

## **Online Supplement**

### **Original Research**

#### **Genetic Evidence for Causal Relationships Between Circulating Cathepsin Levels and Chronic Obstructive Pulmonary Disease: A Mendelian Randomization Study**

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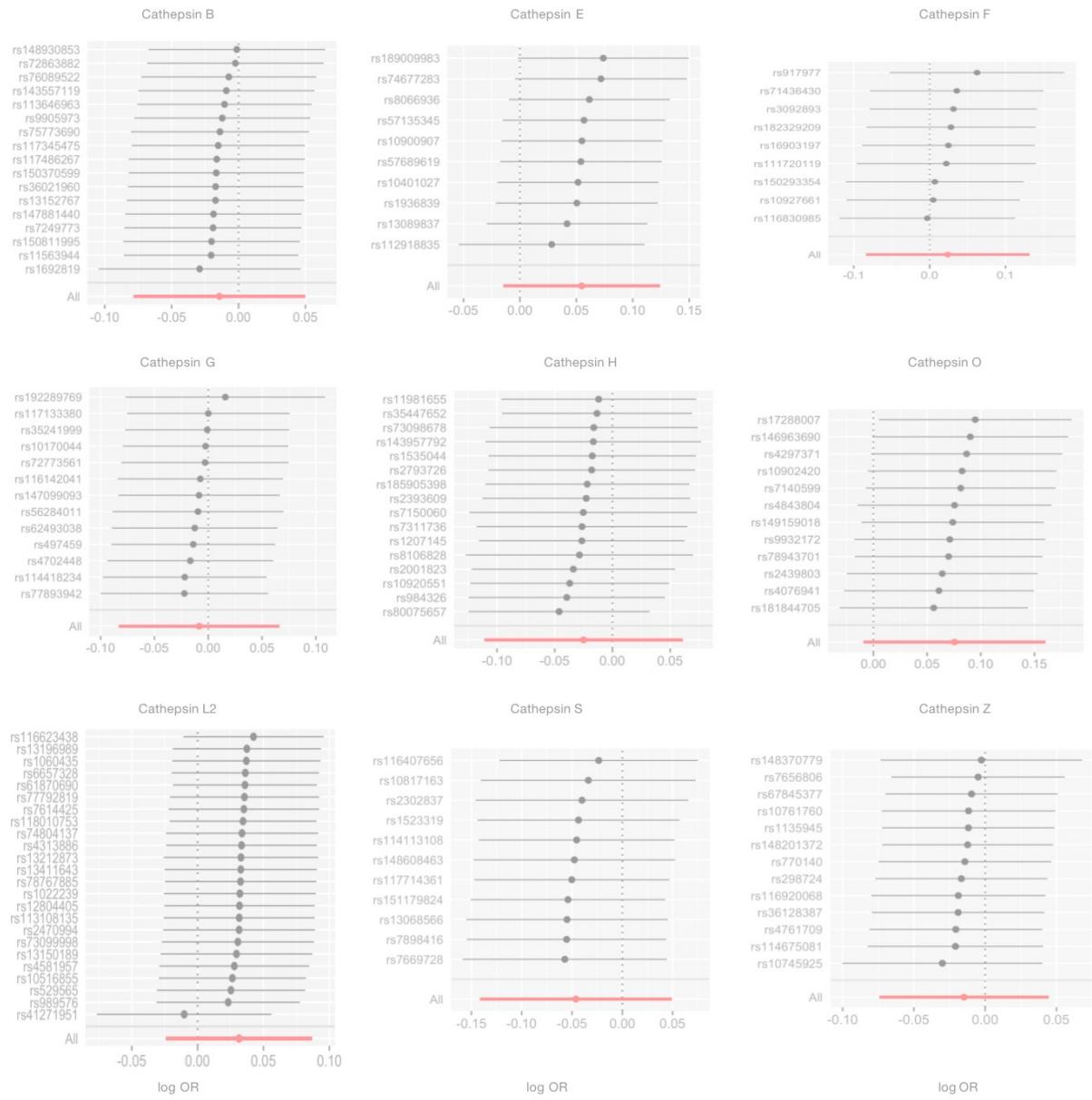
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**Supplementary Table 1.** Results of reverse Mendelian randomization analysis between cathepsins and chronic obstructive pulmonary disease.

Type	MR Method	Odds ratio	p-value	MR-Egger intercept (p)	Heterogeneity test (p)	MR-PRESSO global (p)
Cathepsin B	IVW	1.069	0.145	0.985	0.789	0.803
	MR-Egger	1.071	0.467		0.744	
	Weighted median	1.071	0.308			
	Weighted mode	1.033	0.729			
	MR PRESSO	1.069	0.109			
Cathepsin E	IVW	0.933	0.133	0.786	0.679	0.681
	MR-Egger	0.954	0.617		0.629	
	Weighted median	0.964	0.579			
	Weighted mode	0.957	0.641			
	MR PRESSO	0.933	0.116			
Cathepsin F	IVW	1.027	0.596	0.544	0.250	0.247
	MR-Egger	0.973	0.786		0.225	
	Weighted median	1.022	0.752			
	Weighted mode	1.012	0.909			
	MR PRESSO	1.027	0.600			
cathepsin G	IVW	0.930	0.112	0.670	0.585	0.600
	MR-Egger	0.962	0.683		0.540	
	Weighted median	0.952	0.453			
	Weighted mode	0.965	0.708			
	MR PRESSO	0.930	0.109			
cathepsin H	IVW	1.053	0.264	0.921	0.452	0.441
	MR-Egger	1.044	0.652		0.398	
	Weighted median	1.043	0.536			
	Weighted mode	1.042	0.665			
	MR PRESSO	1.053	0.274			
cathepsin O	IVW	1.055	0.339	0.201	0.058	0.055
	MR-Egger	1.197	0.117		0.076	
	Weighted median	1.097	0.188			
	Weighted mode	1.106	0.292			

	MR PRESSO	1.055	0.348			
cathepsin S	IVW	1.037	0.464	0.783	0.227	0.265
	MR-Egger	1.064	0.556		0.191	
	Weighted median	1.132	0.053			
	Weighted mode	1.140	0.150			
	MR PRESSO	1.037	0.471			
cathepsin L2	IVW	1.091	0.060	0.271	0.454	0.468
	MR-Egger	0.996	0.966		0.468	
	Weighted median	1.117	0.112			
	Weighted mode	1.097	0.356			
	MR PRESSO	1.091	0.071			
cathepsin Z	IVW	1.064	0.177	0.368	0.672	0.668
	MR-Egger	1.145	0.155		0.667	
	Weighted median	1.132	0.066			
	Weighted mode	1.168	0.110			
	MR PRESSO	1.064	0.156			

**Figure S1.** Leave-one-out (LOO) forest plot of univariable Mendelian randomization analysis between the abundance of nine cathepsins (cathepsin B, E, F, G, H, L2, O, S, and Z) and the risk of having chronic obstructive pulmonary disease.



**Figure S2.** Scatterplots to compare four Mendelian randomization analysis methods.

