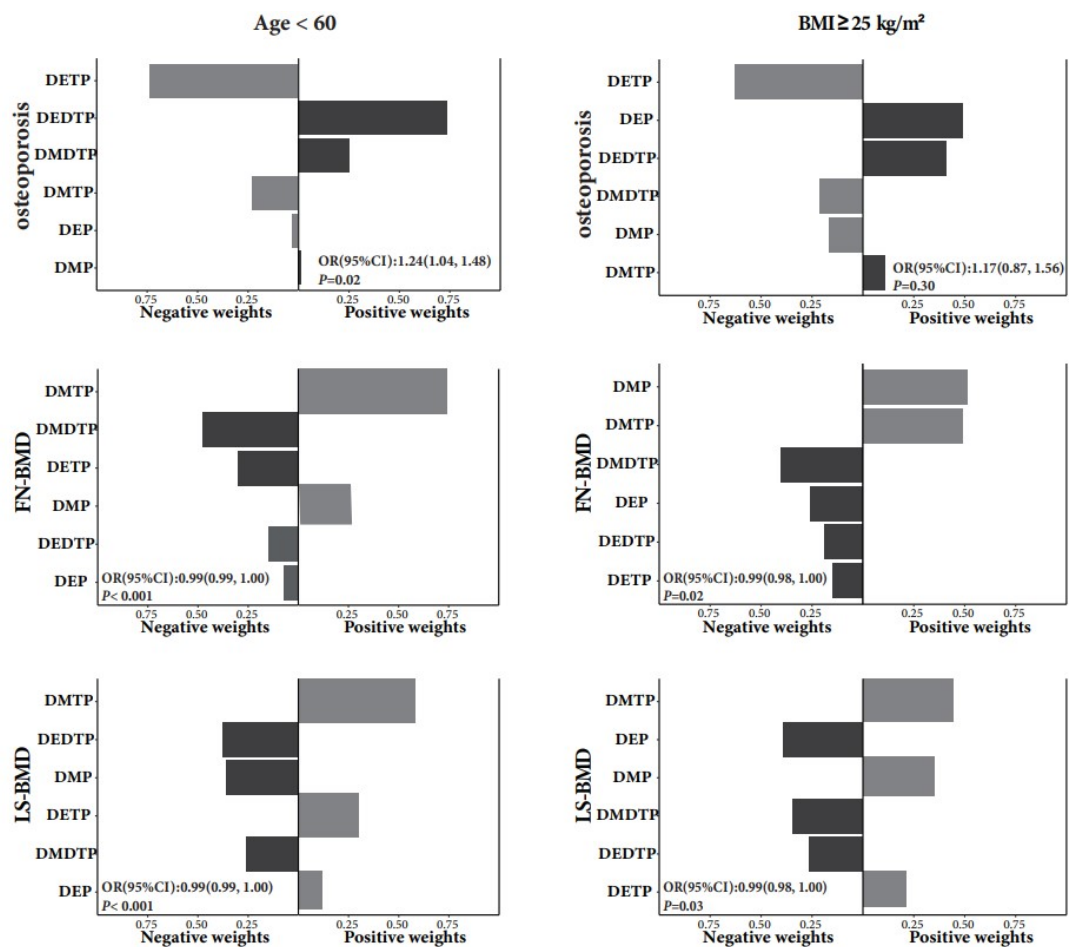
DMP: dimethyl phosphate; DMTP: dimethyl thiophosphate; DMDTP: dimethyl dithiophosphate; DEP: diethyl phosphate; DETP: diethyl thiophosphate, DEDTP: diethyl dithiophosphate; FN-BMD: femoral neck bone mineral density; LS-BMD: lumbar spine bone mineral density.

Model I: Adjusting for age, sex, race, education level, marital status, FIR, and BMI.

Model II: Model I + adjusted for smoking and drinking.

Model III: Model II + adjusted for hypertension, diabetes, and cardiovascular diseases.

Fig S5. Sensitivity analysis: Result of the Qgcomp model.



FN-BMD: femoral neck bone mineral density; LS-BMD: lumbar spine bone mineral density; DMP: dimethyl phosphate; DMTP: dimethyl thiophosphate; DMDTP: dimethyl dithiophosphate; DEP: diethyl phosphate; DETP: diethyl thiophosphate, DEDTP: diethyl dithiophosphate. OR: odds ratio; 95%CI: 95% Confidence interval.

Model was adjusted for age, sex, race, education level, marital status, FIR, BMI, smoking, drinking, diabetes, CVD, and hypertension.