

Supplementary Table S1. IVs used in forward MR analysis.

Disease	Bacterial taxa	Method	nSNP	Beta	SE	p	OR (OR 95% CI)	Heterogeneity	Pleiotropy
RA	<i>Desulfovibrionales</i>	MR Egger	11	-0.40	0.24	0.13	0.67 (0.42–1.08)	0.84	0.26
		WME	11	-0.07	0.07	0.33	0.93 (0.81–1.07)		
		IVW	11	-0.11	0.04	0.01	0.89 (0.81–0.98)	0.78	
		MR-PRESSO				0.65			
	<i>Methanobacteriales</i>	MR Egger	9	-0.12	0.12	0.36	0.89 (0.70–1.13)	0.64	0.78
		WME	9	-0.07	0.04	0.08	0.93 (0.86–1.01)		
		IVW	9	-0.09	0.02	<0.01	0.92 (0.87–0.96)	0.73	
		MR-PRESSO				0.68			
	<i>MollicutesRF9</i>	MR Egger	11	0.23	0.12	0.10	1.26 (0.99–1.60)	0.37	0.54
		WME	11	0.10	0.06	0.08	1.11 (0.99–1.25)		
		IVW	11	0.15	0.04	<0.01	1.17 (1.09–1.25)	0.43	
		MR-PRESSO				0.35			
	<i>Alphaproteobacteria</i>	MR Egger	7	0.21	0.20	0.33	1.24 (0.84–1.82)	0.82	0.89
		WME	7	0.18	0.07	0.01	1.19 (1.05–1.36)		
		IVW	7	0.18	0.03	<0.01	1.20 (1.14–1.26)	0.90	
		MR-PRESSO				0.78			
	<i>Betaproteobacteria</i>	MR Egger	8	0.14	0.22	0.55	1.15 (0.74–1.79)	0.40	0.94
		WME	8	0.13	0.09	0.15	1.14 (0.96–1.35)		
		IVW	8	0.13	0.06	0.04	1.13 (1.02–1.25)	0.51	
		MR-PRESSO				0.65			
	<i>Methanobacteria</i>	MR Egger	9	-0.12	0.12	0.36	0.89 (0.70–1.13)	0.64	0.78
		WME	9	-0.07	0.04	0.07	0.93 (0.87–1.01)		
		IVW	9	-0.09	0.02	<0.01	0.92 (0.87–0.96)	0.73	
		MR-PRESSO				0.69			
	<i>Bacteroidaceae</i>	MR Egger	9	0.23	0.33	0.50	1.26 (0.66–2.39)	0.95	0.82
		WME	9	0.13	0.08	0.11	1.14 (0.97–1.34)		
		IVW	9	0.15	0.03	<0.01	1.17 (1.10–1.23)	0.97	
		MR-PRESSO				0.99			
	<i>Desulfovibrionaceae</i>	MR Egger	9	-0.37	0.25	0.18	0.69 (0.43–1.13)	0.73	0.37
		WME	9	-0.10	0.08	0.21	0.91 (0.77–1.06)		
		IVW	9	-0.14	0.05	<0.01	0.87 (0.78–0.97)	0.72	
		MR-PRESSO				0.58			
	<i>Methanobacteriaceae</i>	MR Egger	9	-0.12	0.12	0.36	0.89 (0.70–1.13)	0.64	0.78
		WME	9	-0.07	0.04	0.08	0.93 (0.86–1.01)		
		IVW	9	-0.09	0.02	<0.01	0.92 (0.87–0.96)	0.73	
		MR-PRESSO				0.69			
	<i>Adlercreutzia</i>	MR Egger	7	-0.11	0.21	0.62	0.90 (0.59–1.36)	0.65	0.26
		WME	7	0.14	0.07	0.04	1.15 (1.01–1.32)		
		IVW	7	0.15	0.05	<0.01	1.16 (1.07–1.25)	0.55	
		MR-PRESSO				0.72			
	<i>Bacteroides</i>	MR Egger	9	0.23	0.33	0.50	1.26 (0.66–2.39)	0.95	0.82
		WME	9	0.13	0.08	0.10	1.14 (0.97–1.34)		
		IVW	9	0.15	0.03	<0.01	1.17 (1.10–1.23)	0.97	
		MR-PRESSO				0.99			
	<i>Butyricimonas</i>	MR Egger	13	0.27	0.13	0.07	1.32 (1.01–1.71)	0.43	0.18
		WME	13	0.08	0.06	0.15	1.08 (0.97–1.21)		
		IVW	13	0.09	0.04	0.03	1.09 (1.01–1.18)	0.35	
		MR-PRESSO				0.37			
<i>Butyrivibrio</i>	MR Egger	14	-0.01	0.10	0.92	0.99 (0.82–1.20)	0.20	0.63	
	WME	14	-0.06	0.03	0.05	0.94 (0.89–1.00)			
	IVW	14	-0.06	0.02	0.02	0.95 (0.90–0.99)	0.24		
	MR-PRESSO				0.31				
<i>Holdemanella</i>	MR Egger	10	0.21	0.11	0.10	1.24 (0.99–1.54)	0.18	0.30	
	WME	10	0.13	0.05	0.01	1.14 (1.03–1.26)			
	IVW	10	0.09	0.04	0.03	1.10 (1.01–1.18)	0.15		
	MR-PRESSO				0.25				

nSNP: Number of SNPs involved in the analysis; Beta: effect estimate; SE: standard error of effect; p: p-value of effect estimate; OR: odds ratio; WME: weighted median estimation; IVW: inverse variance weighted; MR-PRESSO: MR pleiotropy residual sum and outlier.

Supplementary Table S2. IVs used in reverse MR analysis.

Disease	Bacterial taxa	Method	nSNP	Beta	SE	<i>p</i>	OR (OR 95% CI)	Heterogeneity	Pleiotropy
RA	<i>Anaerostipes</i>	MR Egger	43	-0.06	0.03	0.03	0.94 (0.89–0.99)	0.61	0.18
		WME	43	-0.05	0.03	0.06	0.95 (0.91–1.00)	0.57	
		IVW	43	-0.03	0.02	0.05	0.97 (0.94–1.00)		
		MR-PRESSO				0.21			
	<i>FamilyXIIIUCG001</i>	MR Egger	43	-0.06	0.03	0.06	0.94 (0.88–1.00)		0.39
		WME	43	-0.06	0.03	0.04	0.94 (0.89–1.00)	0.41	
		IVW	43	-0.04	0.02	0.03	0.96 (0.92–1.00)		
		MR-PRESSO				0.26			
	<i>Ruminiclostridium9</i>	MR Egger	43	-0.02	0.03	0.51	0.98 (0.92–1.04)		0.18
		WME	43	-0.02	0.03	0.36	0.98 (0.93–1.03)	0.20	
		IVW	43	-0.04	0.02	0.04	0.96 (0.93–1.00)		
		MR-PRESSO				0.22			
	<i>RuminococcaceaeUCG009</i>	MR Egger	43	-0.07	0.04	0.10	0.93 (0.86–1.01)		0.46
		WME	43	-0.06	0.04	0.08	0.94 (0.88–1.01)	0.50	
		IVW	43	-0.05	0.02	0.03	0.95 (0.90–1.00)		
		MR-PRESSO				0.41			
	<i>Prevotella7</i>	MR Egger	42	0.08	0.07	0.25	1.08 (0.95–1.23)		0.56
		WME	42	0.08	0.05	0.15	1.08 (0.97–1.20)	0.61	
		IVW	42	0.08	0.04	0.03	1.08 (1.01–1.15)		
		MR-PRESSO				0.61			

nSNP: Number of SNPs involved in the analysis; Beta: effect estimate; SE: standard error of effect; *p*: *p*-value of effect estimate; OR: odds ratio; WME: weighted median estimation; IVW: inverse variance weighted; MR-PRESSO: MR pleiotropy residual sum and outlier.